

ORIGINAL ARTICLE

The Reliability of Diffusion Tensor Imaging (DTI) Region-Of-Interest (ROI) Methods for Tracking the Corticospinal Tract (CST) In Adolescents

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ABSTRACT

Introduction: Human brain development is a complex process that continues during childhood and adolescence. Development does not end there, as young adulthood also provides new challenges and experiences that may continue to impact brain development. The corticospinal tract (CST) plays a pivotal role, serving as the primary pathway for voluntary motor control. By delineating the CST, researchers can analyse the integrity and connectivity of this tract. Thus, this study aims to evaluate the reliability of DTI ROI methods for tracking CST among adolescents.

Methods: 50 DTI images were post-processed using automated and manual ROI tracking methods. The fractional anisotropy (FA), and apparent diffusion coefficient (ADC) values of the CST were obtained and compared. The observer's agreement between two observers was evaluated using the Bland-Altman test and intraclass correlation coefficient (ICC) test. A paired t-test was used to compare the mean values of the FA and ADC obtained from both methods. One-way ANOVA and independent t-test were conducted to compare the FA and ADC across age group and gender. **Result:** Both the Bland-Altman analysis and the ICC test showed a good agreement between two observers. A paired t-test showed a statistically significant in FA and ADC. One-way ANOVA and independent t-tests were conducted and showed no significant difference between ROI methods across age group and gender different.

Conclusion: Automated and manual ROI tracking methods can provide a robust and dependable way of tracking the CST. Nevertheless, the different operational characteristics of various methods made direct comparison challenging. *Malaysian Journal of Medicine and Health Sciences (2025) 21(SUPP5): 270–276. doi:10.47836/mjmh.21.s5.34*

Keywords: Corticospinal tract, DTI, ROI, fractional anisotropy, apparent diffusion coefficient

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INTRODUCTION

The development of the human brain is a complex yet highly rapid and dynamic process that occurs during the fetal stage [1], infancy, and adolescence [2, 3]. According to the World Health Organization [4], adolescence spans from ages 10 to 19, encompassing the teenage years. The establishment of neural networks linking various brain regions depends on the development of white matter (WM) during adolescence [5]. The maturation of cerebral WM, which includes ongoing axon myelination, is a fundamental developmental process that occurs during adolescence and leads to the formation of a more developed brain [6]. This WM development is important

as it plays a role in providing the structural, architectural organisation of the brain and as a structural correlate of communication within complex neural systems [7]. Among the key neural pathways composed of WM fibers is the corticospinal tract (CST). The CST plays a pivotal role in the central nervous system, serving as the primary pathway for voluntary motor control [8]. Natali et al. [9] reported that disruptions or lesions along the CST may result in a range of motor impairments, such as spasticity, paralysis, and loss of fine motor control. The process of brain development can be evaluated using non-ionising assessments, including prenatal ultrasonography (US) and structural magnetic resonance imaging (MRI) techniques [10, 11]. However, MRI has not yet demonstrated biochemical and microstructural changes in gray matter (GM) and WM [12, 13].

Diffusion tensor imaging (DTI) is an advanced MRI technique that allows for the visualisation of changes in WM by indirectly evaluating the microstructure

and organisation of WM through the analysis of water molecule diffusion [13]. The DTI technique enables the computation of various quantitative metrics, such as apparent diffusion coefficient (ADC), fractional anisotropy (FA), axial (AD), and radial diffusivities (RD) [14]. The analysis of ADC and FA metrics enables the examination of typical and atypical brain development in children. As the brain matures and undergoes myelination, ADC values tend to decrease, indicating reduced water diffusion, while FA values increase, reflecting more organised white matter tracts [5, 15].

Region-of-interest (ROI) analysis is a direct approach for measuring diffusion in the brain in two-dimensional (2D) imaging. It involves selecting specific brain areas manually or automatically from images [16]. Additionally, the ROI methods, either manual or automated fiber tracking, allow researchers to focus specifically on the CST, enabling targeted analysis of this critical neural pathway [17].

The primary ROI method employed in Malaysia for tracking the CST and assessing FA and ADC parameters is the manual ROI method. Nevertheless, previous studies on the reliability of various ROI methods used in evaluating CST have shown inconsistent outcomes [18, 19]. Thus, the objective of this study was to evaluate the reliability of DTI ROI methods for tracking CST in healthy adolescents by comparing the reliability of manual Neuro3D software and automated DSI Studio software.

MATERIALS AND METHODS

Study Setting

This study was retrospective study that involved 50 MRI brain images from healthy volunteers that met the inclusion and exclusion criteria (Table I). The images were obtained using Siemens Magnetom Verio 3.0 Tesla with 64-channel head coil available at MRI Unit, Radiology Department of UKM Specialist Children's Hospital, Cheras, Kuala Lumpur, between March and September 2019.

Table I: Inclusion and exclusion criteria.

Inclusion criteria
1. Brain images of the subjects age between 13 -16 years old
2. Normal brain images
3. Brain images scanned with DTI sequences
Exclusion criteria
1. Brain images with present of noise and artifact
2. Brain images of subject who been diagnose with mental health

DTI post-processing

CST fiber tracking of 50 brain images was tracked using both manual Neuro3D software that is installed on the Siemens Magnetom Skyra 3.0 Tesla system and automated DSI Studio software that installed on a research desktop computer. Two experienced radiographers with more

than ten years of experiences in MRI and comprehensive training in Neuro3D software conducted Neuro3D analysis of the CST. In order to avoid bias, the tracking process was conducted at constant times, both in the morning over the weekend and under the same lighting conditions and at room temperature. The T1-weighted images were reconstructed into axial, coronal, and sagittal planes to produce multiplanar reconstruction (MPR) images. The TENSOR images obtained from DTI sequences was reconstructed into colour-coded fractional anisotropy (FA) maps to delineate the midbrain, which was used as the ROI for evaluating motor control in this study. The MRI brain images were retrieved from DICOM and translated into source code formation (SRC) format for the automated DSI studio tractography. The software then automatically reconstructed the images and generated file information block (FIB) datasets. Fiber tracking of the FIB files was performed using a template provided by Atlas. Bilateral hemispheres were evaluated for both manual and automated CST tracking methods. Since no significant differences were observed between the right and left hemispheres, the average values for both hemispheres were calculated for analysis. The FA threshold for the CST was determined using the tract termination. A minimum FA limit of 0.2 was employed for the CST, while a maximum angle limit of 60 degrees followed the software's standard.

Statistical Analysis

The data was analysed using the Statistical Package for the Social Sciences (SPSS) version 29.0 for Windows (SPSS Inc., USA). An analysis of normality was performed on the data and showed that the data follows a normal distribution. The Bland-Altman test and intraclass correlation coefficient (ICC) evaluation were used to evaluate the inter-observer agreement of the manual Neuro3D method. A paired t-test was used to evaluate the FA and ADC values between manual Neuro3D and automated DSI studio tractography methods in tracking CST. An Independent t-test was used to compare the FA and ADC values between genders, while a one-way Analysis of variance (ANOVA) was used to analyse the values among ages. A p-value less than 0.05 was considered statistically significant.

Ethical clearance

This study has been approved by the Universiti Teknologi MARA (UiTM) Research Ethics Committee with reference number of FERC/FSK/MR/2023/00293 and the Institutional Ethics Committee (IEC) of the National University of Malaysia (UKM) with the reference number of JEP-2023-857.

RESULTS

Demographic Data

In this present study, 50 images that met the inclusion criteria were chosen. These images included 26 males and 24 females, with an average age of 14.46 ± 1.28

years old, ranging from 13 to 16 years old.

Observers’ agreement in tracking the Corticospinal tract (CST)

The Bland-Altman test was employed to evaluate the agreement between the two observers in measuring the FA and ADC values. The Bland Altman test revealed a mean difference of -0.01 (95% CI: -0.03 to 0.02) and 95% limits of agreement ranging from -0.12 to 0.14 for FA. Similarly, for ADC, the mean difference was -0.03 (95% CI: -0.05 to -0.01), and 95% limits of agreement ranged from -0.17 to 0.12, as shown in Fig. 1 and Fig. 2 below. A good agreement between the two observers was demonstrated by both FA and ADC values falling within the limit of agreements. An ICC test was calculated then to assess the reliability of the observers' measurements for FA and ADC. The ICC for FA was shown to be 0.84 (95% confidence interval: 0.71 to 0.92), whereas for ADC it was 0.80 (95% confidence interval: 0.60 to 0.87), as displayed in Table II. Both the FA and ADC results indicate a strong level of agreement between observers.

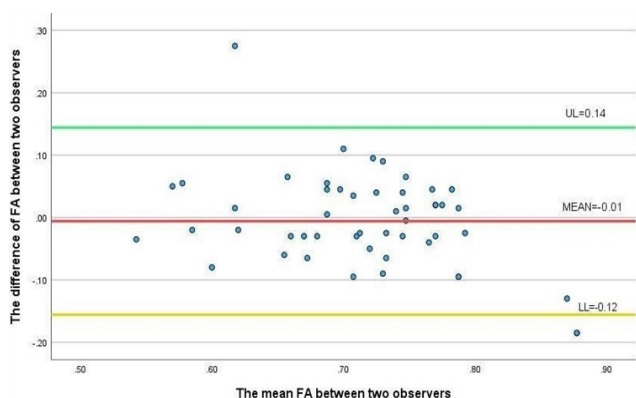


Fig. 1: Bland Altman plots for inter-observer agreement measurement of fractional anisotropy (FA).

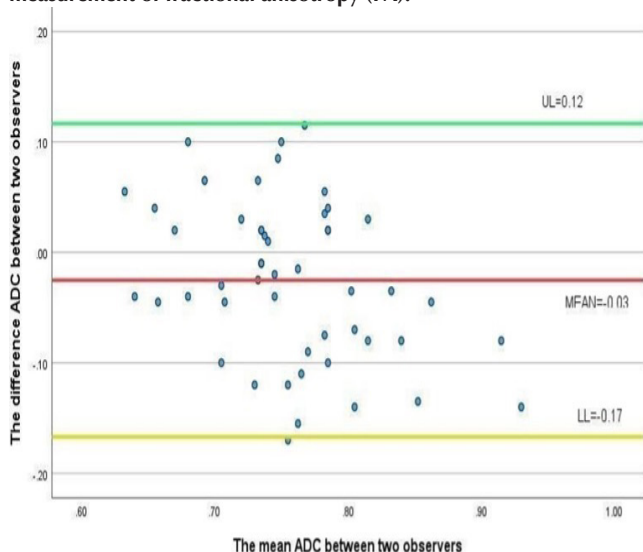


Fig. 2: Bland Altman plots for inter-observer agreement measurement of apparent diffusion coefficient (ADC).

Table II: ICC of fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values between the observers.

	ICC coefficient	95% CI		F-test with true value 0			
		upper	lower	value	df1	df2	sig
FA	0.84	0.92	0.71	7.20	49	49	0.00
ADC	0.80	0.87	0.60	4.40	49	49	0.00

Comparison of fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values from various region-of-interest (ROI) methods

A paired t-test was conducted to compare the FA and ADC values between manual Neuro3D and automated DSI tracking methods in tracking the CST. Significant differences were observed in the mean scores for manual Neuro3D (M=0.72, SD=0.07) and automated DSI methods (M=0.46, SD=0.03); $t(49) = -0.26, p < 0.001$ for FA; and manual Neuro3D (M=0.76, SD=0.06) and automated DSI methods (M=1.29, SD=0.05); $t(49) = -48.13, p < 0.001$ for ADC (Table III).

Table III: Paired t-test of fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values from various ROI methods.

Variables	DSI Studio Mean (SD)	Neuro3D Mean (SD)	Mean difference (95% CI)	t-stats (df)	p-value
FA	0.46 (0.03)	0.72 (0.07)	-0.26 (-0.28, -0.23)	-23.32 (49)	<0.001
ADC	1.29 (0.05)	0.76 (0.06)	0.52 (0.50,0.55)	48.13 (49)	<0.001

Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) by gender

An independent t-test was conducted to compare FA and ADC values between genders. The results showed no significant gender differences in manual Neuro3D tracking between males (M= 0.71, SD = 0.07) and females (M=0.71, SD=0.08); $t(48) = -0.11, p > 0.05$ for FA; and males (M= 0.75, SD = 0.06) and females (M=0.77, SD = 0.07); $t(48) = -0.80, p > 0.05$ for ADC (Table IV).

Table IV: Independent t-test of fractional anisotropy (FA) and apparent diffusion coefficient (ADC) by gender.

Variables	Male Mean (SD)	Female Mean (SD)	Mean diff. (95% CI)	t-stats (df)	p-value
FA	0.71 (0.07)	0.71 (0.08)	0.00 (-0.04,0.05)	-0.11 (48)	0.91
ADC	0.75 (0.06)	0.77 (0.07)	0.02 (-0.05,0.02)	-0.80 (48)	0.43

Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) by age

An ANOVA was conducted to compare the FA and ADC values across three different age groups; 13, 14, and 16 years old. Statistical analysis revealed no significant difference in FA ($F(2,47) = 0.75, p = 0.48$) and no statistically significant difference in ADC ($F(2,47) = 1.15, p=0.32$) among different age groups of adolescents (Table V and Table VI).

Table V: One-way ANOVA of fractional anisotropy (FA) by age.

Variables (FA)	n	Mean FA (SD)	f-stat (df)	p-value
Age	50	0.72(0.07)	0.75	0.48
13	15	0.71(0.06)		
14	16	0.74(0.10)		
16	19	0.71(0.07)		

Table VI: One-way ANOVA of apparent diffusion coefficient (ADC) by age.

Variables (ADC)	n	Mean ADC (SD)	f-stat (df)	p-value
Age	50	0.76(0.06)	1.15	0.32
13	15	0.77(0.07)		
14	16	0.74(0.05)		
16	19	0.77(0.70)		

DISCUSSION

Observers’ agreement in tracking the Corticospinal tract (CST)

The Bland-Atman and ICC tests demonstrate good agreement among observers who track the CST using the manual Neuro3D method, with minimal bias. The remarkable consistency in the measurements may be due to the observers' years of working experience in MRI and DTI and their level of proficiency in the software. Foesleitner et al. [20] reported a similar finding in a study of CST asymmetry in unilateral polymicrogyria by observers with minimum five years of work experience. This highlights the robustness of experienced observers in overcoming potential biases. Furthermore, the presence of adequate and effective training on the software used was another crucial factor in attaining a good agreement among observers. This discovery aligns with previous research studies conducted by Brandstack et al. [21] and Tang et al. [22]. Brandstack et al. [21] evaluated the reliability of tractography-based measurements compared to standard ROI methods, with an objective of minimising the impact on raters' ability by providing necessary training and supervision. Their research emphasised the need to closely follow anatomical delineation guidelines in order to improve the consistency and reliability of measurements. Additionally, Tang et al. [22] emphasised the significant effect of observers' knowledge and familiarity with brain anatomy, especially in tract-specific analyses of the CST.

Another factor contributing to the good agreement among observers in this study was the characteristics of the subjects, individuals with normal and healthy brains. Absence of pathological conditions at the CST minimises the anatomical variability and makes ROI selection more consistent between the observers. For instance, Metwali et al. [23] conducted a study on brain tumours and found that brain tumours can affect DTI images and fiber tracking. Tumors invade the brain tissue, change its diffusivity characteristics, and can displace the tracts. These complexities often lead to decreased inter-observer agreement due to the difficulty

in defining consistent ROIs in the presence of abnormal brain structures. Similarly, Borich et al. [24] conducted a study involving stroke patients and observed poor inter-rater agreement for FA asymmetry. This study stated that anatomical deformations resulting from stroke, such as infarcts, can complicate the placement of the ROIs. These deformations, when combined with the distortions associated with normal images of a template brain, exacerbate the inconsistencies in DTI analysis. The presence of lesions and the resulting structural changes make it challenging to achieve good inter-observer measurements. In contrast, this study shows consistent ROI tracking with good inter-observer agreements between the two observers as the tract's presence without abnormalities.

Comparison of fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values from various region-of-interest (ROI) methods

A paired t-test was performed to compare the reliability of manual Neuro3D and automated DSI studio fibre tracking ROI methods in measuring FA and ADC values. The results showed significant differences in the mean values of FA and ADC between the two methods. Similar results were reported by Ressel et al. [25] and Zhang et al. [26] which compared the reliability of automated and manual tracking of CST. Both studies revealed that the FA values obtained by the automated ROI method were significantly greater than those obtained by the manual ROI method. Nevertheless, the automated ROI method showed inconsistent effectiveness in patients with severe clinical conditions for two primary reasons: 1) severe anatomical deformation leading to the displacement of tracts of interest, and 2) loss of anisotropy resulting in a termination of fibre tracking [26].

Another study comparing manual and automated ROI methods in paediatric populations revealed significant changes in FA in different brain regions using the automated method. The manual method showed only a limited number of significant differences in the brainstem, cerebrospinal fluid (CSF), midbrain, thalamus, and deep right white matter [27]. Nevertheless, this study has demonstrated the limitation of the automated ROI method, which becomes less useful when changes deviate from the anatomical boundaries specified in the atlas or are limited to a small area [27].

Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) by gender

A comparison of the FA and ADC by gender revealed no statistically significant difference between males and females. Narrow age range of the subjects likely contributed to the lack of significant differences between the genders. A study conducted by Lawrence et al. [28] evaluated the differences in white matter microstructure between genders in a developmental sample of children aged 9 to 10. The study revealed that the gender differences in CST were the least significant,

while gender differences in FA during late childhood were found to be specific to geographical regions. Both boys and females exhibited substantial development in white matter microstructure during adolescence, which could be attributed to variations in pubertal maturation as puberty onset in females occurs 2 to 3 years earlier than in males [29].

Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) by age

The FA and ADC values of the participants in this study were compared among across age group; 13, 14, and 16 years old. The results indicate that there were no statistically significant differences in the FA and ADC values across the given age groups. Probably, this was may be attributed to the limited age range of the participants. However, previous studies have found contradictory results [30-35]. Bonekamp et al. [30] and Lebel et al. [31] studies had demonstrated the replicability of the FA and ADC in children between the ages of five and 19 years old, and five and 29 years old, respectively. This study investigated the age-related changes in the microstructure of brain white matter and studied the variations across different regions of the brain. The results showed that the CST continues to develop until the mid-thirties. This result can be achieved by including a broad age range. A positive association was seen between age and FA in nearly all white matter tracts. The age-related difference suggests continuing myelination and axonal packing in children beyond the age range [33]. Conversely, there is a direct negative correlation between ADC and age [35].

CONCLUSION

DTI is a non-invasive MRI technique used to identify tissue microstructural changes via alterations in quantitative parameters. DTI tractography assesses the structural integrity of white matter, and it has been widely used for prognostic and diagnostic purposes in various brain pathologies such as stroke, neurodegenerative diseases, and brain tumours. There were so many methods for tracking the fibers in the DTI including manual and automated ROI tracking. The finding of this study revealed a significant FA and ADC values that, nevertheless, fell within the established normal range for adolescents. Both methods are capable of providing a robust and dependable way of tracking the CST. Nevertheless, the different operational characteristics of various methods made it difficult to compare them directly.

The current study is subject to several limitations. One limitation of this study was the limited age range of the participants, encompassing individuals aged 13, 14, and 16 years old. The limited age range inhibits the evaluation of CST among teenagers accurately. It is advised that future research to include a wider variety of teenage ages in order to obtain more accurate baseline data on

the normative value of the CST. Another limitation of this study was the lack of standardisation in the shape and size of the ROI in the manual tracking method. This significantly affects the accuracy, reliability, and interpretation of outcome assessments.

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