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● *Original Contribution*

QUANTITATIVE 3-D ULTRASOUND OF THE MEDIAL GASTROCNEMIUS MUSCLE IN CHILDREN WITH UNILATERAL SPASTIC CEREBRAL PALSY

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Abstract—Three-dimensional ultrasound (3-DUS) was used to examine the size and appearance of the medial gastrocnemius (MG) muscle in children with unilateral cerebral palsy (CP). Twenty-six children with CP and 10 typically developing (TD) children participated. Three-dimensional US images of both limbs in children with CP and the right limb in TD children were analysed using quantitative methods to determine muscle volume, global echo intensity, global echo pattern and regional echo intensity. Significant differences in MG volume and all echo parameters were found between TD and CP children. The more involved limb was smaller and had higher echo intensity and a more heterogenous echo pattern compared with the TD group. Compared with that of the more involved limb, the MG of the less involved limb was larger but had a similar echo appearance. The MG of both limbs in children with unilateral spastic CP is smaller and, based on quantitative ultrasound, structurally different from that of TD children. (E-mail: s.obst@cqu.edu.au) **© 2017 World Federation for Ultrasound in Medicine & Biology. All rights reserved.**

Key Words: **Children, Cerebral palsy, Muscle, Ultrasound, Echo intensity, Spasticity, Echo pattern.**

INTRODUCTION

Cerebral palsy (CP) describes a spectrum of movement disorders caused by a non-progressive lesion of the developing brain (Rosenbaum et al. 2007). Although the brain lesion is static, secondary changes to the musculoskeletal system, such as muscle contracture and bone deformity (Gough and Shortland 2012; Morrell et al. 2002), are progressive and often the target of intervention (Graham and Selber 2003). Structural differences between CP and typically developing (TD) muscle, including reduced muscle size and abnormal composition (*e.g.,* increased intramuscular fat (Johnson et al. 2009; Noble et al. 2014) and collagen (Booth et al. 2001)), combined with altered neural control (*e.g.,* increased co-contraction and selective activation (Rose and McGill 2005; Stackhouse et al. 2005)), contribute to muscle weakness and stiffness (Barber et al. 2011a, 2011b) in children with CP. Increased passive stiffness of CP muscle, in particular, is strongly linked to abnormal muscle composition wherein muscle cells are shorter and stiffer (Friden and Lieber 2003); muscle fibres are thinner (Friden and Lieber 2003) and stiffer (Mathewson et al. 2014) and composed of longer and fewer sarcomeres in series (Smith et al. 2011); and the extracellular matrix is stiffer and contains inferior and poorly organised collagen (Booth et al. 2001; Pingel et al. 2016). Altered muscle composition in CP may also be more common in muscles required for ambulation (Handsfield et al. 2016; Lampe et al. 2006; Noble et al. 2014) and/or those targeted with chemical denervation treatments (Fortuna et al. 2011; Pitcher et al. 2015) (*e.g.,* botulinum toxin A [BoNT-A]). Identifying changes in the composition of lower limb muscles will be important for the assessment and management of muscle impairment and physical function in ambulant children with spastic CP (Gough and Shortland 2012; Picelli et al. 2012; Pingel et al. 2016).

The gross morphology of CP muscle has been well documented using medical imaging (Barrett and Lichtwark 2010); however, few studies have examined muscle composition (Johnson et al. 2009; Noble et al. 2014; Pitcher et al. 2015). Ultrasound has been used extensively to quantify muscle composition in children with neuromuscular disorders (Heckmatt et al. 1988; Pillen et al. 2008) by analysing the echo intensity and pattern of the images (Pitcher et al. 2015). Ultrasound of normal muscle appears black (low echo intensity), with relatively few white (high

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echo intensity) reflections scattered throughout the muscle cross-section (Heckmatt et al. 1988; Pillen et al. 2008). In comparison, diseased muscle (Pillen et al. 2008) or muscle that contains high concentrations of fat (Reimers et al. 1993a, 1993b) and/or collagen (Pillen et al. 2009) appears predominately white with a large number of high-intensity echo signals diffusely scattered throughout the muscle cross-section (Nielsen et al. 2000, 2006; Pillen et al. 2008). Both echo intensity and echo pattern are used to interpret muscle quality, as muscles with same mean echo intensity can have very different echo patterns (Pillen et al. 2008).

Initial applications of muscle ultrasound used a visual grading system (I–IV Heckmatt scale (Heckmatt et al. 1988)). More recently, quantitative approaches have been developed that evaluate echo intensity using histogram-based statistics (Pillen et al. 2003, 2006) and echo patterns using higher-order texture (Molinari et al. 2015) and spatial analysis (Nielsen et al. 2006) techniques. Quantitative ultrasound using mean echo intensity has greatly improved screening procedures for children suspected of neuromuscular disorders (Brockmann et al. 2007; Pillen et al. 2003, 2006, 2007). Higher-order texture analysis has been used to quantify intramuscular fat in animal muscle (Kim et al. 1998) and can characterise cancer tissue in humans more effectively than histogram-based parameters (Acharya et al. 2014), but has only recently been used to evaluate skeletal muscle tissue (Gdynia et al. 2009; Molinari et al. 2015; Nielsen et al. 2006; Pitcher et al. 2015). Because higher-order analyses are intensity invariant (Acharya et al. 2014; Molinari et al. 2015) and provide information about echo pattern and spatial distribution, they could provide an additional method to evaluate muscle composition in children with CP.

To date, only one study has used quantitative ultrasound to evaluate muscle composition in children with CP (Pitcher et al. 2015). This study investigated medial gastrocnemius (MG) muscle ultrasound in 40 children with spastic motor type CP (Gross Motor Functional Capacity [GMFCS I–V]) and an age-matched cohort of TD children. The authors used 2-D ultrasound to quantify mean echo intensity, image entropy and percentage of connected regions determined using blob analysis (Nielsen et al. 2006). The results revealed significant differences between CP and TD and between GMFCS levels III and I and levels III and II. Consistent with a previous study that used magnetic resonance imaging to quantify intramuscular fat in children with CP (Noble et al. 2014), these authors found a relationship ($r = 0.42$) between mean echo intensity and GMFCS level. The study also reported a correlation between the amount of connective tissue, as measured with blob analysis (Nielsen et al. 2006), and the frequency of BoNT-A injections (Pitcher et al. 2015). Although this study provides preliminary support for quantitative ultrasound in CP research, the authors acknowledge that single-site measurements may not be representative of the whole muscle and may be vulnerable to error (Pitcher et al. 2015). Furthermore, the study did not report the distribution of limb involvement (unilateral or bilateral) in the CP cohort or which limb was measured (less involved or more involved), so it is difficult to interpret the results on the basis of GMFCS level alone (Pitcher et al. 2015). Although muscle impairment is a feature of both unilateral and bilateral CP, the extent and location of the cerebral injury and attainment of developmental milestones differ considerably (Uvebrant 1988).

There is consistent evidence for reduced muscle size, as compared with a TD cohort, of the more involved limb in children with unilateral and bilateral CP (Barber et al. 2011a, 2011b, 2016; Barrett and Lichtwark 2010). Few studies have examined differences in muscle size and structure in children with unilateral CP between the less involved limb and TD children (Bandholm et al. 2009; Elder et al. 2003; Lampe et al. 2006; Malaiya et al. 2007; Mohagheghi et al. 2007) or between the less and more involved limbs (Elder et al. 2003; Malaiya et al. 2007). Compared with TD children, the muscles of the less involved limb in children with CP are smaller in length (Malaiya et al. 2007) and possibly volume (Elder et al. 2003; Malaiya et al. 2007). Compared with those of the less involved limb, muscles of the more involved limb tend to be more stiff (Lee et al. 2016) and smaller in length (Malaiya et al. 2007), volume (Elder et al. 2003; Lampe et al. 2006; Malaiya et al. 2007; Riad et al. 2011), cross-sectional area (Bandholm et al. 2009; Elder et al. 2003) and thickness (Bandholm et al. 2009; Lee et al. 2016; Mohagheghi et al. 2007), but do not differ in fascicle length and pennation (Lee et al. 2016; Malaiya et al. 2007; Mohagheghi et al. 2007). Although differences in muscle size and composition between limbs in ambulant children with unilateral CP might be expected, it is unclear whether the less involved limb would be structurally similar or different to that of TD children. Because the classification of limb distribution is often based on clinical assessment of motor impairment and function, and not structural brain imaging, it may be inappropriate to assume that muscles of the less involved limb are ostensibly normal and comparable in size and composition to TD muscle. To date, no studies of children with unilateral CP have examined muscle size and composition of the less involved limb compared with the more involved limb or compared with the limbs of TD children.

This study used freehand 3-D ultrasound (3-DUS) to evaluate muscle volume and muscle echo intensity and echo pattern of the MG muscle in both limbs in children with unilateral spastic CP as compared to TD children. We hypothesised that the MG muscle of the more involved limb would be smaller and have a brighter and more