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A reliability assessment of constrained spherical deconvolution-based diffusion-weighted magnetic resonance imaging in individuals with chronic stroke

Nicholas J. Snow[a], Sue Peters[a], Michael R. Borich[b], Navid Shirzad[c], Angela M. Auriat[a], Kathryn S. Hayward[a,d], Lara A. Boyd[a,e,*]

[a] Graduate Program in Rehabilitation Sciences, Faculty of Medicine, University of British Columbia, Vancouver, Canada
[b] Division of Physical Therapy, School of Medicine, Emory University, Atlanta, USA
[c] Biomedical Engineering Graduate Program, Faculty of Applied Science, University of British Columbia, Vancouver, Canada
[d] The Florey Institute of Neuroscience and Mental Health, University of Melbourne, Melbourne, Australia
[e] Graduate Program in Neuroscience, Faculty of Medicine, University of British Columbia, Vancouver, Canada

HIGHLIGHTS

- Assessed reliability of constrained spherical deconvolution (CSD) in chronic stroke.
- Reliability was generally good to excellent in the selected white matter tracts.
- CSD is a reliable white matter imaging technique in persons with chronic stroke.

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ABSTRACT

Background: Diffusion-weighted magnetic resonance imaging (DW-MRI) is commonly used to assess white matter properties after stroke. Novel work is utilizing constrained spherical deconvolution (CSD) to estimate complex intra-voxel fiber architecture unaccounted for with tensor-based fiber tractography. However, the reliability of CSD-based tractography has not been established in people with chronic stroke.
New method: Establishing the reliability of CSD-based DW-MRI in chronic stroke. High-resolution DW-MRI was performed in ten adults with chronic stroke during two separate sessions. Deterministic region of interest-based fiber tractography using CSD was performed by two raters. Mean fractional anisotropy (FA), apparent diffusion coefficient (ADC), tract number, and tract volume were extracted from reconstructed fiber pathways in the corticospinal tract (CST) and superior longitudinal fasciculus (SLF). Callosal fiber pathways connecting the primary motor cortices were also evaluated. Inter-rater and test–retest reliability were determined by intra-class correlation coefficients (ICCs).
Results: ICCs revealed excellent reliability for FA and ADC in ipsilesional (0.86–1.00; $p < 0.05$) and contralesional hemispheres (0.94–1.00; $p < 0.0001$), for CST and SLF fibers; and excellent reliability for all metrics in callosal fibers (0.85–1.00; $p < 0.05$). ICC ranged from poor to excellent for tract number and tract volume in ipsilesional (−0.11 to 0.92; $p \leq 0.57$) and contralesional hemispheres (−0.27 to 0.93; $p \leq 0.64$), for CST and SLF fibers.
Comparison with existing method: Like other select DW-MRI approaches, CSD-based tractography is a reliable approach to evaluate FA and ADC in major white matter pathways, in chronic stroke.
Conclusion: Future work should address the reproducibility and utility of CSD-based metrics of tract number and tract volume.

* Corresponding author at: University of British Columbia, Department of Physical Therapy, 212-2177 Wesbrook Mall, Vancouver, British Columbia V6T 1Z3, Canada. Tel.: +1 604 827 3369.
E-mail address: lara.boyd@ubc.ca (L.A. Boyd).

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1. Introduction

For nearly two decades, diffusion-weighted magnetic resonance imaging (DW-MRI) has been used to non-invasively investigate white matter properties within the human brain. DW-MRI-based white matter tractography has shown clinical utility for both neurosurgical planning and the assessment of disease progression and recovery (Ciccarelli et al., 2008). In stroke literature, DW-MRI techniques have been used to help characterize potential biomarkers for functional motor recovery (Lindenberg et al., 2012; Stinear et al., 2007a; Mang et al., 2015; Borich et al., 2014; Cunningham et al., 2015). To date, the majority of this work has examined white matter microstructural properties using diffusion tensor imaging (DTI)-based fiber tractography. However, an increasing body of literature is beginning to explore these properties using non-tensor models (e.g., Tournier et al., 2011). For example, work in both healthy individuals and pre-surgical patients has employed constrained spherical deconvolution (Tournier et al., 2007a) (CSD)-based fiber tractography to reconstruct white matter pathways, which better resembled known anatomical structures than DTI (Farquharson et al., 2013). CSD-based tractography has also been shown to better detect differences in white matter anisotropy in persons with Alzheimer's disease (Reijmer et al., 2012) and bipolar affective disorder (Emsell et al., 2013), versus DTI-based approaches. Similar advantages also extend to the stroke literature (Auriat et al., 2015).

Recently, we conducted a comparison of DTI and CSD in persons with chronic stroke and healthy control participants, wherein we found several advantages of CSD over DTI (Auriat et al., 2015). Specifically, CSD was able to reconstruct a greater number of tracts than DTI for two pathways important to recovery from stroke – the cortical spinal tract (CST) and corpus callosum (CC). CSD identified ipsilesional white matter pathways in stroke participants who did not have identifiable tracts using DTI, and detected significant differences in diffusion metrics between CSD- and DTI-based methods (Auriat et al., 2015). Importantly, CSD-based diffusion metrics were more strongly related to both clinical and functional outcomes in chronic stroke, compared to those derived from DTI (Auriat et al., 2015). Specifically, fractional anisotropy (FA) in the CST of individuals with stroke is more closely related to motor function when tractography is performed with CSD versus DTI, while both motor function and impairment are more strongly correlated with CSD-derived FA in the CC when compared to DTI (Auriat et al., 2015). Moreover, CSD-based fiber tractography in persons with chronic stroke has been used to reveal significant relationships between FA of transcallosal white matter tracts and transcallosal inhibitory interactions between brain hemispheres (Mang et al., 2015). It is becoming increasingly apparent that the use of CSD-based tractography is appropriate for both clinical and research purposes.

Generally, DTI-based fiber tractography utilizes voxel-wise estimates of white matter fiber orientation, by generating a single tensor ellipsoid model that estimates a single three-dimensional fiber orientation per voxel (Basser, 1995). These tensor-based tractography approaches utilize the eigenvalues and eigenvectors of the diffusion tensor ellipsoid to estimate the corresponding fiber orientations (Mori et al., 1999). However, the diffusion tensor is unable to resolve complex intra-voxel fiber architecture, limiting the ability to characterize different fiber orientations in voxels containing multiple fiber populations (Tournier et al., 2011). This is a significant problem because a high proportion of white matter-containing voxels in the human brain contain projections from multiple fiber populations (Jeurissen et al., 2013). DTI-based fiber tractography may misrepresent white matter fiber architecture in brain regions containing crossing fibers and may be vulnerable to partial volume effects (Farquharson et al., 2013; Jeurissen et al., 2013; Kristo et al., 2013; Jeurissen et al., 2011). On the other hand, CSD-based fiber tractography expresses the DW-MR signal as an estimate of the fiber orientation distribution (FOD) response function within each voxel (Tournier et al., 2007b). This method thus provides information regarding the orientations and contributions of multiple fiber populations to voxel-wise estimates of diffusion fiber orientation (Tournier et al., 2011). As such, CSD is robust to the presence of multiple fiber populations and does not make assumptions regarding uniform intra-voxel water diffusion (Farquharson et al., 2013; Tournier et al., 2007b). Taking both deterministic and probabilistic tractography methods into account, CSD provides more accurate estimations of complex local fiber orientations, as well as more accurate estimations of the uncertainty associated with the reconstructed fiber orientations, respectively (Farquharson et al., 2013; Auriat et al., 2015; Jeurissen et al., 2011; Tournier et al., 2008). Moreover, spurious, non-anatomical fiber reconstructions are fewer in CSD-based reconstructions as compared to DTI (Farquharson et al., 2013; Jeurissen et al., 2011). Indeed, there is considerable evidence in favor of using CSD-based fiber tractography as an alternative to DTI, given its greater sensitivity to multiple intra-voxel fiber pathway trajectories.

Given the recognized sensitivity and growing use of CSD-based fiber tractography in clinical-based research in recent years, it would appear timely to establish the reliability of this approach. Multiple studies have demonstrated that CSD is a reliable tractography technique in healthy individuals (Kristo et al., 2013; Besseling et al., 2012). However, establishing the reliability of CSD-based tractography in people with stroke is necessary before it can be used in clinical practice, especially due to the substantial variability in the location and size of lesions that are evident in stroke. Further, manual delineation of white matter regions in the post-stroke brain may be susceptible to variation (Ay et al., 2008), and the outcomes of automated CSD-based techniques could be significantly influenced by the presence of one or more major lesions (Thomas et al., 2013). As such, the aim of the current investigation was to establish the inter-rater and test–retest reliability of CSD-based fiber tractography in three clinically-relevant ROIs in individuals with chronic stroke: inter-hemispheric primary motor connections mediated by the CC (CC_{III}); CST projections; and the superior longitudinal fasciculus (SLF). These regions were selected due to their importance in motor recovery after stroke. Specifically, we chose three major pathways including projection (CST), associative (SLF), and commissural (CC) pathways, that encompass a broad range of fiber orientations that support motor function and recovery after a stroke. These pathways are also prevalent in previous investigations of their white matter properties (Lindenberg et al., 2012; Mang et al., 2015; Borich et al., 2014; Auriat et al., 2015; Borich et al., 2012a), and the reliability of the CSD approach, has yet to be examined.

Presently, we conducted a ROI-based tractography, following whole-brain tractography using a deterministic CSD model. In the present investigation we assessed commonly reported measures of white matter microstructural and diffusion properties: FA, apparent diffusion coefficient (ADC), tract number, and tract volume (Basser, 1995; Basser and Pierpaoli, 1996; Le Bihan et al., 1988). It was expected that CSD-based tractography would provide reliable estimates of these measures within a sample of individuals with chronic stroke. Overall, we aimed to add to the existing body of literature, by providing evidence that CSD is a reliable fiber tractography technique in a sample of persons with chronic stroke. We show that in addition to being a valid DW-MRI analysis technique (Farquharson et al., 2013; Auriat et al., 2015), CSD-based fiber tractography can be a reliable white matter imaging approach.