Advancing the assessment of spasticity in the upper limb post stroke

By Parvin Eftekhar

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Rehabilitation Sciences Institute
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Abstract

Upper limb spasticity can interfere with function and cause pain and contractures. Botulinum neuro toxin A (BoNTA) has been effectively used to reduce spasticity; however, the impact of BoNTA combined with rehabilitation on upper limb function is not clear. One possible reason could be the lack of sensitive clinical assessments to show the changes in the focal muscles after an intervention. Therefore, this dissertation aimed to examine the impact of BoNTA combined with rehabilitation on arm function using sensitive, objective assessments in addition to clinical measures. The present findings affirmed that a combination of BoNTA and one month of upper limb rehabilitation assisted patients after stroke with upper limb spasticity to achieve their goals using the Goal Attainment Scale (GAS). Because there is subjectivity in clinical measures such as the GAS, a Kinematic Upper Limb Spasticity Management (KUSA) protocol was developed to objectively characterize the wrist, elbow and shoulder movements that were identified through the goals selected by patients. Kinematic variables including speed, active range of motion and compensatory trunk movement through KUSA were able to distinguish between
affected and unaffected sides. Furthermore, KUSA provided supplementary information for motion characterization that was not available through clinical measures alone. Further, both clinical and kinematic measures were used to examine the effect of two different phases: upper limb rehabilitation, and BoNTA plus rehabilitation on arm function. It was shown that only two clinical measures (Modified Ashworth Scale and Chedoke Arm and Hand Activity Inventory) significantly changed after BoNTA and rehabilitation; however, no changes in kinematic measures were found. Secondary analysis demonstrated that patients with higher motor recovery on the Chedoke McMaster Stroke Assessment improved in all kinematic variables compared to those individuals with lower initial motor recovery stage. This thesis advances knowledge about the types of assessments that identify change in function following spasticity management intervention and characteristics of patients that best responded to this intervention based on these outcomes. These results would be useful in guiding future research on the effectiveness of BoNTA.
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<td>ADL</td>
<td>Activities of Daily Living</td>
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<tr>
<td>BoNTA</td>
<td>Botulinum toxin A</td>
</tr>
<tr>
<td>CAHAI&lt;sub&gt;9&lt;/sub&gt;</td>
<td>Chedoke Arm and Hand Activity Inventory version 9</td>
</tr>
<tr>
<td>CIMT</td>
<td>Constraint induced movement therapy</td>
</tr>
<tr>
<td>CMSA</td>
<td>Chedoke McMaster Stroke Assessment</td>
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<tr>
<td>GAS</td>
<td>Goal Attainment Scaling</td>
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<tr>
<td>IADL</td>
<td>Instrumental Activities of Daily Living</td>
</tr>
<tr>
<td>ICF</td>
<td>International Classification of Function, Disability and Health</td>
</tr>
<tr>
<td>KUSA</td>
<td>Kinematic Upper Limb Spasticity Assessment</td>
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<tr>
<td>NMES</td>
<td>Neuromuscular electrical stimulation</td>
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<td>UMNS</td>
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Chapter 1: Introduction

1.1 Stroke incidence and prevalence

A stroke is defined by acute focal damage to the central nervous system in a vascular distribution consequently creating neurological signs and/or symptoms persisting for a time period greater than 24 hours (or until death eliminating other diagnoses)\(^1,2\). A local and temporary brain ischemia which lasts less than 24 hours, with no neuropathological evidence, is categorized as a transient ischemic attack\(^1\). There are two types of stroke: 1) ischemic, which encompasses the majority of strokes (87%) and is caused by an infarction in the brain, spinal cord and/or retina\(^1\); and 2) hemorrhagic (13%) which is caused by local bleeding in the brain's ventricular system, parenchyma or subarachnoid space\(^1\). The sequelae of stroke are neurological impairments including hemiparesis, impaired mobility, spasticity, poor proprioception, and cognitive deficits\(^3\).

Stroke is the leading cause of death in the world\(^4\), and is a source of significant disability\(^5\) The prevalence of stroke in Canada is 1.15%, with more than 400,000 Canadians living with the effects of stroke\(^6\). In Canada one person dies from stroke every ten minutes and with the aging population, the incidence of stroke will increase as the majority of strokes happen after age 70\(^4\). Only about half (48-58%) of the individuals who experience stroke return to independence in their self-care activities\(^7\) and 10-29% become institutionalized\(^8\). Due to recent improvements in stroke management, fewer patients die after stroke; in fact, 33% fewer die after stroke compared to a decade ago\(^4\). In addition, from 1987 to 2011, the mortality rate after stroke has decreased\(^9\) as a result of advanced diagnostic, medical technologies and post stroke risk factor management.
treatments. Interestingly, the decrease in stroke incidence was observed only in older adults\textsuperscript{5,9} and not in younger individuals\textsuperscript{9}. In contrast, the rate of stroke has increased in adults between 45-59 years of age\textsuperscript{9} with risk factors such as obesity, hypertension, diabetes and high cholesterol as the main contributing factors\textsuperscript{4}.

1.2 Upper Motor Neuron Syndrome and spasticity after stroke

Stroke can cause Upper Motor Neuron Syndrome (UMNS) which is manifested in two ways: a) loss of motor function such as muscle weakness, limb flaccidity and fatigue, a result of lack of motor activity and, b) muscular over activity such as spasticity, increased tendon reflexes, clonus and extensor/flexor spasm\textsuperscript{3}. Spasticity is more common in younger individuals\textsuperscript{10} after stroke and mostly impacts upper extremities\textsuperscript{11}. Spasticity can occur immediately after stroke or as much as one year later\textsuperscript{12}. It reaches its peak one to three\textsuperscript{13} months after onset\textsuperscript{14}.

Spasticity has been defined as “a motor disorder characterized by a velocity dependent increase in the tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the upper motor neuron syndrome”\textsuperscript{15}. This definition implies that stretch reflex hyperactivity is the sole cause of spasticity\textsuperscript{16}. Pandyan (2005) elaborated on Lance’s definition explaining that there is not enough evidence to indicate that spasticity results only from stretch reflex hyperexcitability. He proposed that the supraspinal systems and afferent pathways may play a role as well, and advanced the following definition: “a disordered sensorimotor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles”\textsuperscript{16}. In 2012, Ward proposed that a universal
definition\textsuperscript{12} was not possible because spasticity was not a “single entity” and that there was considerable clinical manifestation among patients; therefore, there cannot be a universal definition.

Spasticity impacts the individuals' function; in a prospective study, Koski et al., (1996) showed that spasticity may lead to impaired balance and gait, falls and bone fractures. Spasticity may cause pain, contracture and skin breakdown\textsuperscript{17,18}. Welmer et al. (2006) found a moderate correlation between spasticity and quality of life\textsuperscript{19}. In a recent study, it was shown that six months after stroke, 50\% of individuals with spasticity develop contracture\textsuperscript{20}. Usually after stroke, spasticity develops differently in the upper and lower extremities; flexors in the upper limb and extensor muscles in the lower limbs are most typically involved\textsuperscript{21}.

1.3 Prevalence of spasticity

The prevalence of spasticity is variable and ranges from 19\%\textsuperscript{3} to 92\%\textsuperscript{22}. The onset of spasticity also varies and could happen in the short, medium or long-term after stroke\textsuperscript{12}. In the short term, Somerfield and colleagues (2004) showed that in the first week after stroke, 21\% have spasticity\textsuperscript{3}. Similarly, Wissel et al. (2010) followed 103 post stroke patients at six days, six weeks and 16 weeks post-stroke; the results indicated that 24.5\% developed spasticity within two weeks after stroke\textsuperscript{23}. For the medium term, Urban et al., (2010) showed that six months after stroke, 43\% developed spasticity\textsuperscript{24}, and in the long term, a year post-stroke, Lundstrom et al. (2008) showed a rate of 21\%\textsuperscript{10}.

The variability in prevalence estimates of spasticity in the post-stroke population may depend on the tools used to measure it. Reported rates of spasticity might be lower
than the actual rates because of the low sensitivity of measurement tools\textsuperscript{25}. Initially, researchers and clinicians relied on clinical measures such as the Modified Ashworth Scale (MAS) to measure spasticity\textsuperscript{26}. Recent studies indicate that this measurement tool is not sensitive enough to detect spasticity. Malhotra et al. (2008) evaluated wrist spasticity of 100 post-stroke individuals by using the MAS and electrophysiological measures\textsuperscript{27}. The MAS score indicated spasticity of the wrist in only 44\% of the cases; however, the electrophysiological measures identified spasticity in 87\%. This study indicated that the prevalence of spasticity was underestimated when only clinical measurements were used, and that neurophysiological tools had greater capacity to detect spasticity\textsuperscript{27}.

1.4 Outcome measures of spasticity: Clinical tools

Effective treatment is based on accurate assessment and identification of the exact mechanisms of spasticity. Spasticity due to stretch reflex hyperexcitability (neural) could be identified by rapid muscle movements, while the soft tissue changes in the muscles and around the affected joints (non-neural) can be teased out by the resistance to the slow passive range of motion\textsuperscript{28}.

In order to measure the effectiveness of any therapeutic intervention on spasticity, there is a need for an objective, reliable and valid measurement of spasticity in clinical settings. There are a few clinical tools to measure upper limb spasticity, including the Modified Ashworth Scale (MAS), Modified Tardieu Scale (MTS), Numerical Rating Scale (NRS), Penn Spasm Frequency Scale (PSFS), and Range of Motion\textsuperscript{29}. 
The most commonly used tool to assess spasticity in clinical practice is the MAS\textsuperscript{26}. The examined joint is passively stretched rapidly and the rate of perceived resistance through the movement is scored on a five point scale by the examiner. This measure has ordinal scales from 0 to 4, with 0 meaning a normal tone and 4 meaning contracture. There are some limitations with using MAS; this tool is not sensitive enough to distinguish the neural stretch reflex activity and non-neural viscoelastic resistance of joints and soft tissue elements of spasticity\textsuperscript{28,30}. In addition, Fleuren et al. (2010) in a cross-sectional study of the spasticity in the elbow flexors and knee extensors showed that MAS has insufficient construct validity and inter-rater reliability in measuring spasticity\textsuperscript{31}. Platz et al. (2005) questioned the inter and intra rater reliability of this assessment and these researchers suggested that MAS has a higher reliability in the upper than lower limbs which might be a result of having more muscle bulk in the legs than the arms\textsuperscript{32}. Other studies also indicated that the MAS lacks standardization; for example, different movement velocities at different ranges (the most sensitive method to show neural spasticity) could impact the reliability of this tool\textsuperscript{31,33}.

In contrast, the MTS measures spasticity at both fast and slow stretching velocity; the fast stretch elicits stretch reflex and is an indicator of neural spasticity (Lance’s definition), and the slow stretching range of motion determines the soft tissue changes or limitations (non-neural spasticity)\textsuperscript{34}. In this assessment, a spasticity angle is measured; it is the angle between the catch (fast stretch) and the non spastic range. In contrast to MAS, the MTS distinguishes between the neural and non-neural components of spasticity by applying different speeds of movement\textsuperscript{35}. However, the examiners’ perception of spasticity and goniometer alignment impacts the reliability of the
assessment. The test-retest reliability of MTS was moderate to good in patients with severe brain injury. The NRS, in which the patient rates the severity of the spasm, and PSFS, in which patient counts the frequency of the spasm, are measures that are based on the patients’ perception of their spasticity. The reliability of PSFS has not been established but this measure is moderately correlated to the Ashworth Scale in the spinal cord patients. To measure spasticity in patients with multiple sclerosis, the correlation between the changes in NRS and PSFS was significant but it was insignificant between NRS and the Ashworth Scale. Passive range of motion is valuable to measure; however, it does not distinguish between neural and non-neural components. Range of motion measure is reported with excellent validity, and good inter-tester agreement in assessing ankle dorsiflexion motion in healthy population. However, the use of a goniometer impacts the validity and reliability of the test due to the alignment of the goniometer, and the applied force.

1.5 Lab-based spasticity measurements

Among clinical tools, observer bias could play a role in the accurate rating of the spasticity level since it is based on the examiner’s observation. In addition, many clinical measures, such as the Barthel Index, fail to tease out the role of compensatory movement during upper limb function. Biomechanical measures, on the other hand, such as kinematic analysis are quantitative, objective, and robust and offer a reliable and precise assessment. These measures provide three-dimensional information about the movement components and strategies used during linear and angular upper limb movements any slight change in movement is meaningful and could be an indicator of motor recovery.
Recently, kinematic analysis of intervention in patients after stroke has become increasingly popular and used on linear reaching and grasping tasks\textsuperscript{44}. Van Dokkum et al. (2014) showed that in 13 post stroke patients, kinematic parameters such as movement time, smoothness, velocity, and trajectory of the hand were changed and were different in the affected and unaffected limbs. Improved smoothness of upper limb movement explained 62.5\% of Fugl-Meyer Assessment (FMA) variability\textsuperscript{43}. Another kinematic study showed that BoNTA improved velocity and smoothness of elbow movement during reach task in brain injury patients\textsuperscript{45}. In contrast, other studies indicated that via kinematic analysis, BoNTA did not improve upper limb function, but facilitated adaptive and postural upper limb changes\textsuperscript{46,47}. Lemmens et al. (2012) recommended combining objective clinical and biomechanical methods for accurate and comprehensive evaluate upper limb movement\textsuperscript{48}.

### 1.6 Neurophysiology of spasticity

The motor control system encompasses four major components: cerebral cortex, subcortical structures, brainstem, cerebellum and spinal cord. The cerebral cortex is critical for directing signals for preparation and execution of movements through different areas such as premotor and supplementary motor areas which program and plan voluntary movements and the primary motor cortex, which controls execution of movement\textsuperscript{49}. Subcortical centres, including basal ganglia are essential for movement coordination and sustaining tone\textsuperscript{49}. The brainstem plays an important role in stretch reflex, posture and repetitive movements. The spinal cord is the last pathway for motor movement and it encompasses components of spinal circuitry that coordinates movement and alpha motorneurons that innervate muscles\textsuperscript{49}. At the spinal level, motor
function is controlled by three elements: afferent input from sensory receptors, interneurons, and reflex activity. In stroke patients, two categories could mediate spasticity: abnormal intraspinal control of stretch reflex and/or supraspinal control with abnormal descending pathway\textsuperscript{50}. The following sections will discuss the mechanism and neurophysiology of stretch reflex.

1.7 Stretch reflex and intraspinal control

At the spinal level, the stretch reflex is one of the factors that regulate muscle function\textsuperscript{21,51}. Muscle tone occurs due to the excitation of alpha motorneurons located at the anterior horn of the grey matter and ongoing sensory input about the muscle’s length from each muscle to the spinal cord\textsuperscript{52}. In the muscle spindles, the sensory receptors in the intrafusal muscle fibers (i.e. muscle spindles) convey information about muscle length to the spine\textsuperscript{49}. The efferent fibers include alpha motor neurons which innervate extrafusal fibers and gamma neurons that innervate muscle spindles\textsuperscript{53} to help maintain sensitivity to stretch. Stretch reflex continuously generates muscle tone by activating muscle spindles. Muscle tone is a basic muscle function that helps the body to maintain body posture against gravity. When there is a change in muscle length, both gamma and alpha fibers (alpha-gamma co-activation) are excited which leads to the contraction of both extrafusal and intrafusal muscle fibers\textsuperscript{49}.

1.8 Types of interneurons

Interneurons, mediate the integrative functions of the spinal cord; as Lundberg (1979) suggested, different types of interneurons play a role in every segment and in excitatory and inhibitory reflex activity\textsuperscript{54}. These interneurons and their functions include:
1) Recurrent Renshaw inhibition: This type of interneuron is a function associated with alpha motorneurons in which collateral branches from an alpha motorneuron axon stimulate the Renshaw cells. They not only inhibit the same alpha motorneurons but also the synergistic muscles’ motorneurons; however, disinhibition of recurrent inhibition does not cause major spasticity.  

2) Disynaptic Reciprocal Ia inhibition: After a muscle is stretched, the Ia afferent excites alpha motorneurons and simultaneously disynaptic inhibition occurs in the alpha motorneurons of the antagonist muscles. Stretch reflex leads to excitation of the alpha motorneurons, contraction of the muscle and synergistic muscles, and also excitation of the Ia inhibitory interneurons that inhibits the alpha motorneurons of the antagonistic muscles. Diminishing this type of inhibition has been reported as a major cause of spasticity. Decrease in this type of inhibition could contribute to spasticity by causing co-contraction in the antagonist muscles.  

3) Ib inhibition: Ib fibers originate from the Golgi tendon organs which are sensory receptors that transmit information about muscle tension. The Ib fibers terminate at the Ib inhibitory interneurons and synapse with alpha motorneurons in the same muscle as well as different muscles and inhibit muscle contraction from taking place. Disinhibition of Ib interneurons leads to activation of agonist muscles while the antagonist muscles are also contracted. The Ib fibers are similar to Renshaw cell and Ia interneurons as they receive spinal and supraspinal inputs.  

4) Secondary (II) afferent group inhibition: in both human and animals models, these afferent fibers play a role in stretch reflex and also stimulate flexion reflex by
facilitating the level of excitation in flexor motorneurons and dampening the
doroneural excitation of the extensors\textsuperscript{50}.

5) Presynaptic Ia afferent inhibition: a reduction in stretch reflex excitation by
descending pathways influences on inhibitory interneurons, which, through axon-
axonal connections, induces a GABA (gamma-aminobutyric acid)-mediated
inhibition of Ia afferent activity\textsuperscript{21}.

1.8.1 Spasticity and intraspinal processing

After stroke, three different factors could disturb normal intraspinal processing\textsuperscript{46,50}
and cause abnormal tone. First, elevated afferent input causes the hyper-excitation of
spinal motorneurons which lowers the stretch reflex threshold because of the increased
sensitivity of muscle spindles. Second, increased motorneuron excitability is due to
“altered inter-neuronal reflex circuits” which are caused by diminishing reciprocal
inhibition, presynaptic Ia afferent inhibition, and group II and group Ib facilitation (in place
of inhibition). These changes lead to decreased inhibition at the intraneuronal level and
cause spasticity. Third, alteration in the spinal motor neuron properties cause hyper
excitation of α motoneuron and again lowers the stretch reflex threshold leading to
spasticity\textsuperscript{50}. Katz and Rymer (1989) showed that the major cause of spasticity after
stroke is α-motoneuron hyperexcitibility\textsuperscript{51}. Studies indicated that γ-motoneuron hyper
excitability has minimal effect on stretch reflex hyper activation\textsuperscript{57}. Several studies
indicated that the altered intraspinal processing and hyperexcitable α motoneuron is a
neuroplastic rearrangement (i.e. maladaptive neuroplasticity) due to the imbalanced
supraspinal inhibitory and excitatory descending pathways\textsuperscript{50,58,59}.
1.9 The supraspinal systems

The descending pathways encompassing excitatory and inhibitory systems regulate stretch reflex and normal tone through modification of afferent and efferent inputs onto spinal motorneurons\textsuperscript{49,50,58}. Spasticity can be created by a disruption of the balance of inhibitory and excitatory inputs at the motoneuron level\textsuperscript{21,51,59}. In humans, three descending pathways are reported to regulate spinal activity (dorsal reticulospinal, medial reticulospinal, and vestibulospinal). However, research involving both human\textsuperscript{60} and animal models\textsuperscript{61} indicates that integrity of the dorsal reticulospinal tract is essential for keeping levels of spinal excitability in check. The contributions of each pathway to regulation of reflex function and contribution to spasticity will be discussed in the following section.

1.10 Excitatory supraspinal system

The role of the excitatory system is to facilitate stretch reflexes and extensor tone. Two descending pathways regulate excitation of stretch reflex. The first pathway is vestibular spinal (VST) which originates from lateral vestibular Nucleus and remains uncrossed as it descends through the spinal cord. The second one is medial reticulospinal tract (mRST), which originates in the bulbopontine tegmentum\textsuperscript{21}. The VST preferentially excites extensor motorneurons as well as interneurons. This pathway is important in sustaining decerebrate rigidity in animal models but has plays minor role in human spasticity\textsuperscript{62}. The cerebellum through the networks with the vestibular nuclei and reticular formation may modulate stretch reflex and tone\textsuperscript{49}. Animal studies have shown that stimulation of the bulbopontine tegmentum enhances reflexes and extensor tone\textsuperscript{63}.  

The mRST appears to play a bigger role in sustaining the extensor tone than VST.\textsuperscript{21,49,50} As an example, Bucy (1938) observed that after performing cordotomies on 3 children with congenital spastic para or quadriplegia, lesions involving only the anterior part of the ventral columns (i.e. VST) had a slight impact on lessening spasticity\textsuperscript{64}. Bucy concluded that other pathways were capable of maintaining spasticity even after sectioning of anteromedial columns. Brown’s (1994) review suggests the more dorsal mRST would have been spared in Bucy’s experiment, and furthers the view that these excitatory systems maintain tone and, if left unopposed by inhibitory drive, would contribute spasticity\textsuperscript{49,65}.

1.11 The inhibitory system

The inhibitory system lessens the excitability of the stretch reflex through 2 pathways acting in serial: 1) the corticoreticular pathway (CRT) and 2) the dorsal reticulospinal tract (dRST). The CRT originate from the premotor and supplementary motor areas and pass through the genu and anterior limb of the internal capsule\textsuperscript{49}. This pathway maintains a level of excitability onto an inhibitory component of the bulbar reticular formation, which is the origin of the dRST. This inhibitory pathway maintains a tonic level of inhibition on afferents and reflex activity.

Lesions involving premotor and supplementary motor areas contribute to spasticity\textsuperscript{49}. Gilman et al. (1971) indicated that a lesion in the watershed region of the middle cerebral artery, (supplying territories which include both the corticospinal and corticoreticular tracts), causes spasticity\textsuperscript{66}. This is in line with structural neuroimaging data by Cheung and colleagues comparing lesions of individuals with and without
spasticity was in putamen, thalamus, internal and external capsule, and insula\textsuperscript{67}. Disruption of the corticoreticular pathway reduces the inhibitory effect of the reticular formation, resulting in a disinhibitory effect of DRT onto spinal reflex and motorneuron structures. The resulting disinhibition, coupled with unopposed drive from the excitatory system described in Section 1.5.5 results in hyperexcitability at the spinal level, resulting in spasticity. Figure 1.1 summarizes the excitatory and inhibitory systems that contribute to spasticity.

\textbf{Figure 1.1:} An inhibition/excitation model of spasticity. In an intact system, the dorsal reticulospinal tract maintains inhibitory control over spinal reflexes through cortico-reticular drive (solid lines). This is opposed by excitatory medial reticulospinal and vestibulospinal tracts (dashed lines). A brain lesion disrupting the corticoreticular fibers (A) causes disinhibition which leads to unopposed excitatory system and spasticity.
1.12 Hypertonia and spasticity

There are two different mechanisms that cause resistance in muscle movement or hypertonicity; 1) the neural hypertonia which is due to hyperexcitable stretch reflexes and causes velocity-dependent resistance to passive movement (spasticity)\textsuperscript{68,69} and 2) the non-neural or non-reflex hypertonia due to changes in muscle and joint properties which is soft tissue shortening around the affected joint\textsuperscript{34,68}. If the shortening of the soft tissue is fixed, it causes reduced joint range of motion and joint immobilization which is defined as contracture\textsuperscript{70}.

Spasticity is the velocity-dependent aspect of hypertonia; but patients with UMNS also experience hypertonia which is not velocity dependent\textsuperscript{21}. Animal studies have shown that when a muscle in a paretic limb is positioned at a shortened length (flexed), some pathological changes occur in the muscle tissues decreasing the number of sarcomeres, and replacing them with connective tissue\textsuperscript{71}. These changes occur at the early stage of paresis\textsuperscript{72}. This phenomenon may occur in patients with UMNS and leads to contracture that could cause hypertonia which is non-reflexive and not velocity dependent. In a clinical setting, distinguishing between the non-reflexive and velocity dependent hypertonia is difficult; however, physiological measures such as electromyography (EMG) can help with diagnosis. Because EMG as a neurophysiological measure represents levels of muscle activities, it is important to note that these two components of hypertonia are closely associated; for example, a pulling force of a shortened muscle may excite the spindle and stimulate stretch reflex and create spasticity\textsuperscript{21}. Management of hypertonicity depends on the causing mechanism. In the case of spasticity, treatment in the form of active upper limb rehabilitation\textsuperscript{73} is
recommended, as well as using pharmaceutical agents, orally (systematically) or focally. Non-neural hypertonicity can be managed by active and passive movements.

1.13 Pharmacological approaches to manage spasticity

There are oral and focal pharmacological treatments for spasticity; the most common of these include Baclofen, Tizanidine, and botulinum toxin A (BoNTA). Baclofen is the analog of gamma-aminobutyric acid (GABA), the main inhibitory neurotransmitter in mammals found in pre-synaptic Ia sensory neurons, post-synaptic motorneurons and interneurons. It binds to GABA receptors and inhibits stretch reflex. The side effects of Baclofen are weakness and sleepiness, and only 45% of users find it effective. Tizanidine is another oral medication which mainly reduces pre-synaptic facilitation and is effective in reducing tonic and phasic stretch reflex. This medication has been shown to be effective in reducing spasticity with side effects similar to Baclofen.

BoNTA is injected in the motor points in a muscle as a chemodenervator through activity of light and heavy chains in each BoNTA molecule. The heavy chain allows the drug to enter the axon terminal through the presynaptic membrane by binding with the synaptic vesicle protein, AV2. After BoNTA enters the axon, the lighter chain cleaves the SNARE proteins and prevents the neurotransmitters such as acetylcholine (Ach) from being released to the synaptic cleft. The sequestering of Ach induces a focal reduction in capacity for muscle contraction. Due to the focal effect of BoNTA on reducing spasticity, it has become one of the interventions for focal treatments of spasticity.
1.14 Non-pharmacological approaches to manage spasticity

In addition to pharmacological approaches, a multidisciplinary approach to manage spasticity has been recommended. Different rehabilitation modalities have been utilized aiming to assist the neural activation of the affected hemisphere, decrease the soft tissue shortening of the affected joints, and retain the functional level. Two main types of intervention are used to manage spasticity: active and passive movement therapies. The therapeutic modalities that fit in the active movement category include repetitive task training, Neuro Developmental Therapy (NDT), functional neuromuscular electrical stimulation (NMES), constraint induced movement therapy (CIMT), mirror therapy and robot assistance. The passive movement category includes stretching, splinting, and serial casting.

1.14.1 Active movement interventions

Repetitive task training may not only diminish muscle spasticity and weakness by actively stretching the spastic muscles through reaching, grasping and releasing tasks, but it may also improve motor learning during functional tasks. In a recent Cochrane review, it was shown that repetitive task training indicated modest improvement in walking compared to the standard care or placebo but only in the short term. The improvement did not last more than six months.

Neuro-developmental Technique (NDT), as another modality, is one of the more common interventions for stroke rehabilitation among health professionals and its assumption is to instigate normal movement patterns by reducing spasticity. The therapist assists a controlled movement while inhibiting synergic movements. This
approach has been controversial with several studies showing the ineffectiveness of this modality. As a specific example, Dickstein and Pillar (1983) failed to find any effect in decreasing spasticity during NDT treatment using EMG feedback.

NMES is thought to induce specific plasticity at the spinal pathway, whereby motor units are recruited through the motor axons beneath the electrodes. As it stimulates cutaneous sensory receptors, the Ib fiber is activated and facilitates the Renshaw cell recurrent inhibition, Ia inhibition and increased cutaneous sensory stimulation. Applying NMES with the following regime appeared to be effective: the frequency between 30 and 50 HZ, and a pulse width of 0.1 to 0.5 ms for 30 minutes 5 times per week for 3-4 weeks. A recent systematic review and meta-analysis showed that NMES combined with other treatment modalities such as Bobath, stretching, and conventional therapies improves spasticity and increases range of motion after stroke. However, some muscle intrinsic changes negatively impact the effectiveness of NMES including muscle atrophy, loss of sarcomeres, and decreased muscle length. Interestingly, this systematic review indicated that a combination of BoNTA and NMES did not result in the reduction of spasticity significantly; however, the authors related this issue to an insufficient sample size.

Constraint Induced Movement Therapy is based on the "learned non-use" therapy; it aims to force the patient to use the affected limb by restraining the unaffected arm. Patients who have active wrist extension greater than 20° and have active extension greater than 10° at the metacarpal phalangial joints could be part of the CIMT program. This therapy has three components: restraining the unaffected arm, massed and repetetive practice of a task and shaping of each task to each individual with the
additional complexity of a behavioral contract\textsuperscript{89}. This entails what tasks need to be performed unilaterally while the unaffected arm is restrained, and when and which tasks should be done bilaterally. In a systematic review, even though all included studies indicated improvement, due to a lack of homogeneity, this study failed to clearly indicate the effectiveness of CIMT\textsuperscript{90}. Another study indicated that after mCIMT, spasticity in the upper limb was not reduced even after significantly improvement in the upper limb function; in that study chemodenervation was required to manage spasticity\textsuperscript{91}.

1.14.2 Passive movements

The main goal of passive movement and stretching is to maintain joint mobility and prevent soft tissue shortening around the joint\textsuperscript{92}. Stretching causes elongation of the stretched muscle; it is the most common intervention offered in rehabilitation centres\textsuperscript{93}. Stretching puts tension on soft tissues which includes muscles, skin, tendons, and neural and vascular tissues; it may affect the elasticity and excitability of the stretched muscle\textsuperscript{94}. The goal of stretching specifically for patients with spasticity is to decrease abnormal muscle tone, prevent shortening of soft tissue, decrease pain and possibly improve function\textsuperscript{95-97}. Often, stretching is recommended daily for a long period of time. The intensity, velocity, duration and repetition of this intervention varies\textsuperscript{98}. In a systematic review, Bovend’Eerdt et al. (2008) indicated that the effect of stretching on spasticity was inconclusive and further studies are needed\textsuperscript{98}.

Splinting is another intervention to manage spasticity; a splint is a removeable device used to maintain position of the affected limb. It has different goals that include: to avoid contracture, to improve the range of motion, to reduce spasticity and to maintain a certain position\textsuperscript{99,100}. In neurorehabilitation, the goals for applying a splint include: to
decrease spasticity, to diminish and avoid contracture through delivering a constant stretch\textsuperscript{101}, to assist with joint alignment which could lead to improvement in hand and arm function\textsuperscript{101}, and to decrease pain\textsuperscript{102}. In the past, it was believed that splinting prevented muscle contraction but recent views suggest that rather than impacting reflexive muscle movements, splints enable biomechanical gains such as passive prolonged stretch and joint alignment\textsuperscript{99}. Splinting precludes muscle shortening and range of motion in spastic muscles\textsuperscript{99}, but there is no strong evidence that the addition of a splint on standard rehabilitation would prevent contracture in post-stroke individuals nor improve arm function\textsuperscript{99}. Nor does splinting have additional effect on spasticity compared to usual therapy after stroke\textsuperscript{88}.

Serial casting has also been used to manage upper limb spasticity. Casting is the positioning of the limb at a certain angle or position to maintain muscle length for a period of time. The process is repeated as the range of motion slowly increases and continues until it reaches maximum\textsuperscript{103}. Serial casting is redone weekly; after casting the achieved range is maintained by using hand orthoses such as a bivalve cast which is a removable cast or hand splint. This treatment has been applied for decades\textsuperscript{103} and there are two underlying theoretical bases: a) neurophysiological rationale that serial casting prevents muscle shortening, and decreases spasticity by decreasing the excitatory input of muscle spindles\textsuperscript{104}, and b) biomechanical justification that serial casting through “low load and long duration stretches” elongates muscle and avoids contractures\textsuperscript{105}. However, a systematic review studying the effectiveness of casting in adults and children with brain injuries, cerebral palsy and stroke failed to support or disprove the effectiveness of
casting in the upper extremity. Also, no long-term effects or adverse effects of serial casting were found\textsuperscript{103}.

1.15 Role of motor recovery in function

Even though the main goal of BoNTA and therapeutic intervention (hypertonicity management) is to improve function, predominantly, voluntary movement depends on the motor recovery stage of the upper limb at the baseline\textsuperscript{106}. Motor recovery entails trained motor capability which is based on muscle synergies, and the capability of applying those movements in various combinations to perform a task after an upper motor lesion\textsuperscript{107}. Recovery appears if this reacquisition is returned back to the limbs; otherwise, adaptation/compensatory movement presents\textsuperscript{107}. Motor recovery is defined as “the reappearance of elemental motor patterns prior to central nervous system injury”\textsuperscript{107}. In cases where the motor recovery did not occur, such as in patients with severe hemiparesis, compensatory recovery occurs from the remaining or the replacement of normal motor patterns.

Motor recovery leads to functional improvement which is the ultimate goal for both the patients and the clinicians. In patients with severe hemiparesis, compensatory and adaptive motor movement is appropriate\textsuperscript{108}, but patients with mild to moderate hemiparesis would benefit from active movement and a reduction in compensatory trunk movements\textsuperscript{109}. Chang and his colleagues (2009) showed that BoNTA and rehabilitation are necessary to improve function using Chedoke McMaster Stroke Assessment (CMSA)\textsubscript{hand}. CMSA is a motor recovery assessment tool with an outcome scale divided into seven levels. They divided patients at baseline into higher functioning (CMSA \geq 4) and lower functioning groups (CMSA of 3 or 2). They indicated that the hand motor recovery stage greatly impacts the functional gain\textsuperscript{106}. Because baseline impairment
correlates with accessibility to the “motor neuron pool” in their central nervous system, the higher functioning patients have more active motor neurons compared to the lowering functioning. As a result, after decreasing spasticity, the higher functioning group voluntarily activates their agonist muscles and improves their function.

1.16 Conceptual model and key considerations to examine the impact of BoNTA and rehabilitation on arm function

Conceptually, different elements contribute to the impact of BoNTA and rehabilitation on upper limb function (Figure 1.2). Initially, in order to improve function and movement in a limb, there is a need to manage spasticity\textsuperscript{106}. It is caused by upper motor neuron syndrome, but can be modified by extrinsic factors. A systematic review showed that extrinsic factors such as cold, posture, circadian rhythm, skin breakdown and pregnancy would increase spasticity\textsuperscript{110}. In the same review, patients self-identified comorbid conditions such as bowel and bladder infections, menstrual cycle, stress, and tight clothes as other trigger factors\textsuperscript{110}. Although the focus of this thesis is not to investigate those factors, they are relevant to patient goals and capacity to engage in therapy (i.e. Study 1 and 3) and are typically addressed and treated by the interdisciplinary team during the study period in the Spasticity Management Clinic.

As another factor in the model, motor impairment level also contributes to the spasticity level. In the lower stages of CMSA (stage 2), spasticity develops and becomes marked in stage three and from stage four after which, synergistic patterns are diminished and active movements appear\textsuperscript{111}. In Study 1 and 3 the impact of motor recovery on achieving their goals (Study 1) and improving upper limb function will be examined clinically and biomechanically (Study 3).
Even though spasticity after upper motor neuron syndrome is often persisting, interdisciplinary team approach has been recommended to enable patient/family to manage spasticity through rehabilitation and pharmacological agents such as BoNTA. Study 1 and 3 will show the impact of BoNTA on decreasing spasticity. However, the effect of combination of rehabilitation with BoNTA on upper limb function has been equivocal; Study 1 and 3 will shed light further on this topic and it is noteworthy that Study 3 will measure the changes using clinical and kinematic measures which are more objective.

Assessing the effect of interventions is also part of this conceptual model and Study 2 will examine the accuracy and sensitivity of a novel assessment, the Kinematic Upper Limb Spasticity Assessment (KUSA), in distinguishing the affected sides impaired movement components such as velocity, and active range of motion (AROM). Whether BoNTA and rehabilitation impacts the upper limb function and goals will be examined on Study 3 and 2. However, Study 1 is only based on clinical measures but Study 3 will be both clinical and kinematic measurements.

Spasticity may cause flexor synergy where the affected upper limb has limited range of motion and deformity; in longer terms it may lead to contracture and abnormal posture of the upper limb. As a result, cleaning the palm to prevent skin breakdown and personal hygiene, putting the arm down the sleeves (for dressing) may become actively impossible but it can be accomplished by caregivers or with assistance of the unaffected side and these goals are called “passive functional goals” by appropriate positioning through splinting or casting\textsuperscript{112,113}. Study 1 and 3 will examine the impact of interventions
on different types of goals (passive and active goals) that each patient selected individually based on GAS.

**Figure 1.2:** Conceptual model of the thesis. Relationship between spasticity and function: contributing factors that increase spasticity include extrinsic factors, comorbid conditions and severity of impairment. Spasticity management modalities includes rehabilitation and pharmacological/chemodenervation. Different types of assessments aim to measure the impact of intervention on improving function which includes clinical and biomechanical types. Improvement in function leads to enhanced ability to achieve active and passive goals.

### 1.17 Overview and objectives

Managing spasticity and improving function in the upper limb is essential for individuals post stroke to participate in their activities of daily living. In the past, only rehabilitation was used to manage spasticity but recently BoNTA has been added to the treatment plan. However, until now, there has been a paucity of research to show the impact of BoNTA on upper limb function. It is critical to find out if adding BoNTA to the treatment plan is effective in improving arm function which would be beneficial for the patient/families, therapists and managers. Knowing the effectiveness of BoNTA would help the therapist and post stroke clinics to decide whether or not to include it as a
routine care plan and the Ministry of Health to establish more spasticity management clinics to improve best practice.

In order to examine the effectiveness of BoNTA objectively on arm and hand function after stroke, it is important to measure accurately the change of function using clinical and biomechanical measures such as kinematic analysis in the upper limb prior to and after BoNTA. Therefore, the overarching goal of my dissertation was objectively to examine and quantify the changes in upper limb function following spasticity management including BoNTA. My dissertation is comprised of three studies. In the first study, the primary objective was to categorize the patients’ identified goals using Goal Attainment Scale (GAS) and map the goals using the ICF domains in an outpatient clinic. The secondary objective was to explore the characteristics of those individuals who achieved their goals at different levels, as reflected in the changes in GAS scores.

The second study was a methodology paper describing the development of a novel assessment tool that used kinematic measurement of three different tasks (Kinematic Upper Limb Spasticity Assessment (KUSA)) on three patients post stroke at baseline. The objectives of this study were to describe KUSA and demonstrate its ability to quantify spasticity during three multi-joint functional tasks. The details of the kinematic assessment protocol, variables measured, and results from three patients are presented as a case report to demonstrate the value of our novel assessment.

The third study was considered to show the clinical and kinematic changes before and after a BoNTA injection with the hypothesis that treatment with BoNTA would result in improved clinical and kinematic measures. The objectives of that study were 1) To
compare the effect of interventions (upper limb rehabilitation and BoNTA) on affected UL function after stroke using clinical and kinematic measures and 2) Explore the differences between the high functioning and low functioning groups in terms of response to BoNTA.

Together, the chapters that comprise my dissertation inform the type of goals that patients after stroke may have in order to participate in their activities of daily living. Identifying appropriate goals would be helpful for the patients/families and interdisciplinary team to be more focused on their interventions efficiently during the period that patients attend rehabilitation programs which are mostly for a short period. Also, evaluating the result of rehabilitation is important for both patients and rehabilitation team. Including advanced measures in addition to the clinical assessments would objectively indicate the exact amount of improvement and the effectiveness of interventions, while it could be challenging by only relying on the clinical measures. After stroke, almost all patients and their families wish to resume their functional level in full capacity through intensive rehabilitation. With limited resources and the cost of rehabilitation, this study aims to identify to most appropriate type of intervention to patients with different levels of motor recovery and impairment levels. As a result, this thesis would contribute to evidence based practice and patient-centred approach in the clinical settings and the results will guide future research in this area.
Chapter 2: Goal Attainment Scaling in individuals with upper limb spasticity post stroke


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2.1 Abstract

**Background:** Focusing on rehabilitation goals is an effective approach for improving function in individuals with spasticity after stroke.

**Objectives of Study:** The objectives of this study were to examine and map goals of post-stroke individuals with spasticity using the Goal Attainment Scale (GAS) and International Classification of Functioning, Disability and Health (ICF), and to evaluate the impact of botulinum toxin A (BoNTA) on occupational performance based on the type of rehabilitation goals.

**Methods:** Thirty-one patients were recruited from an outpatient spasticity management clinic. Each patient set one goal, was injected with BoNTA in their spastic upper limb muscles, and received standard rehabilitation services twice a week for four weeks.

**Findings:** Twenty-seven participants achieved the expected level and four exceeded the expected level of their rehabilitation goals. Fifty-five percent of the goals were related to Activity/Participation and 45% of the goals were categorized in the Body Structures and Function domain of the ICF. Fifteen goals focused on positioning, while 16 goals focused on (independent) activities of daily living (ADL/IADL). Both the positioning and ADL/IADL groups experienced a reduction in MAS following the administration of BoNTA. The positioning group was older and more impaired.

**Relevance to Clinical Practice:** Mapping goals to ICF identifies specific targets for intervention, establishes a common language within the interdisciplinary team and contextualizes the ways disability impacts goals.
Limitations: This study is limited by a relatively small sample size and absence of a functional measure.

Recommendations for Further Research: Further studies can explore the development of goal/item banks to advance the use of GAS for spasticity management.
2.2 Introduction

Spasticity, a component of the upper motor neuron syndrome, can be observed in individuals who have experienced a stroke\textsuperscript{114}. Spasticity is characterized by an increased resistance to brisk passive movement and often results in abnormal posturing, loss of volitional coordinated movement, and/or length of the muscle affected\textsuperscript{59,69}. The incidence of spasticity is 19\% after three months and 38\% after one year stroke\textsuperscript{115}. The prevalence of spasticity has been reported as high as 87\% when clinical and electrophysiological measures are used for assessment\textsuperscript{27}.

The impairments resulting from spasticity often interfere with activities of daily living. In prolonged and severe cases, spasticity can lead to contracture which increases the difficulty of basic personal care such as dressing, hand hygiene, feeding oneself or toileting\textsuperscript{62}. Limitations such as these can negatively impact quality of life of the individual and can also increase caregiver burden\textsuperscript{116}.

Because of the complex clinical presentation of individuals with spasticity, best practice guidelines recommend that spasticity management be interprofessional\textsuperscript{117}, and follow a multidimensional approach\textsuperscript{118}. This approach may include splinting\textsuperscript{119}, electrical stimulation\textsuperscript{120}, stretching\textsuperscript{121}, as well as pharmacological interventions such as botulinum toxin A (BoNTA) injections\textsuperscript{122}. However, stroke rehabilitation and spasticity management should also be goal-oriented to allow patients and their caregivers to work collaboratively with the healthcare professionals to identify meaningful goals\textsuperscript{117}. This approach motivates patients through a focus on achievable expectations\textsuperscript{112} and can be assessed using a goal setting tool such as the Goal Attainment Scaling (GAS)\textsuperscript{123}. The GAS is a
tool that provides a “measure of the achievement of expectation”\textsuperscript{124} and assists the team with organizing, targeting and defining the rehabilitation process\textsuperscript{125}.

The GAS can be used in combination with standardized clinical assessment tools in the rehabilitation setting. In patients with spasticity, GAS can complement the results of other clinical measures of spasticity, such as the Modified Ashworth Scale (MAS), which measures the resistance of a joint while it is moved passively and is scored from range from 0 (normal tone) to 4 (rigidity)\textsuperscript{26}. In contrast to MAS, a measure of impairment, the GAS is an indicator of goal attained after intervention\textsuperscript{126}. Goals identified by the GAS can be classified using the International Classification of Function, Disability and Health (ICF). The ICF is a model that facilitates the use of common international language to classify the impact of diseases across different health or health-related domains. These include: (1) the body function /structure domain as an indicator of impairment, (2) the activities domain as an indicator of disability, and (3) the participation domain as an indicator of handicap, as well as contextual factors, such as environmental and personal aspects\textsuperscript{127}.

The primary objectives of this study were: 1) to examine and map goals of post-stroke individuals with spasticity using the Goal Attainment Scale (GAS) and International Classification of Functioning, Disability and Health (ICF); and 2) evaluate the impact of botulinum toxin A (BoNTA) on occupational performance based on the type of goals.
2.3 Methods

2.3.1 Design

This study used a cross-sectional retrospective design among community dwellers attending an outpatient spasticity management clinic following their first stroke.

2.3.2 Study sample

Patients were recruited consecutively from those attending the outpatient spasticity management clinic at a rehabilitation hospital from 2012 to 2014. Post-stroke adults with upper limb spasticity, defined as Modified Ashworth Scale (MAS) ≥ 1 (slight increase in tone with resistance at the end range) in any of the muscles of the upper limb, were included. The patients were not naïve to BoNTA. Individuals with joint deformities and contractures, cognitive impairments, or an inability to follow instructions were excluded from the study. Consent was obtained from the patients to use their data for research purposes.

2.3.3 Procedures

Individuals received a BoNTA injection in the involved muscles from a physiatrist at the outpatient spasticity management clinic. The physiatrist selected the muscles, dosage, and type of BoNTA (BOTOX® or Xeomin®) based on best practice guidelines. The injections were guided using electromyography.

Patients received standard rehabilitation twice a week for four weeks following BoNTA injection, which reaches peak effect at four weeks post injection. Rehabilitation was delivered by an occupational therapist and was individualized based on best practice recommendations and included activities such as task oriented intervention, constraint
induced movement therapy, functional electrical stimulation, splinting, casting, and self-management\textsuperscript{121}.

2.3.4 Data collection and measures

Sociodemographic data (age, sex) and stroke-specific information (time since stroke, affected side, type of stroke) were collected to describe the study sample. The Chedoke McMaster Stroke Assessment (CMSA) for arm and hand was administered to measure the extent of motor recovery\textsuperscript{130}. In addition, two clinical measurements, GAS and MAS, were completed at baseline and four weeks post BoNTA injection.

Goals identified in the GAS were categorized based on ICF domains using the linking rules established by Cieza et al\textsuperscript{131}. Each goal was mapped retrospectively as a best match to an ICF category; for example, ”keeping the affected wrist and hand well positioned in the wrist and hand orthotics at night time” was categorized as \textit{b735- Muscle tone functions}. As previously reported by others\textsuperscript{132,133}, second level categories with the three-digit code (\textit{b7351: Tone of muscles of one limb}) offer the most optimal combination of “breadth and depth.”

Patient goals were also categorized into one of the following categories: (1) Activities of Daily Living (ADLs), (2) Instrumental Activities of Daily Living (IADL), or (3) positioning. Activities such as: eating, bathing, dressing, toileting and transferring, and continence were classed as ADL\textsuperscript{134}. IADLs were considered activities that involved interaction with the environment and included such activities as preparing food, shopping, money management, and household chores\textsuperscript{135}. Positioning was defined as the
promotion of normal resting alignment of a joint in order to maintain and stretch soft tissue to prevent shortening and contracture\textsuperscript{136}.

2.3.4.1 Goal Attainment Scale

For this study, each patient was allowed to select only one goal. For example, one patient wanted to “be able to wear a splint at night for 4-5 hours at maximum range of extension of the wrist joint without pain.” Each goal can be calculated as a weighted goal, which takes importance and difficulty into account\textsuperscript{123}. In the present study, only the unweighted GAS scores were considered for data analysis\textsuperscript{137}.

The treating occupational therapist and each patient with his or her family member(s) (based on patient preference) negotiated one goal. There are five levels for the GAS as follows:

\begin{itemize}
  \item +2 “a much better than expected” level
  \item +1 “a somewhat better than expected” level
  \item 0 “the expected level of achievement”
  \item -1 “a somewhat less than expected” level
  \item -2 “a much less than expected” level
\end{itemize}

The goals were set prior to the BoNTA injection and scored on the day of injection (baseline) and then four weeks later (peak). To make sure that the goal was potentially achievable and not overly ambitious, every patient started at the -1 level and if he/she achieved the goal, it was scored as 0, to be consistent with previous studies\textsuperscript{132,137}. If the patient exceeded the goal, the level of GAS increased to a maximum of +2. Consistent with guidelines for GAS\textsuperscript{123}, the patient and therapist identified and agreed on the
specifics of each of the five levels of achievement of the GAS. For example, for the patient whose goal was to wear the splint for 4-5 hours, this would be the expected level of achievement, which if achieved would be rated as 0. Thereafter, the patient and therapist agreed that if the splint could be tolerated for 6-7 hours at night without pain, the goal would be scored at the +1 level; if she tolerated it the entire night without pain, the goal would be +2.

2.3.4.2 Modified Ashworth Scale

The treating occupational therapist measured the Modified Ashworth Scale (MAS; 0 = normal muscle tone, 4 = rigidity) score of the most affected muscle (e.g. elbow, wrist, or finger flexors) while the patient was seated.

2.3.5 Data analysis

Each goal was categorized as Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL) or positioning. Each goal was mapped based on ICF domains by utilizing linking guidelines developed by Cieza and colleagues. The GAS scores were examined at baseline as well as four weeks from the time of injection. MAS was quantified at baseline and at four weeks after injection based on goal category and on GAS. Wilcoxon signed ranks tests were used to determine whether the change in MAS between baseline and week four was statistically significant. Independent t-tests (age and time), Mann-Whitney U tests (CMSA arm and hand) and Chi-square (proportion of sexes) were used to identify differences in characteristics of goal-based subgroups. Statistical significance was set at \( p \leq 0.05 \).
2.4 Results

2.4.1 Patient characteristics

Data from 31 participants (11 female) was included in this study. The mean (sd) of the ages for the whole sample was 56.8 (12.5) years and the average time post-stroke was 4.3 (3.1) years. Ten individuals were determined to have hemorrhagic stroke and 11 individuals had ischemic stroke. The median (range) CMSA score for the arm and hand were 2 (2-5) and 2 (1-4), respectively.

2.4.2 GAS

All patients had improvement based on the GAS. Twenty seven of 31 patients demonstrated improvement by achieving the “expected level of achievement” (GAS = 0). The remaining four patients achieved “a somewhat better than expected” level (GAS = 1). The demographic and clinical characteristics of the GAS subgroups are presented in Tables 2.1 and 2.2.
Table 2.1. Characteristics and clinical information of subgroups.

<table>
<thead>
<tr>
<th></th>
<th>Grouping by GAS score</th>
<th></th>
<th>Grouping by Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GAS = 0 after BoNTA injection</td>
<td>GAS = +1 after BoNTA injection</td>
<td>Positioning Goals</td>
</tr>
<tr>
<td></td>
<td>(n=27)</td>
<td>(n=4)</td>
<td>(n=15)</td>
</tr>
<tr>
<td>Age</td>
<td>56.5 ± 13.3</td>
<td>59.0 ± 8.0</td>
<td>62.9 ± 9.1</td>
</tr>
<tr>
<td>Sex</td>
<td>9 F</td>
<td>2 F</td>
<td>2F</td>
</tr>
<tr>
<td>Type of stroke</td>
<td>9 Hem/18 Isch</td>
<td>1 Hem/3 Isch</td>
<td>8 Hem/7 Isch</td>
</tr>
<tr>
<td>CMSA arm ^</td>
<td>2 (2-5)</td>
<td>2.5 (2-3)</td>
<td>2 (2-4)</td>
</tr>
<tr>
<td>CMSA hand ^</td>
<td>2 (1-4)</td>
<td>2 (2-3)</td>
<td>2 (1-3)</td>
</tr>
<tr>
<td>Years after stroke</td>
<td>4.4 ± 3.2</td>
<td>3.8 ± 2.1</td>
<td>4.4 ± 2.9</td>
</tr>
</tbody>
</table>

Note: Mean ± standard deviation; number in parenthesis indicate min and max; ^Median (min-max), *statistically significant difference between positioning and ADL/IADL groups (p≤0.05); Hem.: Hemorrhagic stroke, Isch.: Ischemic stroke
### Table 2.2: List of goal classifications

<table>
<thead>
<tr>
<th>Goal Classification</th>
<th>Group A (n=27)</th>
<th>Group B (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADL goal list</strong></td>
<td>• Pick up a light object such as a sock from a surface (at the hip level) with the affected hand&lt;br&gt;• Zip/unzip a winter jacket to 1/3 of the zipper length with the affected hand&lt;br&gt;• Use unaffected side to wash the affected armpit&lt;br&gt;• Reach, grasp and lift a glass of water (200cc) with the affected hand&lt;br&gt;• Hold a soap bar with the affected hand and wash the unaffected armpit&lt;br&gt;• Wash the unaffected arm with the affected hand for 2-3 minutes during bathing&lt;br&gt;• Swipe the table with the affected hand while assisted with the unaffected arm&lt;br&gt;• No elbow hiking during walking affected&lt;br&gt;• Hold and drink a cup of coffee with the affected hand, assisted with the unaffected hand</td>
<td>• Tie hair to a pony tail with using both hands</td>
</tr>
<tr>
<td><strong>IADL goal list</strong></td>
<td>• Use the affected arm for gesturing during daily conversation with the family for 3-4 hours a day&lt;br&gt;• Grasp to open the fridge and drawers with the affected hand&lt;br&gt;• Turn on the stove burner with the affected elbow (elbow full extension)&lt;br&gt;• Turn pages while reading a book with the affected hand&lt;br&gt;• Extend the affected elbow to reach the fridge door (with less effort/compensatory trunk movements)</td>
<td>• Use affected hand and arm to gesturing for 3-5 minutes</td>
</tr>
<tr>
<td><strong>Positioning goal list</strong></td>
<td>• Tolerate the wrist and hand orthosis for 7-8 hours at night (n=3)&lt;br&gt;• Position the affected wrist and hand correctly on the resting splint&lt;br&gt;• Rest the affected hand in the pocket while walking with a cane&lt;br&gt;• Stretch the affected wrist and fingers on the table while the unaffected hand stabilizes&lt;br&gt;• Rest fingers on the table caregiver passively stretches the affected fingers straight on the table&lt;br&gt;• Tolerate Saebo Stretch splint 8 hours a day&lt;br&gt;• Be able to reach and put the affected hand in a box&lt;br&gt;• Apply figure 8 oval and Saebo stretch splints together at night time&lt;br&gt;• Tolerate the resting hand and wrist splint every night without any redness in the PIP joints.&lt;br&gt;• Position the affected wrist on the Saebo Stretch&lt;br&gt;• Keep the affected elbow on the wheelchair lap tray</td>
<td>• Tolerate the wrist and hand orthosis all night&lt;br&gt;• Be able to use digital extensor splints 3-4 hours at night time</td>
</tr>
</tbody>
</table>
2.4.3 Mapping onto the ICF

In considering all 31 goals, 45% (n=14) were categorized in the Body Structure and Function domains. Specifically, 38% (n=12) were in neuromusculoskeletal and 6% (n=2) were in the sensory and pain chapters. The remaining 17 goals were fit into the Activities and Participation domain with the following distributions: 15% (n=5) in mobility, 21% (n=7) in self-care, 10% (n=3) in domestic life, and 6% (n=2) in communication chapters (Table 2.3).

When separating the groups based on GAS, analysis revealed that for the GAS=0 group, 44% (n=12) of the goals mapped to the Body Structure and Function domain with the neuromusculoskeletal chapter accounting for 37% (n=10) and the sensory and pain chapter 7% (n=2). The rest of the goals for this group (n=15) were categorized in the Activities and Participation domain including: mobility 19% (n=5), self-care 22% (n=6), domestic life 11% (n=3) and communication 3% (n=1). In the GAS=1 group, 2 goals were categorized at the Body Structure and Function domain with both goals classed in the neuromusculoskeletal chapter. The other 2 goals were in the Activities and Participation domain with one goal in the self-care and the other one in the communication chapters. The small and unequal sample size (n= 27 and 4) did not permit a statistical comparison of changes in MAS between subgroups; however, both groups demonstrated a tendency towards a decrease in MAS 1 month post-injection (Figure 2:1A and B).
2.4.4 Types of goals

Irrespective of GAS score, almost half of the goals, 48% (n=15/31), were in the positioning category, while 26% (n=8) were classified as ADL. The remaining 26% (n=8) were classed as IADL. For those with GAS=0, 48% (n=13/27) were related to positioning, 33% (n=9) were ADL and 19% (n=5) were IADL. For those with GAS=1, 2 goals were classified as positioning, 1 was ADL, and 1 was IADL (Table 2.2).

The characteristics of the positioning and IADL/ADL groups are presented in Table 2.1. As a whole, the positioning group was older (t29 = 2.856, p=0.008), had proportionally more males (χ²1 = 6.229, p = 0.013) and had lower CMSA arm (U=72.5, p=0.23) and hand (U=76, p=0.035) scores. In addition, the reduction in MAS at four weeks post-injection was statistically significant in both the positioning group (Z = -
3.473, p=0.001) and the ADL/IADL groups (Z = -3.624, p<0.001). Figure 2:1C and D show the distributions of MAS scores for each group at baseline and peak.

**Figure 2.1:** Distribution of MAS scores at baseline (left panels) and at one month post-BoNTA injection (right panels) for each subgroup. A: GAS=0; B: GAS=1; C: Position-related goals; D: ADL/IADL-related goals
2.5 Discussion

This study examined and mapped goals of individuals with upper limb spasticity after stroke using the ICF. The characteristics of individuals who achieved their goals as reflected in changes in Goal Attainment Scale (GAS) scores were also examined. All patients achieved or exceeded their rehabilitation goals; the majority of which were related to joint positioning. Two groups emerged: those who achieved the expected level of achievement and those who somewhat exceeded the expected level of achievement. No patient demonstrated a ‘much better than expected level of improvement’. Almost half the goals were considered within the Structure and Function domain of the ICF, specifically under the categories of neuromusculoskeletal and sensory and pain. The rest of the goals were categorized under the domain of activities and participation, specifically mobility, self-care, domestic life and communication. Individuals with positioning-related goals were older and more impaired. The interpretation of these findings is described below.

2.5.1 Use of the GAS as an indicator of efficacy of intervention

The GAS has been used as tool to determine whether a patient’s goals have been achieved following a therapeutic intervention\textsuperscript{138,139}. The GAS can be applied in a heterogeneous neurological population and is not subject to floor or ceiling effects which limit standardized measures\textsuperscript{112}. Indeed, analysis of previously reported findings of McCrory et al\textsuperscript{140} showed that one third of individuals (35%) improved 1 level in their GAS (i.e. from -2 to -1) and 19% achieved their goals and 4% overachieved\textsuperscript{133}. Similarly, Nott et al. (2014) reported that in individuals with acquired brain injury, 50% of the goals were attained and they did not report any goal overachieving\textsuperscript{132}. In our study,
all patients achieved or exceeded their goals, and 13% overachieved. The low rate of overachievement of goals may suggest that some of the goals may have been over-ambitious given the chronicity (4yrs) and impairment level (CMSA = 2) of the study cohort. While the differences in rates of goal attainment or over-achievement between studies can be attributable to number of goals, ambitiousness of goal or experience with the tool, the evidence demonstrates that the GAS is a useful tool for quantifying outcome.

The GAS may be more sensitive than global clinical measures for determining response to treatment\textsuperscript{112}. However, there may also be components related to the implementation of the GAS that may limit its utility as a robust measure of outcome in a rehabilitation setting. There is an assumption that the goals are unbiased and balanced between exceeding and falling short of the expected level but sometimes goals can be either not sufficiently challenging or are too unrealistic\textsuperscript{141}. In addition, the five-point ranking of the GAS are ordinal values but are treated as interval data which causes non-linearity in the scores\textsuperscript{142}. Applications of models to alter the components of the GAS have identified differences in the proportion of instances of clinically-significant changes in GAS scores\textsuperscript{142}, suggesting that the results for GAS could be dependent on how the measure was applied rather than an outcome of patient improvement.

2.5.2 Establishing goals based on impact of disease: mapping the GAS onto ICF domains

When mapped on to ICF domains, the majority of goals (44\%) were categorized in body structure and functions. This is not surprising considering majority of the patients who were included in this study had CMSA of 2 in the upper limb. In studies by
Nott et al., (2014) and Turner-Stoke et al. (2010), 24% and 28% of the goals, respectively, were mapped to this domain. The rest of the goals in our study (55%) were categorized in the activities and participation domain, in contrast to 76% and 72% in the Nott and Turner-Stokes studies\textsuperscript{132,133}. A number of reasons could explain the divergence between findings. Turner-Stokes and colleagues’ (2010) results were based on two cycles of BoNTA injections and ours on one. For peak results, the measurements were completed at eight weeks after BoNTA injections in previous studies and ours at four. The longer time frame may explain the greater emphasis on goals in activities and participation domain compared to impairment. The patients in this study were older than in Nott et al. (2014) which may explain the greater focus on long-term impairments such as contractures and position of the affected limbs. Indeed, the individuals in the present study with positioning-related goals were older and more impaired. These person-specific factors may have also been influenced by the family’s or treating team’s perspectives on setting goals related to long-term impairments since the aim is to prevent the affected joint from developing contracture by improving positioning. The use of rehabilitation in conjunction with BoNTA and the type and dosages of BoNTA used in this study may also account for differences between studies.

2.5.3 Use of goal banks to facilitate goal setting

The results of this study build on previous findings that GAS, at this time, may be best used as a framework for facilitating communication and discussion in terms of helping teams to assess and reflect on their service delivery and discuss the progress with patients and families. As a way of enhancing the utility of this tool in this regard, goal/item banks which appropriately identify achievable goals could be developed\textsuperscript{142}. 

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For therapists, setting and wording of a Specific, Measurable, Attainable, Realistic, and Timely (SMART) goal can be a prolonged process\textsuperscript{133}. Setting “free-flowing” goals could be subjective and take time and effort to describe\textsuperscript{133}. As a result, setting individual goals could be costly in terms of training the clinicians and spending sessions for negotiating and setting goals at the beginning rather than starting intervention immediately. Thus, having a list of preset goals with standard scales (i.e. for pain scale 0-10) adds the objectivity of goal setting and expedites the goal setting process. This list of goals compiled in this study could be used as a start of a goal/item bank thus facilitating the process for therapists.

2.6 Study limitations

There are a number of limitations that must be considered when interpreting the results of this study. The sample size was limited and the treating and assessing therapist was the same person which could have biased the results. Functional measures of the upper limb were not administered. Finally, the practice setting pre-determined that only one goal would be set. Nevertheless, the results of this study can serve as the basis for future studies to examine the role of goal attainment scaling in rehabilitation, whether as a communication tool or outcome measure to assess the effectiveness of intervention.

2.7 Conclusion and relevance to clinical practice

The GAS can be a beneficial tool for interacting with patients with spasticity in rehabilitation settings in order to facilitate discussion and agreement on mutual goals. Knowing whether the patients’ goals are in the body structure or activities/participation domains help guide the treatment plan. Further studies are required to explore how to
best utilize the GAS in the management of individuals with spasticity and the potential for linking it with the development of a goal/item bank.
Chapter 3: Implementation of kinematic upper-limb spasticity assessment (KUSA): a case series

3.1 Abstract

**Background**: Upper limb spasticity is common after stroke and severely impacts activities of daily living. Current clinical measures of spasticity are subjective and lack the sensitivity needed to track a patient’s progress and compare different therapies. Kinematic analysis provides an objective measure of movement to evaluate the effects of rehabilitation. This paper presents a novel assessment for upper limb spasticity: the Kinematic Upper-limb Spasticity Assessment (KUSA) and demonstrates its potential benefits by comparing results with existing clinical measurements.

**Methods**: Three participants with stroke completed the Modified Ashworth Scale, the Chedoke McMaster Stroke Assessment, and the KUSA. The KUSA incorporates a motion capture system to evaluate upper limb movement and spasticity using the following kinematic measures: active range of motion, speed and amount of compensatory trunk movement. Participants performed three multi-joint functional tasks: wrist and elbow extension/flexion, and shoulder flexion/abduction.

**Results**: Results demonstrate the ability of KUSA to distinguish between unaffected and affected upper limb motion. Furthermore, KUSA provides supplementary information for motion characterization that is not available through clinical measures alone.

**Conclusion**: The KUSA provides clinicians with valuable information that, in conjunction with clinical measures, can be used to monitor patient progress and modify rehabilitation.
Keywords: stroke, tasks, kinematic analysis, clinical measurement, model, kinematic variables
3.2 Introduction

Spasticity is a type of disordered sensori-motor control, manifesting as limb tightness or stiffness, caused by involuntary activation of muscles. It commonly occurs after stroke, with a prevalence rate of 38%, and mostly affects upper extremities. It can result in pain, fatigue, involuntary limb movement, and difficulty performing activities of daily living (ADL). As most ADL require the use of the hands and arms, upper limb spasticity is particularly debilitating for individuals and increases caregiver burden.

3.2.1 Measuring spasticity

A variety of clinical tools have been used to measure spasticity. For instance, the Modified Tardieu Scale is a subjective measure of a muscle’s response to different speeds of movement. The Penn Spasm Frequency Scale is a self-reported measure based on the number of spasms that occur, while the Numeric Rating Scale is a patient-rated measure of the intensity of spasms. However, the most commonly used assessment of muscle spasticity in stroke populations is the Modified Ashworth Scale (MAS), which is a rating scale that reflects the extent and location of resistance of a muscle during quick passive stretches. The MAS has five levels: 1, 1+ and 2 (mild spasticity), 3 (moderate spasticity), and 4 (severe stiffness).

Studies of the validity and reliability of MAS have reached variable conclusions depending on testing protocols. The MAS implicitly assumes that spasticity is measured by resistance to passive movement, which may not hold universally. It also lacks sensitivity to distinguish neural (i.e. hyper-excitability of spinal reflexes) and non-neural (i.e. shortening of soft tissue around the joint) aspects of spasticity. By nature,
the MAS is a subjective rating, which may explain its poor inter-rater reliability, as factors such as velocity of passive movements can confound results\textsuperscript{31}. When compared to objective measures of reflex muscle activity (surface electromyography and dynamometry recordings), the MAS appeared to be poorly related\textsuperscript{31}. These results indicate that clinicians should be wary of relying solely on the MAS to make decisions when treating and managing spasticity. The Chedoke McMaster Stroke Assessment (CMSA) is another commonly used clinical assessment, although it measures the extent of motor recovery after stroke and does not explicitly indicate functional impairment caused by spasticity\textsuperscript{130}. It consists of a series of tasks designed to test impairment level in different body parts, each rated on a scale of 1-7, where higher scores mean less impairment.

3.2.2 Kinematic analysis

Current clinical assessments fail to distinguish and differentiate the effect of an intervention on movement and provide an incomplete view on a patient’s recovery. As a result, different objective measures such as kinematic analysis using robotic technology or motion capture systems are increasingly used to examine the changes after stroke.

Recently, studies have used robotics to enhance objectivity and sensitivity to measures of proprioceptive deficits on arm function after stroke\textsuperscript{155,156}. Through robotic technology Semrau et al. showed that 61% of patients after stroke had kinesthetic deficits which were significantly related to clinical measures including FIM, and CMSA\textsuperscript{155}. Additionally, Dukelow and colleagues\textsuperscript{157}, used a robotic exoskeleton to determine that two-thirds of patient with left side hemiparetic and one third of right hemiparetic patients demonstrated impairment in sense of limb positioning, They also
reported good interrater reliability of KINARM with the clinical Thumb Localizing Test. Importantly, these examples not only identify tools to enhance sensitivity of measurement, they also demonstrate association with clinical outcomes.

Traditional kinematic analysis, typically involves the use of a motion capture system to model an individual’s body segments and track their movements with sub-millimeter accuracy in 3-dimensional space. Motion capture systems consist of a set of video cameras that track reflective markers placed on the patient. The use of kinematic analysis for evaluating upper limb movement has been reported in several studies in patients with upper limb spasticity using a wide range of outcome measures including peak velocity, duration of a reaching task, the number of velocity peaks during a prescribed movement, distance, total movement time, trunk displacement, the number of velocity peaks, and the direction of trajectory. We hypothesize that kinematic analysis can offer more detailed information about motion components and strategies than existing subjective clinical measures like the MAS and CMSA. In addition, kinematic measurement can more precisely describe changes in movement patterns and strategies over time, which can assist in the evaluation of the effectiveness of rehabilitation interventions by measuring changes from one therapy session to the next.

The use of kinematic measures has recently become more common when examining functional changes after rehabilitation; however, there is a lack of consistency in methods, outcome measures and a misalignment of movements performed by patients with those that are clinically relevant. For example, Bensmail et al. (2010) measured peak hand velocity, number of movement units, movement time,
and jerk during reaching tasks\textsuperscript{160}. Fridman et al. (2010) recorded peak velocity, movement time and distance during reaching, grasping and transferring of an object\textsuperscript{161}. In another study, a drinking task was measured with additional parameters such as inter-joint coordination and compensatory trunk movement\textsuperscript{162}. Most recently, Van Dokkum et al. (2014) used a reach to grasp task with the following kinematic variables: movement time, time for maximum velocity, trajectory length and number of peak velocity\textsuperscript{43}. These studies focus on upper limb function after stroke but used different tasks and kinematic variables to define functional improvement. None of the existing methods provide a comprehensive assessment of upper limb movement that includes multi-joint functional tasks which are necessary components for any upper limb functional movement and provide a comprehensive characterization of a patient’s movement quality after stroke.

3.2.3 Kinematic Upper-limb Spasticity Assessment (KUSA)

In this paper, we describe our novel Kinematic Upper-limb Spasticity Assessment (KUSA) for quantifying spasticity during three multi-joint functional tasks in patients after stroke. We present details of the KUSA protocol and data from three patients as a case series to demonstrate the potential for this assessment to provide objective measures of upper limb spasticity as a supplement to the two most commonly used clinical measures, MAS and CMSA.
3.3 Methods

3.3.1 Participants

Three patients were recruited in this study; their demographic and clinical characteristics are listed in Table 3.1. This study was approved by the University Health Network Research Ethics Board and written consent was obtained from all participants.

**Table 3.1: Characteristics and clinical information of the sample**

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Details of stroke</th>
<th>Composite MAS</th>
<th>CMSA&lt;sub&gt;hand&lt;/sub&gt; †</th>
<th>CMSA&lt;sub&gt;arm&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>49</td>
<td>Hemorrhagic stroke; left arm affected</td>
<td>8</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>72</td>
<td>Ischemic stroke and right arm affected</td>
<td>13</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>69</td>
<td>Ischemic stroke and right arm affected</td>
<td>7</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

*Composite MAS= the Modified Ashworth Scale sores in five joint of hand, wrist and elbow
†CMSA= Chedoke McMaster Stroke Assessment, Case 1 and 3 have higher motor recovery than case 2.

3.3.2 Clinical measures

The MAS and the CMSA were used to capture and describe the quality and levels of the upper limb impairment. In this study, MAS was calculated as a composite score of five joints (elbow, wrist, metacarpal phalangeal, proximal and distal inter phalangeal joints) with maximum score of 25. The CMSA was administered for both the arm and hand.

3.3.3 Experimental setup

Data was collected using a three–camera Vicon motion capture system (shown in Figure 1a). Vicon Nexus 1.8.1 software (Vicon Motion System, UK) was used for
processing to output 3D coordinates for all markers. Data was sampled at 100 Hz and filtered with a 6 Hz low pass Butterworth filter to remove noise. One digital video camera was also connected to the Vicon system to record video during all data collection sessions. Seven spherical reflective 12 mm markers were placed on each upper limb. Placement locations were the second and fifth metacarpophalangeal, the styloid process of the radius and ulna, the lateral epicondyle, the middle of elbow crease (anteriorly), and the acromial end (Figure 3.1b). In addition, three markers arranged in a triangular cluster were attached to the upper chest (5 cm above xiphoid process of sternum) as a landmark to locate the trunk during arm movements (Figure 3.1b). Both affected and unaffected sides were measured in each task and all tasks were completed in the seated position on a chair with a height of 50 cm and a height adjustable hand therapy table (Hausmann Industrial Inc.) (Figure 3.1a).

![Figure 3.1: Kinematic data collection components. a) Position of the infrared cameras and the video camera relative to the participant’s seating area. b) Location of kinematic markers on the hand, arm, and trunk.](image)

3.3.4 Tasks

The three tasks used to observe upper limb movement in this study were chosen based on their importance for performing activities of daily living (ADLs) and instrumental activities of daily living (IADLs). These tasks were performed near the
midline of the body to represent the types of movements that are needed for ADL and IADL, such as dressing, eating, using a computer, etc. In addition to ADLs, wrist, elbow and shoulder motions are also important for stability to prevent falls.

3.3.4.1 Task 1 – Wrist motion

Participants performed five cycles of active wrist extension and flexion. The elbow was flexed at 90 degrees and shoulders neutral. The forearm was positioned at 45 degrees from the midline and was secured to the apparatus with two straps (Figure 3.2a) to minimize compensatory movement. The Task required the participant to move the wrist from midline to extension and then flexion five times at a comfortable pace to prevent eliciting spasticity by increasing velocity during the movement. To provide feedback about appropriate arm position, a switch was positioned to the dorsal side of the forearm (2 cm above the wrist markers). Participants were instructed to keep their forearm in continuous contact with the switch during the five repetitions. If the switch was not held down, a buzzer would sound and an LED would be illuminated (Figure 3.2 a & b) indicating a failed trail which needed to be repeated. The participant’s hips were rotated 45 degrees axially relative to the front edge of the table to bring the arm to be tested closer to the testing surface while keeping maintaining neutral trunk, hips and shoulder positions during the task.
Figure 3.2: Apparatus used for Task 1 (wrist extension and flexion motion). a) Diagram of the apparatus. The switch box (green tab) indicates whether the forearm is moved out of position. b) Positioning of the participant within the apparatus. Marker positions are visible throughout the motion.

3.3.4.2 Task 2 – Elbow motion

Task 2 involved five cycles of active elbow flexion and extension. The desk surface was raised such that the participant was able to rest his or her arm on the surface with the wrist, elbow and shoulder aligned while preventing any shoulder horizontal abduction or extension. The subjects’ hips were positioned relative to the table surface the same way as in Task 1. The start position required the elbow to be at midline (180 degrees of extension). The subject was asked to bend the elbow bringing the forearm towards the trunk and back to the starting point, five times at comfortable pace. Participants were required to make contact with a switch to mark the start and end of each movement. The first switch was mounted such that it came into contact with the dorsal aspect of the forearm proximal to the wrist while the elbow was in full extension (unaffected side), and the other switch was positioned such that it came into contact with the ventral side of the forearm when the elbow was in maximum flexion (Figure 3.3a). For every occurrence in which the arm reached maximum extension or
flexion, the switch was engaged resulting in sounding of a buzzer and activation of a flashing green light (Figure 3.3b) to indicate the full range of motion was successfully achieved. In all three participants, the affected side could not reach both switches during trials.

![Figure 3.3: Apparatus used for Task 2. a) Location of switch boxes (green tabs) to determine whether elbow flexion and extension movements took place through full range of motion. b) Position of the participant in the apparatus. Marker positions are visible throughout full range.](image)

### 3.3.4.3 Task 3 – Shoulder motion

Participants performed five cycles of active shoulder horizontal abduction and flexion. When in the starting position, the forearm was rested on the desk on the desk. Participants were required to raise the arm and land it on top of a 15cm high box 5 times. The box was positioned on the side of the desk. The shoulder was positioned in neutral and the forearm was flat on the desk with palm down. This task was adapted from the Wolf Motor Function Test (raising the forearm from a lower surface to surface raised by 6 inches)\textsuperscript{163}. In this task, the table was raised to navel height and the participant’s elbow resting on the table was flexed at 90 degrees with the participant’s hips parallel to the table. Two switches were mounted to the lower surface and two more on the top surface (Figure 3.4a). The participants were instructed to complete the
movement such that they depressed both switches momentarily on both the bottom and top surfaces. A buzzer sounded to indicate a successful movement was achieved with both the proximal and distal ends of the forearm making contact with both the top and bottom surfaces and the hips were parallel to the desk. (Figure 3.4b).

Figure 3.4: Apparatus used for data collection in Task 3. a) Switches positioned on each box (green tabs) were used to determine a movement cycle (start and end of movement). b) Diagram showing positioning of a participant in the apparatus. Markers were visible throughout the movement.

3.3.5 Measuring kinematics

3.3.5.1 Task 1 – Wrist motion

The marker configuration is shown in Figure 3.5a, where $\mathbf{E}_A$, $\mathbf{E}_B$ are elbow markers, $\mathbf{W}_A$, $\mathbf{W}_B$ are wrist markers, and $\mathbf{D}_2$, $\mathbf{D}_5$ are digit markers (at the knuckle of the 2nd and 5th metacarpal, respectively).

To measure the angle of wrist flexion/extension, a rotation axis is defined using wrist markers $\mathbf{W}_A$ and $\mathbf{W}_B$ and two rigid bodies – the forearm and the hand – are defined that share this rotation axis. Figure 3.5b illustrates the system with the forearm defined by three points ($\mathbf{E}_A$, $\mathbf{W}_A$ and $\mathbf{W}_B$) and the hand defined by three points ($\mathbf{D}_2$, $\mathbf{W}_A$ and $\mathbf{W}_B$).
The angle of wrist flexion/extension can then be computed as the angle between the forearm and hand planes. While some markers are not directly used in the computation, they are necessary for the motion capture system to achieve good accuracy. A full description of computations can be found in the Appendix.

![Figure 3.5: Task 1 kinematic landmark: a) marker configuration at elbow, wrist and fingers; b) measuring the motion angle in Task 1 through two forearm and hand planes.](image)

### 3.3.5.2 Task 2 – Elbow motion

Elbow flexion/extension is tracked using 4 markers, as shown in figure 3.6a. The upper arm is defined by shoulder marker $\mathbf{S}$ and elbow marker $\mathbf{E}_A$, while the forearm is defined by elbow marker $\mathbf{E}_A$ and wrist marker $\mathbf{W}_A$ (see Figure 3.6b). The angle of elbow flexion/extension is computed as the angle between the upper arm and forearm. Please consult the Appendix for detailed calculations.
Figure 3.6: Task 2 motion analysis: a) location of each of the markers and the expected range of motion and trajectory during the elbow flexion/extension movements, b) the motion angle between upper arm and forearm.

3.3.5.3 Task 3 – Shoulder motion

Task 3 evaluates the motion of the shoulder joint (Figure 3.7). The displacement of the elbow marker (Ea) and shoulder marker \( \bar{s} \) are tracked over time. The elbow movement is computed relative to the shoulder marker position.
3.3.6 Outcome measures

A selection of outcome measures were calculated for each task, based on the kinematic data described above. It was expected that compared to the unaffected side, the affected side would have less AROM and speed and displacement, but more compensatory trunk movements.

*AROM (degrees) (task 1 and 2):*

The difference between the maximum and minimum joint angles

*Maximum speed of flexion and maximum speed of extension (degrees/s) (all tasks):*

The highest rate of joint flexion and extension observed in a trial; the average speed of movement, combining both flexion and extension.

*Distance traveled (mm) (task 3):*
A measure of the distance that the elbow marker travels (with respect to the shoulder marker) in each direction.

Compensatory Trunk movement: Root Mean Square of contralateral shoulder motion (mm) (all tasks):

It is expected that if a participant is using their trunk to compensate for restricted movement in the upper body, it will manifest as a twisting of the torso, and can be detected in shoulder motion. The amount of trunk compensation is quantified by considering shoulder motion as lying within a 3D volume. To determine the size of this volume, principal component analysis is applied to the shoulder motion trajectory to compute the three principal components of the motion, similar to fitting an ellipsoid. Instead of using volume, which would be small if one of the principal components has a small magnitude, the metric for trunk compensation is computed as the root-mean-square (RMS) of the three principal components, and is used for both contralateral and ipsilateral shoulder markers.

\[
RMS_{shoulder\ motion} = \sqrt{\frac{1}{3} (S_{h_x}^2 + S_{h_y}^2 + S_{h_z}^2)}
\]

where \( S_{h_x} \), \( S_{h_y} \), and \( S_{h_z} \) are the three principal components of the shoulder marker motion.

3.4 Results

Given the locations of markers tracked using the motion capture system, signals were extracted to describe the characteristic motions for each task. Examples of these signals are shown in Figure 3.8 for both the unaffected and affected limb. This motion is
described by the joint angle of the wrist and the elbow for tasks 1 and 2 respectively. For task 3, the vertical motion of the elbow is indicative of the motion of interest. These signals provide insight regarding the types of kinematic variables that can differentiate between the unaffected and affected sides. For example, the differences in range of motion and velocity can qualitatively be observed. Using the kinematic variables chosen in KUSA, the magnitude of difference between motion of the unaffected and affected limbs can be quantified.

**Figure 3.8:** Single subject representation of movement trajectories for the three Tasks collected through KUSA.

Figure 3.9 shows a comparison between the unaffected and affected sides for the four kinematic variables measured in Task 1. For all three cases, wrist motion of the unaffected side had a higher AROM and speed, and lower trunk compensation.
Figure 3.9: A comparison between the unaffected and affected sides for the three kinematic variables measured in Task 1: (a) Active range of motion, (b) Speed, (c) Trunk compensatory movement. The affected side is the lighter and the unaffected is the darker shades.

Kinematic variables measured during Task 2 are shown in Figure 3.10. The unaffected elbow motion consistently had a higher AROM and speed than the affected elbow motion. Higher trunk compensation was found in the affected side for Cases 2 and 3 but not Case 1.

Figure 3.10: A comparison between the unaffected and affected sides for the three kinematic variables measured in Task 2: Task 2 kinematic variables: (a) Active range of motion, (b) Speed, (c) Compensatory trunk movement. The affected side is in lighter and the unaffected is darker shades.
The kinematic variables measured during Task 3 (shoulder motion) are shown in Figure 3.11. Higher speed and lower trunk compensation were observed in the unaffected side compared to the affected side in all three cases. However, the distance travelled by the elbow yielded different results for different cases.

![Figure 3.11: A comparison between the unaffected and affected sides for the four kinematic variables measured in Task 3: Task 3 kinematic variables: (a) Active range of motion, (b) Speed, (c) Trunk compensatory movement. The affected side is in lighter and the unaffected is darker shades.]

3.5 Discussion

The results suggest that KUSA was able to differentiate between the unaffected and affected side with the exception of two instances: trunk compensation for Case 1 elbow motion (Task 2) and distance traveled for Case 3 shoulder motion (Task 3). For task 2, Case 1, the participant suffered from multiple comorbidities including chronic obstructive pulmonary disorder, which may have increased fatigue during the task, resulting in similar amounts of trunk compensation for both the unaffected and affected
sides. For Task 3, Case 3 had pectoral muscle tightness that may have contributed to shoulder joint movement.

The kinematic variables measured by KUSA provide an objective evaluation of upper limb motion and more detailed information than clinical measures alone. While MAS and CMSA are useful as coarse measures of impairment and motor recovery, they ignore the unique presentations of motor symptoms in different individuals. MAS is rated based on resistance to passive stretching, while CMSA staging is based on the ability to perform specific tasks relevant to motor recovery. KUSA seeks to supplement existing clinical measures by building a richer language for description and comparison of movement profiles. While there are intuitive expectations of movement kinematics with respect to motor recovery and consequently, the clinical measures, KUSA has revealed interesting results that warrant further examination.

3.5.1 The relationship between clinical and kinematic measures

In this study, the relationship between clinical and kinematic measures was not consistent. This could be attributed to the type of tasks included in the KUSA and/or type of clinical measures such as composite MAS rather than the MAS of the task specific joint in isolation. However, it should be noted that Task 3 movement was based on shoulder and upper arm muscles movements (i.e. shoulder flexors, abductors) rather than single isolated joint.

Active range of motion corresponded with MAS and CMSA\textsubscript{hand} in Task 1. Case 1 with the mild spasticity (MAS=8) and higher motor recovery stage (CMSA\textsubscript{hand} =4) had the higher AROM at wrist joint compared to the other Cases. Interestingly, based on the clinical measures, it would be expected that Case 3 with higher level of motor recovery
(CMSAarm=4) and moderate spasticity (MAS=7) should have had higher AROM during Task 2 and/or 3 compared to other two Cases. This discrepancy could be due to generalized fatigue since the affected limb needed to travel a larger distance in Task 2 and 3 than Task 1. Also the impact of stroke on the trunk muscles could be a contributing factor in Task 3 movements which was not measured in this study.

Movement speed also corresponded with clinical measures during Task 1. Case 1 and 3 with mild spasticity (MAS=7-8) and higher motor recovery (CMSA\textsubscript{hand} = 3-4) also had higher speed in comparison to Case 2. Yet, the speed in Task 2 and 3 did not have congruity with clinical measures, It was expected Case 3 with lower spasticity (MAS=7) and higher motor recovery level (CMSA\textsubscript{arm} = 4) to have higher speed than Cases 1 and 2.

The compensatory trunk movement variable corresponded almost to the clinical measures. Case 2 with the higher level of spasticity (MAS=13) and lower motor recovery (CMSA\textsubscript{hand} and arm=2,3) had the highest compensatory trunk movement compared to Cases 1 and 3 except in Task 2, in which Case 3 had the least spasticity and higher motor recovery compared to the Cases 1 and 2. In general, the clinical and kinematic assessments coincided but there were inconstancies which require further studies by increasing the sample size and different kinematic and clinical measures.

3.5.2 Task 1 – Wrist motion

Cases 1 and 3 had a higher AROM and speed compared to Case 2, which was consistent with the clinical assessment, since Cases 1 and 3 were at a higher stage of hand motor recovery (higher CMSA\textsubscript{hand}) and had lower spasticity (lower MAS). The low speed in Case 2 is corroborated by CMSA\textsubscript{hand} stage 2, for which the patient has no
volitional movement in the hand. Case 2 also exhibited most compensatory trunk movement, which is supported by higher spasticity scores and lower motor recovery. In contrast to clinical measures, KUSA determined that Case 3 had faster movement speed than Case 1, which was surprising considering Case 1 was CMSA_hand stage 4, while Case 3 was CMSA_hand stage 3. This poses an interesting question regarding the sensitivity and interpretation of the CMSA. As the CMSA has a total of 7 stages (where 7 represents normal motion), it should be noted that both CMSA stage 3 and 4 are still significantly impaired. While CMSA_hand assesses the ability to perform certain tasks (including wrist flexion and extension), the speed of task completion is not explicitly evaluated. This contradicts the assumption that smoothness improves with motor recovery. A similar observation was made by Rohrer et al. (2002), where they cautioned it cannot be assumed that less smooth movements are necessarily more impaired or less skilled.\textsuperscript{164}

3.5.3 Task 2 – Elbow motion

Although Case 3 had the highest CMSA_arm (stage 4) and lowest spasticity (composite MAS of 7), their elbow motion had a lower AROM and speed and higher trunk compensatory motion compared to Cases 1 and 2 (both CMSA_arm stage 3). The inconsistencies with regards to trunk compensatory motion could indicate that trunk compensation may not be a key determining factor in clinical measures. In CMSA, trunk compensation is not explicitly mentioned in the impairment inventory until stages 4 and higher. Therefore, in earlier stages of stroke recovery as defined by CMSA, less emphasis may be placed on reducing trunk compensation. Rehabilitation strategies
could be improved by incorporating kinematic analysis that measures the magnitude of compensatory mechanisms.

3.5.4 Task 3 – Shoulder motion

Even though Cases 1 and 2 had equal CMSA\textsubscript{arm} stages, KUSA results showed differences between distance traveled and trunk compensation while performing shoulder motion. However, in the remaining two kinematic variables (speed and trunk compensation), Case 1 had the best performance. This lends further evidence to the idea that clinical measures are missing valuable information by adopting a one size fits all approach. KUSA can support existing practices by using objective measurements to interpret movement patterns and inform tailoring of rehabilitation regimens to specific patient needs.

3.6 Conclusion

The KUSA was able to differentiate between unaffected and affected sides and the results generally were agreed with clinical measures. This system provided more detailed information on the patient’s functional changes after intervention in the upper limb as supplementary to the traditional clinical measures.

3.7 Limitations

As this study represents a case series of the KUSA, it is not possible to draw any conclusions about its generalizability to a larger population. In addition, a single clinician performed the clinical assessments; therefore, results may be influenced by clinician experience and familiarity with the system. The KUSA also requires
sophisticated motion capture equipment, which would be prohibitively expensive outside of a clinical environment.

3.8 Future directions

While the kinematic variables gathered by KUSA have the potential to improve stroke rehabilitation, further studies must be conducted to understand their clinical relevance and impact on functional outcomes. Larger samples of both patients and clinicians will be gathered to determine if KUSA has the ability to distinguish between pathological and healthy motion patterns. Testing with more clinicians will ensure the system generates reproducible results. Consumer grade motion capture solutions, such as the Microsoft Kinect, will also be explored. Their relatively low cost would improve clinical availability of kinematic assessments.
Chapter 4: Examining the impact of Botulinum toxin A (BoNTA) combined with rehabilitation on upper limb function after stroke

Eftekhar P., Li M., Dutta T., Richardson D., Brooks D., Mochizuki G. Examining the Impact of Botulinum toxin A (BoNTA) combined with rehabilitation on upper limb function after stroke. Topics in Stroke Rehabilitation (in progress).
4.1 Abstract

**Background:** Spasticity negatively impacts upper limb function and quality of life after stroke. Botulinum toxin A one intervention is used to manage spasticity.

**Objectives:** To compare the effect of upper limb rehabilitation to BoNTA combined with upper limb rehabilitation on upper limb function.

**Methods:** Eleven post-stroke patients (56.2±18.5 years) were recruited. Using a pre-post pilot study design, the impact of upper limb rehabilitation only, followed by upper limb rehabilitation combined with BoNTA were examined. Outcome measures during the “Rehab phase” were captured at baseline (M0), at one month (M1), and three months (M3). At the end of M3, BoNTA was injected by the physicians and the M3 measurements were considered as baseline for the “Rehab + BoNTA phase”. Assessments at four months (M4) and six months (M6) measured the combined effects of BoNTA and rehabilitation. Both clinical and kinematic measures were used to measure changes. Clinical measures included the modified Ashworth scale (MAS), Chedoke McMaster Stroke Assessment (CMSA) of arm and hand, Goal Attainment Scale (GAS), and the Chedoke Arm and Hand Activity Inventory version 9 (CAHAI9). Kinematic measures included active range of motion, number of velocity peaks, speed, and trunk compensatory movement accompanied to improve the sensitivity of measurements.

**Results:** Statistically significant improvements were found in the MAS (p < 0.0001) and CAHAI (p = 0.05). The changes in kinematic variables were not statistically significant.
However, there was a trend of improvement in all kinematic variables in the subjects who achieved CMSA\textsubscript{hand or arm} of 4 or higher at any point in time during the study.

**Conclusion:** This study indicated that combination of BoNTA with upper limb rehabilitation is more beneficial in patients with higher stages of motor recovery at baseline in the upper limb after stroke.

**Keywords:** clinical assessments, kinematic analysis, stroke, spasticity, upper limb
4.2 Introduction

Spasticity is a common consequence of stroke, with a prevalence of 38% within the first year\textsuperscript{143}. One of the main features of spasticity is an increased excitability of the stretch reflex\textsuperscript{69}, but it has also been characterized as altered sensori-motor control, featuring involuntary activation of muscles\textsuperscript{165}. The view that spasticity represents a change in motor control implies that there is a negative impact on function, which subsequently contributes to the extent of disability\textsuperscript{130}. In turn, a tailored treatment plan with goal-directed rehabilitation may increase function and reduce the extent of disability.

Rehabilitation approaches that have been used to manage spasticity include splinting, casting, stretching and constraint induced movement therapy (CIMT); however, the impact of these interventions is temporary and do not persist over time\textsuperscript{166,167}. In people with mild hemiparesis and slight spasticity, activity-based rehabilitation such as CIMT has been effective\textsuperscript{168}. In severe cases, administration of botulinum toxin A (BoNTA) has been used focally to effectively reduce spasticity\textsuperscript{129,169,170} by blocking the release of acetylcholine, which raises the threshold of the stretch reflex and diminishes the sensitivity of the muscle spindles.

In the international consensus statement for best practice guidelines for spasticity management, it is recommended that the use of BoNTA should be coupled with comprehensive rehabilitation services\textsuperscript{171}. Coupling approaches to concomitantly reduce spasticity and improve motor output is believed to have the added advantage of unmasking the active movement by lessening spasticity. However, the results of empirical studies examining the effect of combining BoNTA with upper limb
rehabilitation are mixed in terms of efficacy for improving motor function\textsuperscript{172}. A Cochrane review examining the effectiveness of multidisciplinary rehabilitation after BoNTA showed a low quality evidences for this approach\textsuperscript{173} and the authors in the study recommended further work in this area. In contrast, in a retrospective study, Hara et al. found an improvement in active arm function after BoNTA injection combined with multidisciplinary rehabilitation in an inpatient setting\textsuperscript{174,175}. The variability in findings reveal that there may be interplay of several factors that contribute to detection or realization of functional gains following intervention.

One of the potential factors that may contribute to the discrepancy in these findings is the approach used to assess efficacy. Recently, kinematic analysis has been used to assess the changes in movement characteristics after intervention which complements clinical measures by providing quantitative and objective information about the patterns and quality of movement\textsuperscript{43} that are common among individuals with upper limb spasticity\textsuperscript{176}. Such measures also reveal changes in movement patterns and strategies that occur during the recovery process\textsuperscript{162}.

Spasticity may cause pain, fatigue and limit active movement and participation in activities of daily living\textsuperscript{124,177}. As a result, the affected upper limb could experience limited active range of motion, slower and unsmooth movement which could lead to the development of compensatory trunk movements\textsuperscript{47}. Optimized motor function involves the movement of joints across a specific range to reach, grasp and release items with appropriate speed and coordination\textsuperscript{43,47,162}. Kinematic data could provide valuable information in conjunction with clinical assessments to patients/families and the
interdisciplinary team during the time course of rehabilitation to characterize the impact of interventions for spasticity management on motor output.

The goal of this study was to determine whether the differential effects of upper limb rehabilitation alone or in combination with focal BoNTA injections could be detected using kinematic outcomes. It was hypothesized that the combination of BoNTA and upper limb rehabilitation would improve arm function in individuals with spasticity after stroke compared to rehabilitation alone as identified by measures of active range of motion, movement velocity, and compensatory movement of the trunk.

4.3 Methods

4.3.1 Participants

Twelve participants were enrolled in the study. One participant dropped out of the study due to geographic relocation. Thus, a total of 11 post-stroke patients (> 18 years) were recruited and enrolled from the outpatient spasticity management clinic at Toronto Rehabilitation Institute over a three year period (2014-2016). Patients were eligible to participate if they were candidates for BoNTA injection in their elbow, wrist, and/or finger flexors (defined as a Modified Ashworth Scale score (MAS) ≥ 1+ in any of the muscles of elbow, wrist and fingers), assessed as having a Chedoke McMaster Stroke Assessment (CMSA) hand or arm score ≥ 2, and were naive to BoNTA at the time of recruitment. Individuals with joint deformities and contractures, cognitive impairments, or an inability to follow instructions were excluded from the study. This study was approved by the Research Ethics Board and written consent was obtained from the participants.
4.3.2 Study design

A pre-post study design was employed to examine the impact of upper limb rehabilitation only (Rehab phase), followed by upper limb rehabilitation combined with BoNTA (Rehab +BoNTA phase). The within-person design of the study was used given the difficulty of comparing the effect of BoNTA between groups and the heterogeneity in individuals with spasticity after stroke. Assessments were conducted at multiple time points during the interventions. During the Rehab phase, assessments were performed at baseline (M0), at one month (M1), and three months (M3). At the end of M3, BoNTA was injected by the physicians and the M3 measurements were considered as baseline for the Rehab+BoNTA phase. Subsequently, assessments were conducted at four months (M4) and six months (M6) (Figure 1).

4.3.3 Intervention

In the Rehab phase, participants received conventional therapy for spastic upper limb hemiparesis from an occupational therapist twice a week, one hour each session for 3 months. This included therapies such as splinting, casting, stretching, Functional Electrical Stimulation, Neuro Developmental Therapy, modified Constraint Induced Movement Therapy (mCIMT), repetitive task training, strengthening exercises, and pain and swelling management\textsuperscript{77,81,93,178,179}. In the Rehab+BoNTA phase, participants received focal injections of BoNTA (either BOTOX\textsuperscript{®} or Xeomin\textsuperscript{®}) of a maximum of 620 units in the elbow, wrist and/or finger flexors. Following injection, participants received the same type of rehabilitation as in the Rehab phase twice a week for 3 months. The intensity and type of therapeutic interventions were monitored in both phases through documentation and physicians’, patients’ and their family
members' feedback. The intensity of the intervention was progressed as tolerated by the patients.

4.3.4 Outcome measurements

Outcome measures of interest comprised domains of the International Classification of Function (ICF) model\textsuperscript{180}. Specifically, the following clinical measures were considered: MAS, of the arm and hand (impairment level), and the Chedoke Arm and Hand Activity Inventory version 9 (CAHAI) (activity level)\textsuperscript{26,130,181}. The Goal Attainment Scale (GAS) (participation level) was also administered. Kinematic measures including active range of motion speed, and compensatory trunk movement were collected to improve the sensitivity of measurements (activity level).

\textbf{Figure 4.1:} The study timeline: Rehab phase (M0-M3); Rehab +BoNTA phase (M3-M6). BoNTA was introduced at the end of M3. M3 served as baseline for the Rehab+BoNTA phase.
4.3.5 Data collection

4.3.5.1 Clinical measures

The clinical measures (MAS, CMSA arm and hand, CAHAIs, and GAS) were collected at each of the five assessment time points. The clinical assessments were completed in a seated position at the same time of day and location for each time point.

4.3.5.2 Kinematic measures

Kinematic data were collected using a novel protocol: Kinematic Upper-Limb Spasticity Assessment (KUSA) (Eftekhar et al. under review)\textsuperscript{182}. Briefly, this protocol involved 2 tasks (wrist flexion/extension and elbow flexion/extension) that were performed with both the affected and less affected limb. For Task 1 (wrist), the participant started with the wrist in neutral. In participants for whom neutral position of the wrist could not be achieved, the fixed position of the wrist was taken as ‘neutral’ (i.e. position 0 for the purpose of quantifying movements speed described below). For Task 2 (elbow), the starting point was the elbow on the midline in extended position.

The limb segment proximal to the joint being assessed was secured to the table with a large Velcro strap to reduce compensatory movements. Participants were instructed to perform five repetitions of each movement at a self-selected speed while sitting at a table. A switch positioned at the end of the range of motion identified the end of the target range. A custom fabricated low-friction panel that housed the straps and switch were mounted to the table. Reflective markers (12mm diameter) were placed onto both upper limbs at the following locations: second and fifth metacarpophalangeal, the styloid process of the radius and ulna, the lateral and medial epicondyle, the acromion process, and a cluster of three markers on the chest (5cm above the xiphoid
process of sternum). Vicon motion capture cameras (Centennial, Co) were used to collect kinematic data. Figure 4.2 illustrates the apparatus and marker location for Task 1 (wrist flexion and extension). The detailed information about the location of markers in each task was presented previously (Eftekhar et al. under review)\textsuperscript{182}.

![Figure 4.2: Marker location and participant positioning for Task 1. The forearm is secured to the table. A contact switch provides feedback about movement of the arm away from its intended position during movements of the hand.](image)

4.3.6 Data analysis
4.3.6.1 Kinematic measures

The kinematic variables were chosen based on their representation of movements during performance of the tasks and are consistent with those previously used in other studies examining biomechanical outcomes as indicators of recovery\textsuperscript{43,45-47,162,183}. Three variables were selected to measure the impact of interventions:

- **Active Range of Motion (AROM) (degrees)** measured as the total range between full extension and flexion of wrist and elbow joints from the midline (marked on the testing surface) for Tasks 1 and 2, respectively. This variable was reported as the average across five repetitions.

- **Speed (degrees/s)** was the speed of joint movement in flexion and extension, averaged across five repetitions for Tasks 1 and 2.
Compensatory trunk movement (mm) was computed based on the average distance the contralateral shoulder marker moved away from the midline, during performing each task for five times.

4.3.7 Statistical analysis

All statistical analyses were performed using SAS 9.3 (Statistical Analysis Software, version 9.3 for Windows). Descriptive statistics were used to characterize study outcomes. The analysis comprised of five clinical outcome variables (MAS, CMSA<sub>arm</sub>, and CMSA<sub>hand</sub>, CAHAI<sub>9</sub>, and GAS) and three kinematic variables (active range of motion, speed, and compensatory trunk movement). A MAS score of 1+ was interpreted as a score of 2. Normality and homogeneity of variance of the data were determined using the Shapiro–Wilk test and variance homogeneity test, respectively. Graphical analyses were also used, which included box plots of residuals, histogram of residuals, and normal probability plot of residuals.

To test the primary hypothesis that the combination of BoNTA and upper limb rehabilitation would improve arm function in individuals with spasticity after stroke compared to rehabilitation alone, a one way repeated-measures analysis of variance (ANOVA) was used to identify differences in the change in outcome measures across all time points in the kinematic outcomes and composite MAS and CAHAI<sub>9</sub>. ANOVA was also used to test contrasts between baseline and trough time points across the two phases (M3-M0 and M6-M3). A Proportional odds model was used to examine differences in GAS (categorical variable), CMSA<sub>arm</sub>, and CMSA<sub>hand</sub> across time points and in the specific contrast described above. For all analyses, p≤0.05 was considered as statistically significant.
4.4 Results

A total of 11 patients (4 females, 56.2±18.5 years) participated in this study. Six participants had left-sided hemiplegia. Two participants had hemorrhagic stroke. On average, the entire cohort was in the chronic stage of recovery (3.5 ±1.36 years post stroke) and the majority (82%) had ischemic stroke. The median (range) of CMSA<sub>arm</sub> and CMSA<sub>hand</sub> scores at baseline were 3(2-4) and 2(2-4), respectively. Details regarding this measure for arm and hand across five time points are presented in Table 4.1.

<table>
<thead>
<tr>
<th></th>
<th>M0</th>
<th>M1</th>
<th>M3</th>
<th>M4</th>
<th>M6</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMSA&lt;sub&gt;arm&lt;/sub&gt; median (range)</td>
<td>3(2-4)</td>
<td>3(2-4)</td>
<td>3(2-4)</td>
<td>3(2-5)</td>
<td>3(2-5)</td>
</tr>
<tr>
<td>CMSA&lt;sub&gt;hand&lt;/sub&gt; median (range)</td>
<td>2(2-4)</td>
<td>2(2-4)</td>
<td>2(2-4)</td>
<td>2(2-4)</td>
<td>2(2-4)</td>
</tr>
</tbody>
</table>

Details regarding the administration of BoNTA are presented in Table 4.2. Doses ranged from 200-620 units. Across all participants, no fewer than 2 muscles were injected and no fewer than 3 total injection sites were used.
<table>
<thead>
<tr>
<th>Participant</th>
<th>Targeted muscles and sites</th>
<th>Dose (units)</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pronator teres (2 sites), brachialis (2 sites), Biceps brachii (2 sites), Flexor Carpi Radialis (FCR) (2 sites), Flexor Carpi Ulnaris (FCU) (2 sites)</td>
<td>500</td>
<td>BOTOX</td>
</tr>
<tr>
<td>2</td>
<td>Brachialis (2 sites), Brachioradialis (2 sites), Biceps brachialis (2 sites), Pronators teres (2 sites), FCR (2 sites), FCU (2 sites)</td>
<td>560</td>
<td>BOTOX</td>
</tr>
<tr>
<td>3</td>
<td>Brachialis (2 sites), Brachioradialis (2 sites), FCR (2 sites), FCU (1 site), Pronator teres (2 sites), FDS (2 sites), FDP (2 sites)</td>
<td>620</td>
<td>BOTOX</td>
</tr>
<tr>
<td>4</td>
<td>FDS (2 sites), FDP (1 site)</td>
<td>200</td>
<td>BOTOX</td>
</tr>
<tr>
<td>5</td>
<td>Biceps Brachial (2 sites), Brachialis (2 sites), lumbricals (4 sites), Brachialis (2 sites), Brachioradialis (2 sites), Biceps (1 site), pronator teres (2 sites), FDS (1 site), FCR (1 site)</td>
<td>300</td>
<td>BOTOX</td>
</tr>
<tr>
<td>6</td>
<td>Brachialis (2 sites), Brachioradialis (2 sites), Biceps (1 site), pronator teres (2 sites), FDS (1 site), FCR (1 site)</td>
<td>400</td>
<td>Xeomin</td>
</tr>
<tr>
<td>7</td>
<td>Triceps (2 sites), FDS (4 sites), FDP (4 sites)</td>
<td>500</td>
<td>BOTOX</td>
</tr>
<tr>
<td>8</td>
<td>Brachialis(2 sites), FCR (2 sites) FCU (2 sites), FDS (4 sites), FDP (4 sites)</td>
<td>560</td>
<td>BOTOX</td>
</tr>
<tr>
<td>9</td>
<td>Brachialis (2 sites), brachioradialis (2 sites)</td>
<td>200</td>
<td>BOTOX</td>
</tr>
<tr>
<td>10</td>
<td>FDS (2 sites), FDP (2 sites)</td>
<td>400</td>
<td>BOTOX</td>
</tr>
<tr>
<td>11</td>
<td>Brachialis (2 sites), FCR (2 sites), FCU (2 sites), FDS (4 sites), lumbricals (4 sites)</td>
<td>600</td>
<td>BOTOX</td>
</tr>
</tbody>
</table>
4.4.1 Clinical measures

The mean composite MAS scores are presented in Figure 3a. Analysis of the change in composite MAS scores identified a significant main effect of time ($F(4, 40) = 79.06, p<.0001$). The change in composite MAS at M3-M0 and M6-M3 was $-0.3\pm 0.9$ and $-6.8\pm 2.9$ points respectively. The contrasts comparing the change in composite MAS between phases also identified a statistically significant difference in the extent of change between phases ($F(1, 40) = 33.91, p<.0001$). Similarly, the CAHAI$_9$ scores were determined to have changed significantly over time ($F(4, 40) = 5.53, p=.001$). The change in CAHAI$_9$ was significantly greater ($F(1, 40) = 3.92, p = 0.05$) between M6-M3 (6.3 ± 8.3) in comparison to the change between M3-M0 (0.3 ± 2.2).

In contrast to MAS and CAHAI$_9$, proportional odds analysis determined that while the GAS changed significantly over time ($F(4, 104) = 4.54, p = 0.002$), the change in GAS within each phase did not differ ($F(1, 104) = 0.00, p = 0.98$). From a total of 22 goals (two per patient) set during the Rehab phase, 19 goals were not achieved, and 3 goals were achieved, and 0 goals were overachieved. In the Rehab+BoNTA phase, 6 goals were not achieved, 12 goals were achieved, and 4 goals were overachieved. In addition, neither CMSA$_{arm}$ ($F(4, 38) = 1.73, p = 0.16$), nor CMSA$_{hand}$ ($F(4, 39) = 0.97, p = 0.43$) changed significantly over time. Change scores for CMSA$_{arm}$ ($F(1, 38) = 0.91, p= 0.34$) and CMSA$_{hand}$ ($F(1, 39) = 0.88, p = 0.35$) were not significantly different between phases.
Figure 4.3: Clinical measures: A) CAHAI\textsubscript{9} at five data points with mean± SD; B) Composite MAS at five data points in five joints of hand and forearm (total of 25); BoNTA was injected at the end of M3 data point. Different shapes represent different patients.

4.4.2 Kinematic measures

4.4.2.1 Task 1 (T1)

Across all participants, the mean AROM ranged from 33.1±11.7 to 35.2 ± 10.6 degrees across all time points (Figure 4.4a). The difference across all visits for AROM was not statistically significant (F (4, 40) = 0.79, p = 0.54). Contrast analysis revealed that the change in AROM between M3-M0 and M6-M3 was not statistically significant (F (1, 40) = 2.32, p = 0.13). There was no main of effect of time for movement speed (F (4, 40) = 1.34, p = 0.27), nor was there a statistically significant difference in the change in movement speed between M3-M0 and M6-M3 (F (1, 40) = 0.53, p = 0.46; Figure 4.4b). There was no statistically significant main effect of time (F (4, 40) = 0.31, p = 0.87) for compensatory trunk movement (Figure 4 4c). The difference in the change in
compensatory trunk movement between phases was also not statistically significant ($F(1, 40) = 0.03, p = 0.87$).

4.4.2.2 Task 2 (T2)

Statistical analysis of the kinematic parameters for Task 2 demonstrated similar outcomes as Task 1 in that there were no statistically significant main effects of time on AROM ($F(4, 40) = 0.76, p=0.55$), movement speed ($F(4, 40) = 1.93, p = 0.12$), or compensatory movement ($F(4, 40) = 0.08, p = 0.98$). In addition, analysis of the contrasts between phases (M3-M0 and M6-M3) demonstrated an absence of a statistically significant difference in the change in AROM, speed, and compensatory movement ($F(1, 40) = 0.09, p = 0.76$, $F(1, 40) = 1.92, p = 0.17$, $F(1, 40) = 0.14, p = 0.71$, respectively). Data for Task 2 are presented in Figure 4.4 d-f.
Figure 4.4: Kinematic measures at five data points for Task 1 and 2. A) Task 1- Active Range of Motion; B) Task 1- Speed; C) Task 1- compensatory trunk movement; D) Task 2- Active Range of Motion; E) Task 2-Speed; F) Task 2- Compensatory trunk movement. Solid lines are indicators of mean ± SE and the vertical lines at M3 are indicators of BoNTA injections at the end of M3. Each dotted line represents a different patient.

4.4.3 Secondary analysis

A closer examination of the characteristics of the study cohort revealed a dichotomy with regard to level of impairment. One subset achieved CMSA_{hand or arm} ≥ 4 in at least 1 of the assessments. The other subset never achieved CMSA_{hand or arm} of 4 at any assessment (i.e. they were CMSA ≤ 3 at all-time points). This threshold for separating the data was based on examination of the change in the kinematic and clinical data at different time points, informed by stages of motor recovery of the Chedoke McMaster Stroke Assessment Impairment Inventory, in which Stage 4 is defined as ‘diminished spasticity synergies can be reversed’\textsuperscript{130}. In addition, based on the published and clinical evidence that a change in active function of the arm in individuals with spasticity was observed only in patients with CMSA_{hand} ≥ 4\textsuperscript{106}. Descriptive information of the subgroups is presented in Table 4.3.
Given the small and uneven sample size that existed following the categorization of the data, quantitative statistical analysis was not performed. Figure 4.5 (A-F) shows the differences in kinematic outcomes between subgroups over all time points in both Tasks 1 and 2. These measures indicated a tendency for improvement in kinematic outcomes in the high function group during the Rehab+BoNTA phase. In the low function group, there were no apparent changes in any of the kinematic measures during the two phases.

Table 4.3. Demographic and clinical characteristics of the high and low function subgroups: the subgroup with CMSA ≥ 4 at any time point during the study and another subgroup with CMSA ≤ 3 across all time points.

<table>
<thead>
<tr>
<th></th>
<th>High Function CMSA ≥ 4 (n=4)</th>
<th>Low function CMSA ≤ 3 (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>54.7(15.5)</td>
<td>58.7(21)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>4 M (100%)</td>
<td>3 M (43%)</td>
</tr>
<tr>
<td><strong>Time since stroke</strong></td>
<td>3.2 (1.5)</td>
<td>3.6 (1.2)</td>
</tr>
<tr>
<td><strong>Affected side of body</strong></td>
<td>3 Left</td>
<td>3 left</td>
</tr>
<tr>
<td><strong>Type of stroke</strong></td>
<td>100% ischemic</td>
<td>85% ischemic</td>
</tr>
<tr>
<td><strong>CMSA\text{\textsubscript{hand}}</strong></td>
<td>4 (3-4)</td>
<td>2 (2)</td>
</tr>
<tr>
<td><strong>CMSA\text{\textsubscript{arm}}</strong></td>
<td>4 (4-5)</td>
<td>3 (2-3)</td>
</tr>
</tbody>
</table>

Data are presented as counts or means (SD), except for CMSA, which is presented as median (range).
Figure 4.5: Kinematic measures at five data points for Task 1 (top panels) and Task 2 (bottom panels) in high and low function groups: A, D) Active range of motion; B, E) Movement speed C, F) Trunk compensatory movement. The solid vertical line at M3 denotes timing of administration of BoNTA. The black solid line depicts mean ± SE for the high function group and the dashed grey line illustrates the mean ± SE for the low function group.

4.5 Discussion

When comparing the effect of the combination of upper limb rehabilitation and BoNTA to upper limb rehabilitation alone, the combined neurotherapeutic approach led to improvements in two clinical outcomes: MAS (a measure of spasticity) and CAHAI (a
measure of upper limb function). In contrast to the hypothesis, improvement in upper limb function based on kinematic outcomes was not observed at a group level. Secondary analysis involving the separation of the data based on CMSA (impairment) revealed a dichotomized clustering of outcomes. Individuals with low to moderate levels of impairment tended to improve on kinematic outcomes in contrast to those individuals with high levels of impairment. In this study, patients with low levels of motor recovery were recruited as the objectives were to pragmatically examine the effectiveness of the intervention in a ‘real world’ clinical setting, rather than to examine the efficacy of the intervention under ‘ideal circumstances’.

4.5.1 Impairment vs functional changes

Of the two impairment-based outcome measures (MAS and CMSA) and two function-based assessments (CAHAI9 and GAS), only the MAS and CAHAI9 showed significant changes after the Rehab+BoNTA phase. The change in MAS was expected as other studies have demonstrated that BoNTA significantly reduces spasticity129,184, 185 and, while the relationship between MAS and kinematic outcomes was not included in this study, previous work demonstrates that a reduction in spasticity does not automatically imply an increase in function170. For example, reducing spasticity in patients with lower motor recovery may cause flaccidity of the limb rather than improving active movement and function186. In order to advance towards generating and controlling voluntary movements, reducing spasticity would not be adequate as the affected limb would be required to have a minimal level of recovery at baseline to maximize the potential benefits of activity-based upper limb rehabilitation (i.e. CIMT)187.
At a group level, the combination of Rehab+BoNTA did not significantly improve level of motor recovery, as indicated by the CMSA. While both measures are indicators of impairment, MAS is more likely to capture the chemodenervating effects of BoNTA given the focal nature of assessment and intervention. In contrast, CMSA measures the level of neurological impairment after an upper motor neuron lesion such as stroke by identifying the level of active, coordinated movement of the limb/segment of interest\textsuperscript{130}. Because a score at a given level is dependent on the performance of a number of tasks, it may be more difficult to quantify change based on a focal intervention.

The issue that remains to be resolved is whether the combination of Rehab+BoNTA improves function. Based on the GAS, the evidence indicates that the combination of therapies did not lead to statistically significant achievement of patient goals. It is possible that the patients selected goals that required higher levels of function and motor recovery. Because the majority of patients had high levels of motor impairment, their identified goals may have been overambitious. This view is supported by a previous retrospective study in which changes in GAS scores were significant after BoNTA in the upper limb only in patients with higher functional level\textsuperscript{112}. From this perspective, the present finding that CAHAI\textsubscript{9} demonstrated significant improvement could be interpreted as indicating that the improvement was driven by those individuals with a higher functional status. It is possible that in the high functioning patients, BoNTA effectively reduced spasticity. Their elevated functional status subsequently allowed them to optimally engage in therapy and maximize the potential benefit of the intervention in further improving function, which was reflected in the CAHAI\textsubscript{9}. 
4.5.2 The relationship between kinematic outcomes and motor recovery level

In contrast to the study hypotheses, the kinematic measures did not reveal improvements following Rehab+BoNTA. Prior work has demonstrated that kinematic outcomes (velocity and smoothness) do improve following the administration of BoNTA and rehabilitation in the absence of change in clinical outcomes (i.e. Action Research Arm Test (ARAT) and the Box and Blocks Test)\textsuperscript{45}. It should be noted that in the study by Bensmail and colleagues (2010), participants were relatively high functioning (mean ARAT score of 37.5/57) and the measures were taken after two cycles of BoNTA injections (in contrast to the present study in which only a single cycle of BoNTA was probed)\textsuperscript{45}. Two cycles of BoNTA injection may provide a longer period of recovery in high functioning patients by decreasing spasticity and strengthening weak antagonist muscles\textsuperscript{188-190}. Similarly, Fridman et al. also showed that in high functional patients after stroke (Functional Independence Measurement = 126 out of 126\textsuperscript{191} and Medical Research Council strength grading scale of ≥3+/5, indicating of fair muscle strength\textsuperscript{192}) improved in reaching, grasping and transporting an object and showed improvement in kinematic variables including movement time, peak velocity and distance\textsuperscript{46}. Differences in types of movements employed between the studies may have also contributed to the differences in study findings. In addition, the work by Bensmail et al. (2010) used a multi-joint reaching movement, whereas a single joint movement was chosen in the current study. Many studies examined reaching tasks which is a multi-joint task\textsuperscript{43,45,46,162}; however, since BoNTA is a focal treatment, examination of the effects of BoNTA on single joint movement would provide clear information on the impact of the intervention in a specific joint.
4.5.3 Effect of level of impairment on responsivity to therapy

Though not the primary question of the present study, one key observation was change in upper limb function occurred in individuals with a lower level of impairment in arm and hand. This important finding reinforces work that has been previously published. Similar to this study, Chang et al. (2009) showed that in clinical practice, BoNTA combined with upper limb rehabilitation improves upper limb function of individuals with less baseline hand impairment\(^{106}\). They classified CMSA hand 2 and 3 as low and CMSA stages 4 and 5 as higher functioning groups and they suggested that greater functional gain is expected to occur in individuals with less baseline impairment in the clinical settings. The results of Fridman et al. (2010) also show that the combination of BoNTA with upper limb rehabilitation significantly improved peak velocity, distance and movement time in post stroke individuals who were younger (53.7 years) and able to independently complete the three tasks of reaching, grasping and transporting phases\(^{46}\). Patients who were CMSA= stage 4 or higher have a better potential and capacity to engage, recover and benefit from therapy\(^{106}\). In addition, evidence indicating functional improvement in individuals with less impairment led to the suggestion that offering intensive upper limb rehabilitation to patients with severe impairment and low motor recovery in rehabilitation settings is not encouraged because the chance of improvement is low\(^{193}\). Taken together, the results of the current study aligns with previous work in support of the view that intensive rehabilitation should be provided to patients with higher motor recovery, while those with lower levels of recovery should continue to be monitored. The purpose of continued monitoring would facilitate prevention of the development of contracture and further deterioration of joint mobility and to identify changes in functional status which may indicate that patient may
benefit from a BoNTA and rehabilitation intervention. Ultimately, this approach could inform best practice guidelines for the clinicians and interdisciplinary team in stroke and acquired brain injury programs and also support decision making at the program management level in regards to cost effectiveness of rehabilitation services.

4.6 Limitations

The small sample size limits the generalizability of the study results. Furthermore, this study lacked blinding and treatment control groups which may cause bias in the results. Patients were not homogeneous from a motor recovery point of view and different muscle groups in the upper limb were targeted; therefore, muscles and dosing were not standardized across patients. However, it would be very difficult to find homogenous patient with same pattern of spasticity. A further study with a larger sample size, blind assessor, different kinematic variables and multi-site randomized design is required.

4.7 Conclusion

The combination of BoNTA with upper limb rehabilitation failed to show improvement in kinematic outcomes; however, there were changes in clinical outcomes of function and spasticity. The kinematic measures identified changes in function in individuals with a low level of upper limb impairment. These findings suggest that the Rehab+BoNTA may lead to greater improvements in upper limb function in a higher functioning group than a lower functioning group of individuals post stroke.

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Chapter 5: General Discussion and Conclusion

5.1 Summary of Findings

This dissertation aimed to examine the impact of BoNTA combined with rehabilitation on upper limb movement in individuals with spasticity after stroke. To achieve this goal, three studies were completed. Study 1 used the Goal Attainment Scale (GAS) to characterize the types of goals identified in patients with upper limb spasticity who received BoNTA as desired outcomes of neurorehabilitation interventions. The identified goals were mapped to the ICF model with the aim of facilitating a common language amongst members of the interdisciplinary spasticity management team. We examined the goals selected by the patients, then identified two emergent categories: positioning and ADL/IADL. The results demonstrated that the spasticity level was significantly decreased at peak (after one month of BoNTA injection) in all participants. Individuals who were at lower stages of upper limb motor recovery selected limb-positioning goals (i.e. impairment based goals) as the most commonly desired outcome. Patients with higher motor recovery identified functional goals related to their daily life. These findings identify an approach for establishing outcomes to individualize a treatment plan.

Analysis of the identified goals in Study 1 revealed that many of the goals involved active and/or passive movement of wrist, elbow and shoulder joints. Building on these findings, a kinematic model (Kinematic Upper-Limb Spasticity Assessment, KUSA) was developed to objectively quantify the movement changes as wrist, elbow and shoulder movements after intervention. Study 2 enabled a quantitative and objective characterization of the features of movement that comprise basic upper limb
function. The KUSA model consisted of three functional tasks based on the identified goals in Study 1 and contained selected kinematic variables. Three patients recovering from stroke were recruited consecutively from an outpatient spasticity management clinic. Analysis of the kinematic outcomes indicated that the KUSA was able to distinguish between the affected and unaffected limbs and frequently agreed with clinical measures.

Study 3 involved application of the KUSA and clinical outcomes to measure the impact of BoNTA and upper limb rehabilitation on upper limb movement. From four clinical measures, only two measures, Modified Ashworth Scale (MAS) and Chedoke Arm and Hand Activity Inventory (CAHAI), demonstrated a statistically significant difference when combining BoNTA and rehabilitation, in comparison to using rehab alone. The selected kinematic outcomes did not differ between interventions; however, when the patients were grouped based on their stage of motor recovery stage (CMSA arm or hand ≥ 4 at any point during the study), a trend indicating the kinematic variables improved after Rehab + BoNTA was observed.

5.2 Integration of findings

Together, the individual chapters of this thesis advance knowledge of the effect of BoNTA and upper limb rehabilitation on function. This work is important because it quantified the effects spasticity management intervention based on individual patient goals, clinical outcomes, and quantitative measures. As such, it provides a multi-faceted view on the extent to which interventions for reducing spasticity impact function. Half of the patients who attended an outpatient spasticity management clinic identified their goals in the positioning category and the rest in the ADL and IADL groups. This
appeared to be related to their motor recovery stage. This view was reinforced by the observations in Studies 1 and 3 that patients with a lower motor recovery stage had less active functional movement (Study 3) and their goals were in the positioning category (Study 1). Both Studies 1 and 3 identified a decrease in spasticity after BoNTA; the change in MAS was significant in Study 1 at peak (one month after injection) and Study 3 at peak and three months after the injection. In Study 1, the most common multi-joint upper limb movements necessary to participate in ADL/IADL were identified and incorporated in Study 2 by developing the KUSA model. Based on those movements, the KUSA was comprised of three multi-joint functional tasks including: wrist and elbow extension/flexion and shoulder flexion/abduction. In Study 2, the KUSA distinguished between affected and unaffected sides through measuring the kinematic variables measured, which included: active range of motion, and speed, and the amount of compensatory trunk movement at baseline. In spite of this level of sensitivity, Study 3 revealed that it was the clinical measures, not the kinematic outcomes that identified change following intervention. However, patients with higher motor recovery demonstrated improvement in all kinematic variables as well as clinical measures. These findings indicate that goal-based, clinical, and kinematic outcomes can be effective in identifying responsivity to treatment, so long as there is sufficient functional capacity to begin with.

5.3 Characteristics of impairments and types of goals in patients with upper limb spasticity

The international consensus statement of managing spasticity using BoNTA has recommended that best practice should include setting and reviewing goals before and after injection to evaluate the impact of a BoNTA on the individual. The rehabilitation
team helps the patient and their families select goals and provide appropriate intervention. In Studies 1 and 3, GAS was used to identify and characterize whether goals were achieved following administration of BoNTA. The types of goals were closely examined in Study 1 with 87% achieving their goals and 13% overachieving. Interestingly, in two relevant BoNTA studies, the results were lower; with Notte et al. (2014) reporting that only 50% achieved their goals and Turner-Stokes et al. (2010) reporting that 4% overachieved. In consideration of the differences between the current study and those of Notte et al (2014) and Turner-Stokes et al. (2010), specifically in age, patient population, and type and dose of chemodenervating agent, it is clear that the impact of BoNTA on goals is very specific to the individual and the nature of their impairment. Indeed, regardless of the ways in which goals were examined (i.e. mapping goals to the ICF model and categorizing them as positioning (impairment-based) and ADL/IADL (functional)), individual goals could be identified. And, while there was sufficient overlap to advocate for goal banks, the importance of each goal to the individual cannot be overlooked.

5.4 Objective versus subjective measures

In order to measure changes after intervention, different types of assessments are used: 1) subjective measures, which are based on the examiner’s interpretation, and 2) objective assessments which rely on quantitative outcomes that describe the function. The objective assessments are assumed reliable, but subjective measures are typically assumed to be biased or unstable. There are advantages and disadvantages for each of them. In subjective measures, the examiner’s skill level may play a role in the concise utilization of an assessment and tend to be influence by clinical
impressions. The pros and cons of these features are evident: using the clinician’s expertise and experience in decision making, contrasted against the variability that the extent of experience may have on assessment. The advantages of these assessments include: ease of administering the tools, cost effectiveness and not requiring special training or equipment, and being less time consuming. Those tools are routinely clinical setting to assess and re-evaluate changes after interventions. However, the assessments are typically scored on nominal or ordinal scales, which could be less sensitive or less robust for statistical analysis.

In contrast, the objective measures are considered more precise, objective and less affected by the examiner’s skill and statistically more robust since their scores are interval/ratio levels. However, these are mostly lab-based assessments (i.e. in a research setting) and are less clinic-friendly and are more costly. Haas and Crow (1995) stated that objective measures such as the electromyogram, electrophysiological testing or isokinetic measures should be the yardstick to evaluate the subjective measures. However, studies have shown that the objective assessments do not always correlate with a particular clinical measure. Priebe et al. suggested that the lack of correlation between the kinematic and clinical measures was attributable to the fact that different clinical measures gauge various aspects of spasticity. In order to measure the changes in spasticity after intervention and its impact of function, both objective and subjective measures are recommended.

Because spasticity is not a single entity and it is multidimensional, procedures for assessing it should incorporate both objective and subjective measures in order to capture all aspects of the clinical manifestation of the spasticity. Subjective measures
such as MAS are valuable for timely and efficient measurement in the clinical settings. These could be complemented by objective measures (made more user friendly and designed for the clinical setting), which would provide specific impairment-related detail and characterize quality of movement. Future work should focus on two areas: 1) improving technology on making accessible and user-friendly objective assessments in the clinical settings and 2) improving the validity and reliability of current measures such as MAS.

Attainable goal setting for patients with spasticity is recommended to measure the effectiveness of intervention. However, in this study, some of the low motor functional level patients selected functional goals of relating to more advanced skills (i.e. chopping onion with the affected hand while their CMSA arm and had was stage 2). As a result, the changes in GAS between two phases were not significant, even though their rehabilitation was planned based on their selected goals. It is expected that other subjective and objective assessments to indicate changes after interventions in those individuals.

5.5 Assessing the impact of BoNTA on upper limb movement

BoNTA is a focal treatment and objective assessments are critical in measuring changes after intervention. Measures of gross motor function may not have the sensitivity to assess changes in the movement parameters that comprise functional tasks, which may also better reflect the focal effect of BoNTA. In Study 2, The KUSA model demonstrated the ability to distinguish between affected and unaffected upper limb motion and also provided supplementary information for motion characterization that is not available through clinical measures alone. Study 2 showed that the variables
included in the KUSA model (i.e. measures of range of motion, speed, and compensatory trunk movement) provided additional information in conjunction with clinical measures that could assist with the patient’s progress evaluation. For example, movement speed provides accurate information on the quality and quantity of the movement. Improvement in speed during real life upper limb activities such as reaching, grasping and drinking are indicators of improvement in function\textsuperscript{45,162}. Clinical assessments do not measure speed directly; improved movement speed can only be inferred through functional assessments such as CAHAI\textsuperscript{193}. Similarly, clinical measures are not able to measure compensatory trunk movements, which are indicative of the severity impairment after stroke\textsuperscript{200}. Together, the measures and tasks that comprise the KUSA enable quantitative assessment of movement patterns that are functionally relevant.

In Study 3, the KUSA model in conjunction with clinical measures examined the impact of BoNTA combined with rehabilitation in upper limb movement. Study 3 indicated that the changes after BoNTA were significant in the two clinical assessments (MAS and CAHAI) but kinematic variables including active range of motion, speed, and compensator trunk movement variables, as a measure of active limb movement, failed to show significant changes. However, subgrouping patients indicated those with higher CMSA improved in all kinematic variables. Those with lower initial levels of impairment were likely better able to engage in therapy, subsequently resulting in better outcomes.

The observed differences in results for the clinical and kinematic outcomes warrant discussion. The reduction in MAS score was expected as it has been shown in randomized studies that BoNTA significantly decreased spasticity and MAS is a
measure of impairment rather than function\textsuperscript{201-203}. Similarly, the significant changes observed in the CAHAI (a clinical indicator of upper limb active function), primarily driven by improvement in the patients with advanced motor recovery. In contrast, improvements in CMSA (measure of impairment) were not expected because the six month duration of the study was not long enough to notice changes in motor recovery in individuals with chronic post stroke\textsuperscript{50}. In contrast to the clinical measures, no significant changes in the kinematic variables were observed. Possible reasons for this could be that the tasks that were included in the KUSA were suitable for the patients with higher motor function but not for the lower level of motor function. In addition, the selected outcome measures might have not been as appropriate and/or sensitive as the clinical measures. Although the kinematic measures are sensitive and lack subjectivity, in assessing patients with spasticity, clinical measures would allow for considering all the contributing factors such as environmental, behavioral and cognitive factors which play a crucial role. In other words, kinematics measures may have been sensitive to variability in movement patterns across participants, but may have missed other important factors that contribute to change in function over time. Further studies need to be done to validate the tasks for different levels of motor recovery where psychometric properties have been established.

In contrast to Study 3, Bensmail et al. showed that velocity and smoothness changed significantly after two BoNTA injections\textsuperscript{45}. However, they recruited only a high functional group in the acute stage of recovery after stroke. In addition, Chang et al. showed that patients with higher CMSA\textsubscript{hand} gained more functional improvement than the patients who had lower motor recovery in their hand\textsuperscript{106}. By using BoNTA and
rehabilitation in combination, the researchers in that study speculated that patients with a higher motor recovery would also have a larger number of motor units which leads to a rise in the strength of agonist muscles. These findings raise an important point regarding goals and expectations for changes in specific outcomes and their associations with functional status at the start of the intervention. Individuals, who are at a moderate-high level of recovery at the start of intervention, may have a better capacity to engage in the types of therapies that typically accompany injections with BoNTA. This would subsequently increase the likelihood that individuals will achieve goals related to ADL/IADL and will also be able to achieve measurable change in the patterns and quality of movement.

The task(s) that were used in the work of Bensmail et al. and the ones used in Study 3 of the thesis were different\textsuperscript{45}. While our study focused on two different multi-joint tasks, they only tested a reaching task. The tasks in Study 3 were two plane (X,Y) while Bensmail et al. study was in one plane (Y) and performing tasks in two plane requires more coordination and high level of motor recovery\textsuperscript{204}. As it was shown in Study 1, patients with low motor recovery do not have active goals and struggle with active upper limb movements. Together these findings suggest that there is an interaction between intervention, recovery, and outcome measure that should be considered on an individual basis.

In light of the results presented in Chapters 2-4, the conceptual model presented in Chapter 1 of this dissertation can be re-examined. Even though the comorbid conditions and environmental factors were not controlled in these studies, Studies 1 and 3 showed that BoNTA significantly decreased spasticity. Study 3 also suggests that the
ability to identify changes in function using kinematic outcomes is dependent on the stage of upper limb motor recovery at baseline. Furthermore, a combination of rehabilitation with BoNTA assists the patients to achieve their goals whether passive or active. Based on the stages, scales or score of assessments, which could be biomechanical or clinical, the functional levels are defined and determined.

Figure 5.1: The revised conceptual model of the thesis. Contributing factors that increase spasticity (and impact function) include extrinsic factors, comorbid conditions and severity of impairment. Severity of impairment, also impacts the type of assessments used in measuring the changes in function. Biomechanical assessments may be more appropriate for patients with higher upper limb motor recovery stages. Assessments inform the level of function which is demonstrated as active or passive goals.

5.6 Limitations

The findings from our rehabilitation centre may not be applicable to other rehabilitation centres in Canada or worldwide because of the specific types of interventions that were offered, the specific characteristics of the patient population, and
the skill set of the interdisciplinary team. Also, the small sample size and lack of a blind assessor in Studies 1 and 3 limit generalizability. However, the study design and the patients’ treatment schedules (i.e. having to wait for the efficacy time-course of BoNTA) impacted recruitment and study activities. The study was comprised of two phases and each phase lasted three months; patients had to commit to six months of participation which was difficult for some patients and their family member due to geographical distance. In addition, the requirement that study participants had to be naïve to BoNTA and could not be receiving any oral antispasticity medication contributed to the limited sample size of the study. Study 1 was a retrospective study in which the participants were in various stages of motor recovery with spasticity in different muscle groups in the upper limb. Study 3 had the same limitations with physicians using EMG guided injections but with varying dosages, muscles and types of BoNTA. While this is problematic from a research perspective, it is a reflection of current standard care of spasticity management. Types of goals were directly related to the recovery stage of the participants. Our sample was a heterogeneous population which limited our statistical analysis. For example, if the sample was only higher function patients, the type of goals would have been different. Because we had a disproportionately higher number of low function patients, it impacted the types of goals (Study 1) and changes in arm function (Study 3). In addition, that selected kinematic measures (Study 3) may not have been sensitive enough to detect changes in lower functioning patients; therefore, it is possible that other kinematic measures may indicated changes after Rehab+BoNTA in this group.
5.7 Future research

The impact of BoNTA combined with rehabilitation may be conducted in multicenter randomized trials with more homogeneous participants. Different clinical measures such as measuring passive range of motion of affected joints which can be used for contracture prevention, and the level of skin condition/moist in palm, elbow crest and under arm, would be applied to measure improvement in passive goals and joint positioning. A study should be conducted with a larger sample size using KUSA in a high function group. Since there are few studies indicating the cut off point for motor recovery stage limit and functional capacity after stroke, more studies are require to investigate objectively the impact of Rehab+BoNTA on upper limb function in high function population using appropriate and different kinematic and clinical measures.

5.8 Conclusion

This dissertation aimed to examine the impact of BoNTA combined with rehabilitation on upper limb movement and achieving identified goals in patients post stroke. The evidence indicates that positioning goals at the impairment level are common in patients with upper limb spasticity who attended the outpatient spasticity clinic. A combination of BoNTA and upper limb rehabilitation improved only clinical measures and failed to show improvement in the kinematic variables using the KUSA. However, closer examination of the data indicated that the kinematic variables in patients with higher function and higher motor recovery showed an improvement which was not the case in patients in low motor recovery stage. Together, the chapters that comprise this thesis contribute to the body of knowledge on the impact of BoNTA and upper limb rehabilitation on function in individuals post stroke. The chapters examined
the impact of rehabilitation on function through identifying participant’s goals, and achieving those goals using clinical and kinematic measures. This approach provides a complementary view on the changes after BoNTA and rehabilitation on arm function. This thesis contributes to the best practice knowledge indicating that active movement is highly possible in patients with higher motor recovery stage.
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Appendix A: Kinematic calculations

Task 1 – Wrist flexion/extension

Wrist kinematics are measured as the rotation that occurs about the axis defined by markers $\vec{W}_A$ and $\vec{W}_B$. Two rigid bodies were defined: (1) the forearm and (2) the hand, which share the common wrist axis as shown in Figure 5b.

Since the left and right hands are mirror images, the wrist axis was reversed in left hand trials to maintain the convention of positive angles corresponding with flexion, and negative angles corresponding with extension.

$$\vec{v}_{wrist\ (right)} = \vec{W}_A - \vec{W}_B$$

The forearm vector was defined between the elbow and wrist markers, and the hand vector was defined between the wrist and index finger markers, as shown in Figure 5c.
Orthogonal coordinate systems were defined for each rigid body using the wrist axis and the respective motion vector (i.e. $\vec{v}_{\text{hand}}$ and $\vec{v}_{\text{forearm}}$). The following example outlines the construction of the coordinate system for the hand. The wrist axis was normalized to define the X-axis. Normalizing the vector means shortening the length of the vector to 1 unit, while maintaining its direction. This is achieved by dividing the vector by its length.

$$\vec{x}_{\text{hand}} = \frac{\vec{v}_{\text{wrist}}}{\|\vec{v}_{\text{wrist}}\|}$$

A secondary axis, Z, was defined as the cross product of the X axis and the hand vector. This axis was also normalized to length 1.

$$\vec{z}_{\text{hand}} = \frac{\vec{x}_{\text{hand}} \times \vec{v}_{\text{hand}}}{\|\vec{x}_{\text{hand}} \times \vec{v}_{\text{hand}}\|}$$

The final axis was defined as the normalized cross product of the previous two axes.
\[
\vec{Y}_{\text{hand}} = \frac{\vec{Z}_{\text{hand}} \times \vec{X}_{\text{hand}}}{\| \vec{Z}_{\text{hand}} \times \vec{X}_{\text{hand}} \|}
\]

The coordinate system \( R_{\text{hand}} \) is then defined as a 3x3 matrix made up of the three axes as its columns. \( R_{\text{hand}} \) describes the orientation of the hand with respect to the Vicon reference frame.

\[
R_{\text{hand}} = [\vec{X}_h \quad \vec{Y}_h \quad \vec{Z}_h] = \begin{bmatrix}
R_{1,1} & R_{1,2} & R_{1,3} \\
R_{2,1} & R_{2,2} & R_{2,3} \\
R_{3,1} & R_{3,2} & R_{3,3}
\end{bmatrix}
\]

The same method was used with the forearm vector and wrist axis vector to calculate the forearm coordinate system \( R_{\text{forearm}} \). Since both bodies have coordinate systems with respect to a common origin (i.e. the Vicon system), the relative orientation of the hand with respect to the forearm can be calculated.

\[
R_{\text{forearm to hand}} = R_{\text{forearm}}^{-1} R_{\text{hand}}
\]

The two rigid bodies share a common axis (i.e. the wrist axis), so the relative rotation matrix simplifies:

\[
R_{\text{forearm to hand}} = \begin{bmatrix}
1 & 0 & 0 \\
0 & R_{2,2} & R_{2,3} \\
0 & R_{3,2} & R_{3,3}
\end{bmatrix} = \begin{bmatrix}
1 & 0 & 0 \\
0 & \cos(\theta) & -\sin(\theta) \\
0 & \sin(\theta) & \cos(\theta)
\end{bmatrix}
\]

From this matrix, the rotation about the subject’s wrist can be calculated using an inverse trigonometric function:

\[
\theta_{\text{wrist}} = \text{atan} \left( \frac{R_{3,2}}{R_{3,3}} \right)
\]
In Figure 6b, elbow flexion angle was measured as the angle separating the upper-arm and forearm vectors:

\[ \vec{V}_{\text{upper arm}} = \vec{E}_A - \vec{S} \]
\[ \vec{V}_{\text{forearm}} = \vec{W}_A - \vec{E}_A \]

The elbow flexion angle is calculated as the inverse trigonometric tangent (arctan) of the magnitude of the vector cross product divided by the vector dot product:

\[ \theta_{\text{elbow}} = \arctan\left( \frac{||\vec{V}_{\text{upper arm}} \times \vec{V}_{\text{forearm}}||}{\vec{V}_{\text{upper arm}} \cdot \vec{V}_{\text{forearm}}} \right) \]