DIFFUSION TENSOR IMAGING AND FIBRE TRACTOGRAPHY OF LEUKOARAIOSIS

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SCHOOL OF HEALTH SCIENCES
UNIVERSITI SAINS MALAYSIA
2016

DIFFUSION TENSOR IMAGING AND FIBRE TRACTOGRAPHY OF LEUKOARAIOSIS

by

FATIN AYUNI BINTI HANAPI

Dissertation submitted in partial fulfillment
of the requirements for the degree
of Bachelor of Health Science (Honours)
(Medical Radiation)

May 2016

CERTIFICATE

This is to certify that the dissertation entitled " DIFFUSION TENSOR IMAGING AND FIBRE TRACTOGRAPHY OF LEUKOARAIOSIS" is the bona fide record of research work done by Ms FATIN AYUNI BINTI HANAPI during the period from November 2015 to May 2016 under my supervision. I have read this dissertation and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation to be submitted in partial fulfillment for the degree of Bachelor of Health Science (Honours) (Medical Radiation).

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.....

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DECLARATION

I hereby declare that this dissertation is the result of my own investigations, except where otherwise stated and duly acknowledged. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at Universiti Sains Malaysia or other institutions. I grant Universiti Sains Malaysia the right to use the dissertation for teaching, research and promotional purposes.

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FATIN AYUNI BINTI HANAPI

Date: .....

ACKNOWLEDGEMENTS

Bismillahirrohmanirrohim.

First of all, I am very grateful to The Almighty God for pleasing me to complete this study. I wish to express my deep and deepest appreciation to Dr.Hartini Bt. Mohd Taib as my supervisor for supporting me during the research time.

Also thank to Pn.Suzana Mt Isa(Science Officer) and En. Hanif(Radiographer) for their helping me in acquiring all the data images while in IPPT.

I also place on record, my sense of gratitude to one and all who, directly or indirectly, especially my final year project (FYP) teammates that have lent their helping hand in this study.

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LIST OF SYMBOLS AND ABBREVIATIONS

DTI = diffusion tensor imaging

MRI = magnetic resonance imaging

MD = mean diffusion

FA = fractional anisotropy

LA = leukoaraiosis area

ROI = region of interest

CC = corpus callosum

CST = corticospinal tract

FLAIR = fluid attenuation inversion recovery

CSF = cerebrospinal fluid

NABT = normal appearing brain tissue

NAWM = normal appearing white matter

ABSTRAK

Imbasan pengimejan tensor difusi (DTI) adalah satu teknik penting dalam pengimejan resonans magnetik (MRI) yang digunakan dalam pengimejan otak. DTI mengesan dan mengukur pergerakan molekul air dalam sel-sel biologi. Ia menyediakan indeks skalar iaitu purata kemeresapan (MD) dan pecahan anisotropi (FA). Tambahan pula, berkas gentian neuron boleh dilihat dengan menggunakan teknik khas dalam DTI iaitu gentian tractography. Leukoaraiosis adalah sejenis penampilan yang tidak normal di kawasan jirim putih otak manusia dan rantau ini menunjukkan hyperintense pada imej wajaran - T2 dan pengecilan cecair penyongsangan pemulihan (FLAIR) resonans magnet (MR). Ia biasanya dijumpai di kalangan warga tua yang berkaitan dengan strok iskemia dan penyakit serebrovaskular. Objektif kajian ini adalah untuk membina semula peta parametrik DTI dan serat tractography dan mengukur nilai DTI dan bilangan gentian dalam corpus callosum (CC) dan saluran kortikospina (CST). Ia juga adalah untuk membandingkan nilai FA dan MD diperolehi antara kiri dan kanan CST. Subjek mempunyai leukoaraiosis di sebelah kanan kawasan hadapan jirim putih dan data analisis tepat telah diperolehi dengan menggunakan perisian komersial, NordicICE Versi 2.3.13. MD, FA, dan peta warna berkod FA dan gentian tractography telah dibina. Daya tarikan rantau terletak di corpus callosum dan di sebelah kanan dan kiri saluran kortikospina . Untuk CST tiada perbezaan dijumpai untuk nilai MD dan FA di kedua-dua belah kawasan. Gentian tractography menunjukkan bahagian kanan CST mempunyai gentian 17.4% lebih rendah berbanding bahagian kiri CST. Manakala, untuk corpus callosum nilai MD adalah 96.52 ± 30.34 dan FA adalah 0.56 ± 0.19 dengan bilangan 11451 gentian. Kesimpulannya, peta parametrik DTI dan serat tractography telah dibina semula serta boleh mengukur nilai DTI dan bilangan gentian

dalam CC dan CST. Perbandingan nilai DTI antara kanan dan kiri cst juga berjaya diperolehi.

ABSTRACT

Diffusion tensor imaging (DTI) is an important technique in magnetic resonance imaging (MRI) which is utilized in brain imaging . DTI detects and measures mobility of water molecules in biological cells. It also provides scalar indices which is mean diffusivity (MD) and fractional anisotropy (FA). Futhermore, the neuron fibre bundles can be visualized by using special technique in DTI, namely fibre tractography. Leukoaraiosis is a type of abnormal appearance in the white area of human brain and this region appears hyperintense on T2- weighted and fluid attenuation inversion recovery (FLAIR) magnetic resonance (MR) images. It is commonly found in normal elderly which is related to ischemic stroke and cerebrovascular disease. The objective of this study is to reconstruct the DTI parametric maps and fibre tractography and measure the DTI values and number of fibres in corpus callosum(CC) and corticospinal tract(CST). It is also to compare the FA and MD values obtained between right and left of CST. The subject had leukoaraiosis at right side frontal white matter region and data analysis was acquired by using commercial software, NordicICE Version 2.3.13. MD, FA, and colour coded FA maps and fibre tractography were constructed. Region of interest were located at corpus callosum and at right and left side of corticospinal tract. For CST no differences was found for MD and FA values at both sides. Fibre tractography showed right CST have 17.4% lesser number of fibers compared to left CST. Whereas, for corpus callosum the MD value is 96.52 ± 30.34 and FA is 0.56 ± 0.19 with 11451 number of fibres. In conclusion, DTI parametric maps and fibre tractography has been reconstructed, DTI values and number of fibres in CC and CST also can be measured. The comparison of DTI values between right and left side of CST was successfully obtained.

CHAPTER 1

INTRODUCTION

1.1 Background of study

Diffusion tensor imaging(DTI) is an important technique in magnetic resonance imaging(MRI) which is utilized in brain imaging. DTI detects and measures mobility of water molecules in biological cells. It is an imaging modality that can show detailed anatomy of the white matter, provide quantitative analysis of the magnitude and directionality of water molecules and can generates contrast that are sensitive to fiber orientations (Mori and Tournier,2014).

The two main parameter indices measurable from DTI are mean diffusivity(MD) or in the other term, apparent diffusion coefficient(ADC) as well as fractional anisotropy(FA). MD represents the diffusivity of water along the axons whereas fractional anisotropy(FA) describes the directionality of the water diffusivity. Besides, by using a special technique in DTI, namely fibre tractography, the neuron fibre bundles can be visualized. Specifically, tractography is a unique 3D reconstruction technique in DTI that uses the information from the scalar parameter indices to form the mathematical model of the neural tracts fiber bundles (Mohd Taib et.al 2015).

Leukoaraiosis is a type of abnormal appearance in the white area of human brain. White matter consist a huge bundle of axon that connect with grey matter of the brain and carry nerves fibres between neurons. Leukoaraiois region appears hyperintense on T2-weighted and FLAIR MR images.Its commonly found in normal elderly (Zhang and kang,2013). There is/are studies that relates leukoaraiosis to cerebrovascular disease (Grueter and Schulz,2011) and a pedictor of ischemic stroke (Kuller et.al, 2004).

1.2 Problem Statement

Assessment of leukoaraiosis is usually done using semi quantitative approach, that is by visual rating on FLAIR image.The rating is based on size, shape and distribution of the lesion (Kim et.al,2008). Therefore, in this study, DTI will be used to assess leukoaraiosis via quantitative values provided by this technique.

1.3 Aim of the study

The purpose of this study is to measure DTI values (MD,FA) in a subject with leukoaraosis and compare the values between that of measured in normal and leukoaraiosis area.

1.4 The specific objective

a) To reconstruct the DTI parametric maps and fibre tractography.

b) To measure MD, FA and number of fibres in corpus callosum and corticospinal tract.

c) To compare the DTI values obtained between right and left of corticospinal tract.

CHAPTER 2

LITERATURE REVIEW

2.1 Brain White Matter

In human brain there are two type of brain tissue which is gray matter and white matter. White matter cover almost half the human brain which composed of neuronal fibres (axons) and myelin in each image pixel(Burke,2006).Oligodendrocytes as glial cell made up from mylein sheaths that wrap the axons to ensure fast and efficent tranmission of electrical signals through them.

Myelin as an essential part of the white matter will cause conduction of impulses along nerve fibres slow down if they got damaged. Then lead to lost of brain functions.

2.2 Principles of Diffusion Imaging

A study conducted by(Mukherjee et.al, 2008), diffusion describes the random motion of molecules and also called as Brownian motion. Temperature is a factors that exhibit all molecules in this kind of motion. The rate of diffusion at constant temperature can be described by the Einstein equation: $< r^2 > = 6Dt$,

Where $<r^2>$ = mean squares displacement of the molecules

t = diffusion time

D = Diffusion constant (mm^2/s),

In clinical MR, the diffusion properties of water molecules are measured. In the human brain, diffusion is highest in the ventricles, where there are few barriers for the diffusion of water molecules. The diffusion of water in the brain parenchyma is significantly slower because of the presence of various structures, such as membranes and myelin sheaths, which obstruct the translation of water molecules.

2.3 Principles of Diffusion Tensor Imaging

The imaging data derive directional information of the neural tracts by using at least six diffusion gradient directions, which are adequate to compute the diffusion tensor. Fractional anisotropy (FA) that indicate the degree of a preferred diffusion direction in each voxel can be use for assessing of white matter fiber tract integrity, and notify about fibre directionality (Pierpaoli et.al, 1996). Beside that, diffusion in biological tissue was characterized by mean diffusivity (MD), which is calculated as the mean of the three eigenvalues of the diffusion tensor (Mori, 2007). MD measures the overall, non-directional mobility of water molecules in the brain tissue.

According to (Jones et.al,1999), leukoaraiosis refers to area of nonspecific increased signal in T2 weighted MRI. Leukoaraiois that always found in elderly population which suffers from hypertension show significant reduction in FA values in the areas of T2 hyperintensity ,as well as diffusion changes in the NAWM.Similarly, in previous study (0' Sullivan,2001) reported area affected by leukoaraiois have increased mean diffusivity (MD) and reduced anisotropy (FA).

2.3.1 Isotropic and Anisotropic Diffusion

In isotropic diffusion, represent as a sphere show equal directions of molecular motion. Body temparature at pure water gives isotropic diffusion, quantifies as appearent diffusion coefficient (ADC) of approximately 3.0×10^{-3} mm^2/s. In human brain, barriers to diffusion in white matter tracts include axonal proteins myelin. So that this diffusion considered as isotropic because ADC is same for all direction(Mukherjee et al, 2008).

Meanwhile, for anisotropic diffusion in terms of an ellipsoid describe different in all directions of molecular mobility. More than 1 diffusion-encoding direction needed to characterize regions of anisotrpic diffusion due to water displacement of white matter tract perpendicular to the direction of fibers, resulting in larger ADC.

2.4 Fiber Tractography

In methodology, according to (Mukherjee et.al, 2008) DTI fiber tracking was purposely to detemine intervoxel connectivity on the basis of the anisotropic diffusion of water.In white matter, the orientation of axonal fibers tends to be parallel to the direction of the major eigenvector of the diffusion tensor . Fiber tracking uses the diffusion tensor of each voxel to generate 3D fiber tractography in human brain.

Recently for clinical application, DTI has been used to identify and characterize novel defects in axonal growth and guidance in development disorders . An divergent fiber pathway, called as " asymmetric sigmoid bundle" was first identified with DTI fiber tracking in individuals with dysgenesis of the corpus callosum(Paul et.al,2007)

For fiber tracking, the corpus callosum was choosen as ROI due to largest white matter bundle in the brain. It have million of axons developing in brain that cross in the middle to connect homologous regions between both sides of hemisphere. (Vargas *et.a, 2011*). Otherwise, in voluntary movement corticospinal tract plays an important neural tracts. Its connect impulse from the brain to the spinal cord which control distal extremities movement.(Sun Yoo *et.al,2014*).

A few studies (Berman et.al,(2003)(Dubois et.al,2006) for many neurological disorders about 3D visualization have used fiber tracking to describe clearly white matter tracts for quantitative analysis. 3D regions of interest can be created specifically to an entire white matter tract by using this DTI fiber tracking.

CHAPTER 3

MATERIALS & METHODS

3.1 Data

A retrospective data was used in this study. The data consist of DTI and T1-weighted images obtained using 1.5 Tesla MRI System (Signal HDxt, GE Healthcare) available at Advanced Medical and Dental Institute Universiti Sains Malaysia (AMDI-USM). The subject was healthy male aged 67 years old when the scan was performed. The images were retrieved from USM PACS system and sent to an independent workstation for post processing and futher analysis. Post processing and analysis will be carried out using commercial software, nordicICE version 2.3.13. Subject never had any brain injury, neurological and/ or cardiovascular illness. Informed consent form was signed in compliance with the regulations of the institutional ethics committee.

3.2 MR Imaging Protocols

The DTI data was acquired using the protocols shown in Table 3.1. A parallel imaging technique, specifically Array Spatial Sensitivity Encoding Technique (ASSET) with acceleration factor (R) of 2 was applied during the scanning to shorten the scan time.

3.3 Image Processing and Fibre Tracking

Post processing and analysis data was carried out using commercial software, nordicICE Version 2.3.13 (NordicNeuroLab). Using this software, diffusion tensor elements, and anisotropy at each voxel were calculated. MD, FA, and colour coded FA maps and fibre tractography were constructed.

3.3.1 The data analysis were performed according to the following steps

Step 1: Importing DICOM data into the nordicICE DICOM Database

The DICOM Database was accessed as follows:

- The DICOM Database icon was clicked.
- Then 'File->Open DICOM Server' on the main menu was clicked.

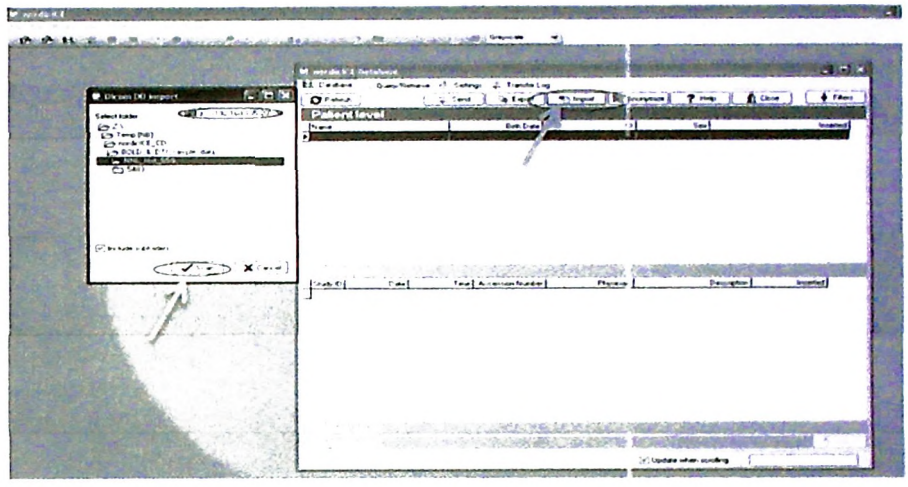


Figure 3.1 Database menu

Then the 'Import' button was clicked to import images into the nordicICE database. The folder to locate the imported DICOM data was selected by ticking off "Include subfolders", clicking "Scan". After clicking 'OK' the import results was displayed after the importing process completed.

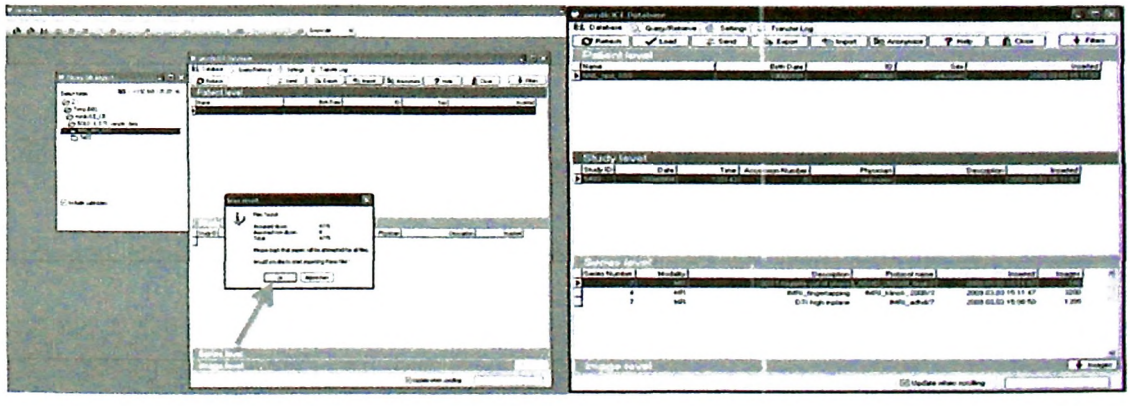


Figure 3.2 NordicICE Database

Step 2: Starting the BOLD/DTI Wizard

After nordicICE was launched, the BOLD/DTI Wizard was opened by clicking on the BOLD/DTI Wizard icon

Step 3: Selecting the patient

The patient was selected by clicking on the name. Then, to start the analysis the 'Next'-button was clicked.

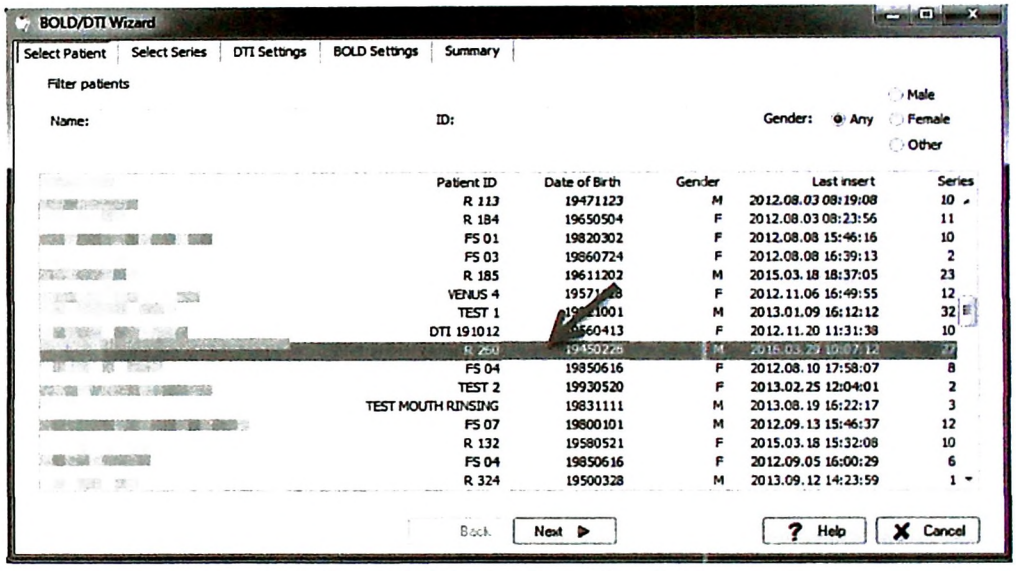


Figure 3.3 Selecting of patient

Step 4: Selecting image series

The dataset were selected. For each image series, some of the crucial DICOM attributes are listed, e.g; Series number, Modality, Series description, Protocol name and number of images. Structural and DTI data set was choosen and the 'Next' button was clicked to continue to the next step. The data that have been selected will now be loaded and are ready to configure the analysis settings.

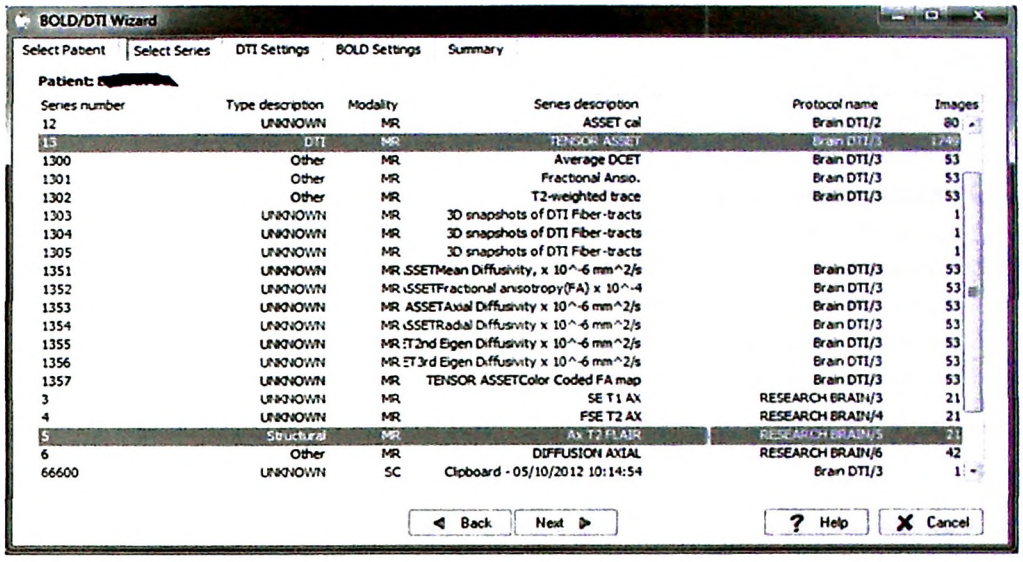


Figure 3.4 Selecting image series for selected patient

At a field called 'Type description', it contains image series like BOLD, DTI, and Structural datasets to distinguish the different image series. Next, 'Type description' of the image series was specified by clicking at right-click on an image series and the type of description was selected from the pop-up menu:

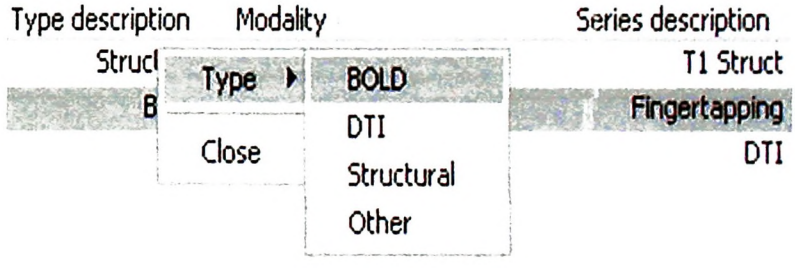


Figure 3.5 Selection of image description series

Step 5: Configure DTI setting

After that, the analysis settings for the DTI dataset was specified. In the DTI Acquisition specifications, the DTI parameters particularly the diffusion gradient directions and the b-value were displayed.

The ' Co-register to structural' box was clicked to allow DTI data set to be co-registered to the structural set and to make sure that reconstructed white matter fibre tracts will be aligned with the structural volume dataset.

The button 'Setting' was clicked to allow the Diffusion Tensor Imaging setting window appear and the various acquisition parameters and processing options was showed.

In this step, the noise level cutoff was set .Next, averaging of multiple b_0 and smoothing of all images was carried out to further reduce noise . Finally, by this software, motion correction and Eddy current correction was performed for correction of any motion artifacts or image distortion .

Fiber tracking was initiated by drawing seed region of interest (ROI) manually on sagittal images of colour-coded FA map at frontal lobes. Fiber tracking was performed using FA threshold of 0.1 and maximum turning angle of 45° .

After finished with the settings, 'OK'-button was clicked to close the settings window and ' Next'- button was aclicked to proceed to the next step.

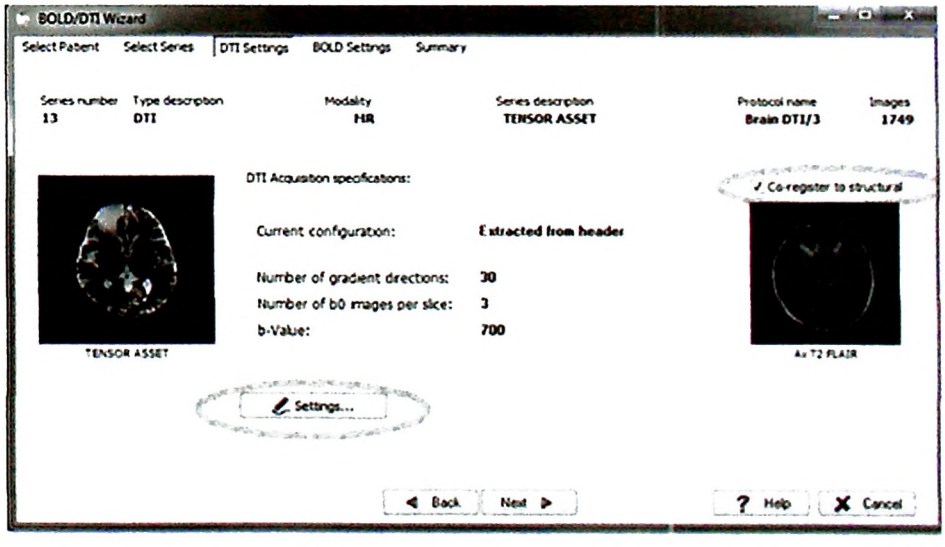


Figure 3.6 Co-register to structural of DTI data set

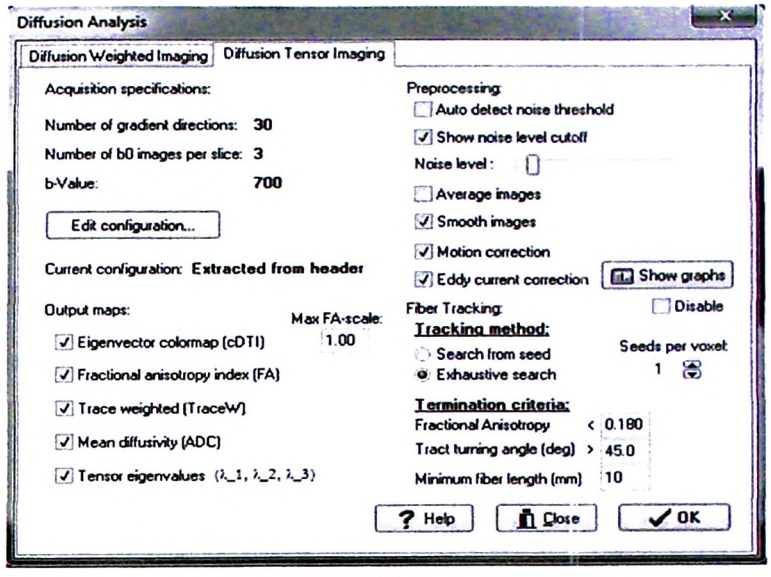


Figure 3.7 DTI data setting

Step 6: Start the analysis

Finally, the summary page was displayed showing which datasets have been selected for this session. Then the 'Finish'button was clicked to complete the Wizard and start the analysis

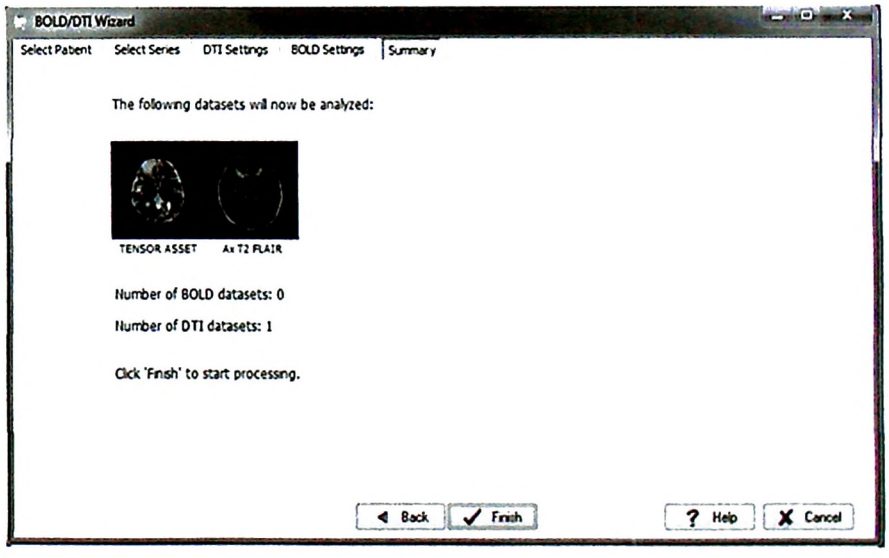


Figure 3.8 Analyzing of the datasets

Step 7:Performing co-registration

The purpose of this processing was to minimize effects of patient motion during data acquisition. The three steps in co-registration are:

- Applying motion/eddy current correction
- Analyzing Diffusion data- calculating DTI maps
- Analyzing Diffusion data- Reconstructing fibers

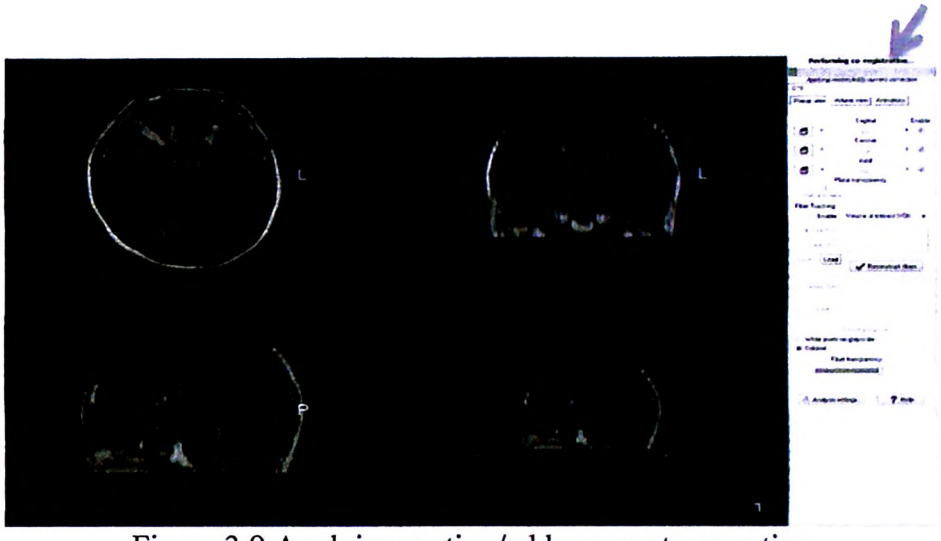


Figure 3.9 Applying motion/eddy current correction

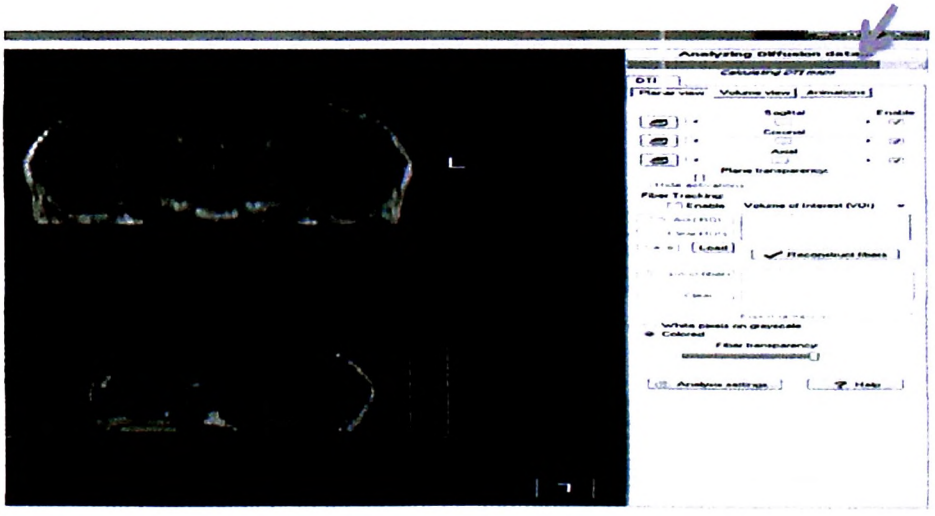


Figure 3.10 Analyzing Diffusion data- calculating DTI maps

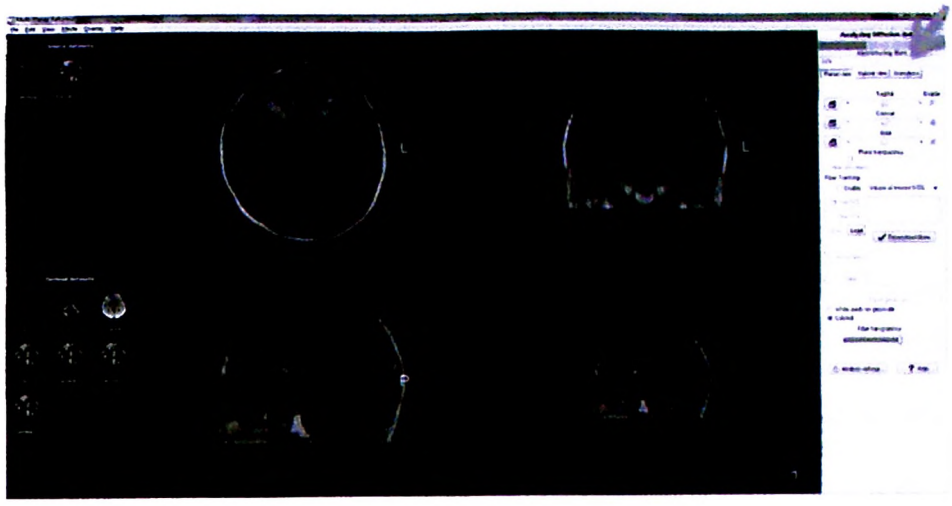


Figure 3.11 Analyzing Diffusion data- Reconstructing fibers.

Step 8: Graph analysis

For graph analyzing, ' Show graphs' button was clicked.The result for co-registration analysis were displayed as graph as shown in Figure. Results for co-registration analysis were displayed in the form of graph which are in rotations, translation and shear movement.

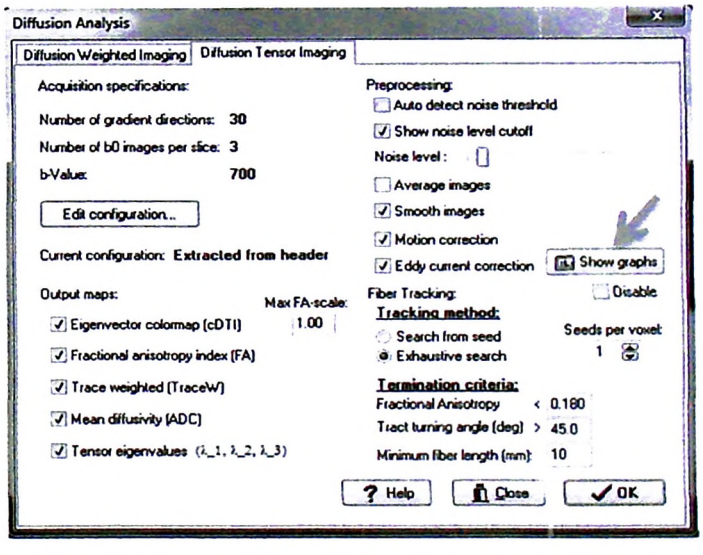
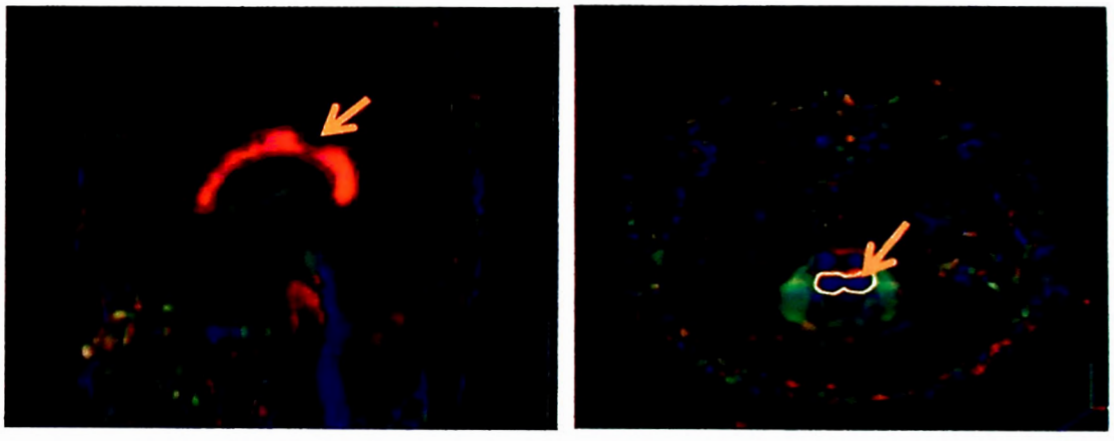


Figure 3.12 Graph analysis setting

Step 9: Region of Interest (ROIs) placement

In this study, two fibre bundles were analyzed specifically callosal fibres and corticospinal tract fibres. These fibre bundles are the major fibre bundles in the brain.The ROI was drawn manually using freehand ROI tool. For the callosal fibres, the ROI was drawn at the area of corpus callosum, as depicted in Figure 3.12(a). Whereas for corticospinal tract, the first ROI was drawn at the posterior limbs of the internal capsule (PLIC) as shown in Figure 3.12(b). Then, the second ROI was drawn at the right and left side of corticospinal tract to make a comparison of no.of fibres and quantitative parameters between them.



(a) **(b)**

Figure 3.13 (a)1st ROI was drawn at callosal fibre on sagittal slice followed by second (b)ROI at corticospinal tract on coronal slice

Step 10: Fiber reconstructing

Once ROIs placement, ' Add ROI' was clicked and 'Enable'box was checked.After ROIs/VOIs has been defined, the fibre reconstruction was performed by showing no of fibers and other quantitative parameters like FA, ADC and eigenvalues.

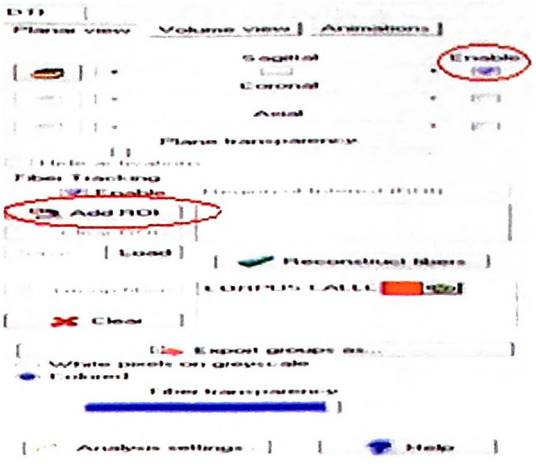


Figure 3.14 Reconstruct Fibres setting

Figure 3.15 Images after fibre reconstruction for each ROI

CHAPTER 4

RESULT

4.1 Co-registration Analysis

From co-registration analysis, three graph were showed which indicates the movement of patient during scanning procedure as shown in Figure 4.1. Results are displayed in the form of (a)rotation ,(b) translation and (c)shear – scale graphs. Based on the graph, we can conclude that there is a slight movement of patient during scanning.

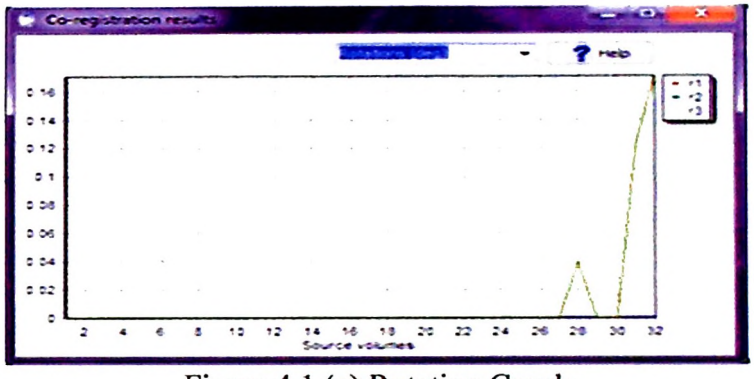


Figure 4.1 (a) Rotation Graph

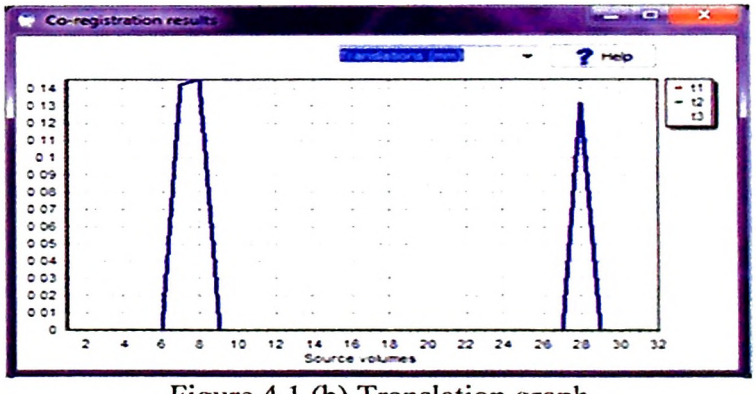


Figure 4.1 (b) Translation graph

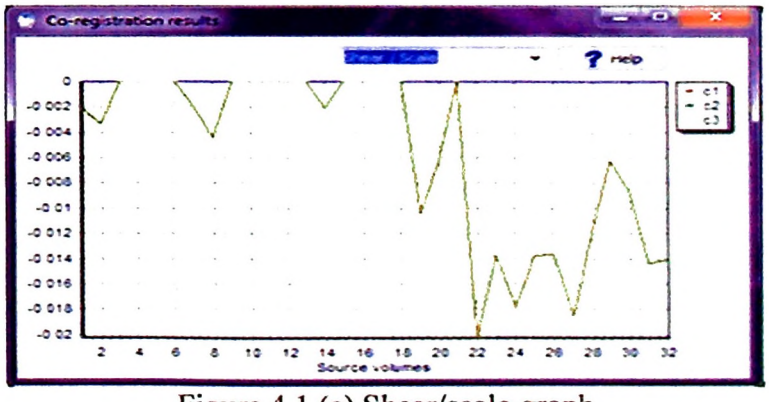


Figure 4.1 (c) Shear/scale graph

4.2 DTI Parametric Maps

After DTI dataset were analyzed , $\lambda_1, \lambda_2 \lambda_3$,Trace, ADC, FA, cDTI maps are reconstructed as displayed in Figure 4.2. The structural images,which is FLAIR image is also shown in Figure 4.2. Fiber tractography appeared a discontinuity of nerve fibre tracts at the area of leukoaraiosis that is in the right frontal white matter region as in Figure 4.3.

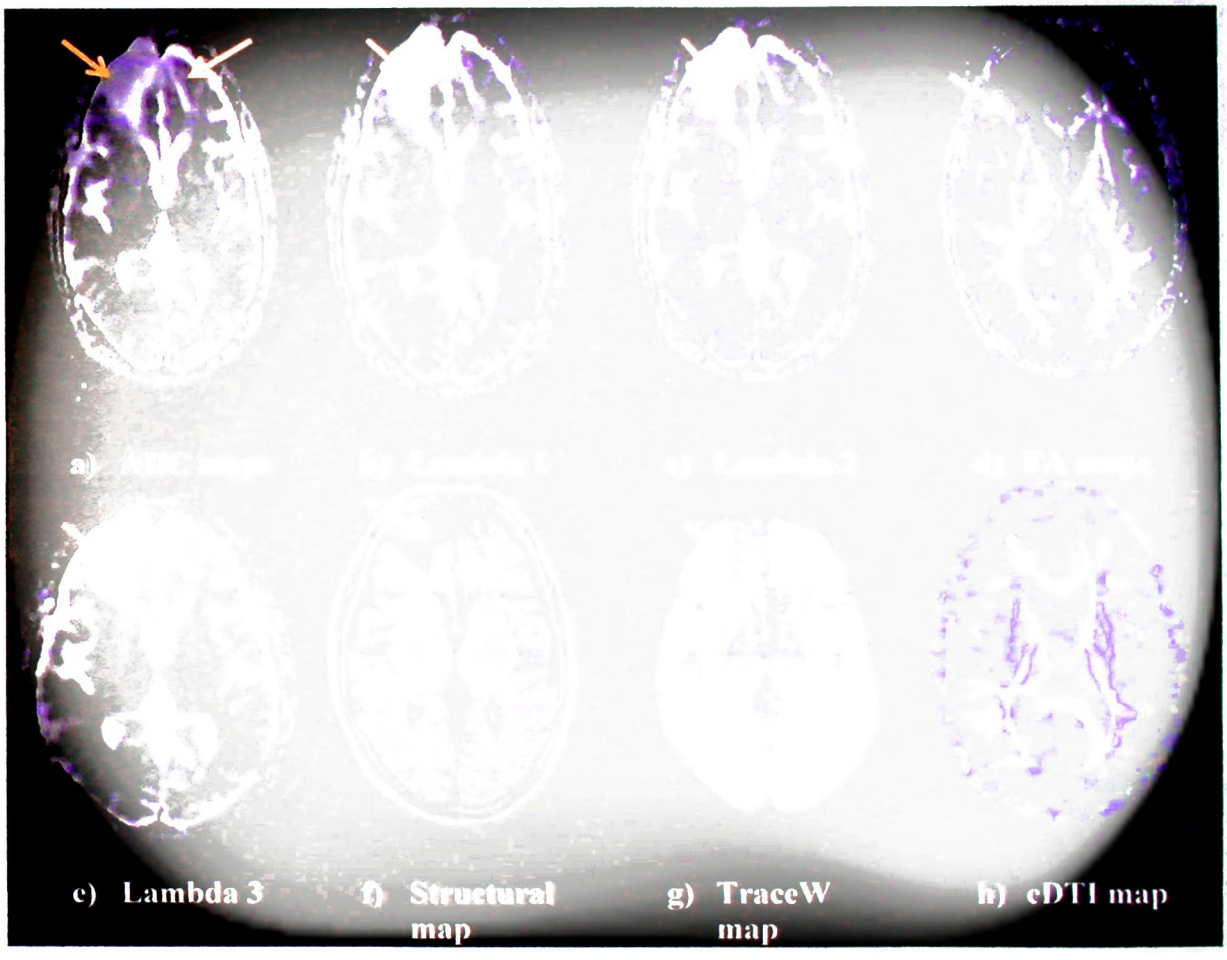


Figure 4.2 DTI parametric maps of normal and leukoaraiosis area of brain. The arrow shows area of leukoaraiosis in the frontal white matter. The bright appearance of leukoaraiosis was noted in ADC map. Its show high diffusivity with low anisotropy in the cDTI map.

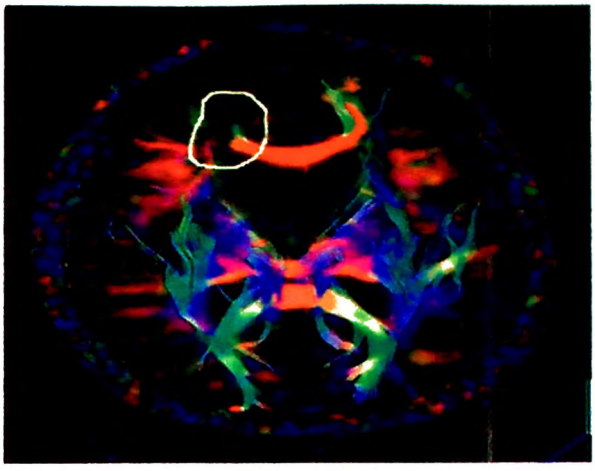


Figure 4.3 A discontinuity of nerve fibre tracts at the area of leukoaraiosis in the right frontal white matter

4.3 Comparison of DTI values and tractography between right and left CST

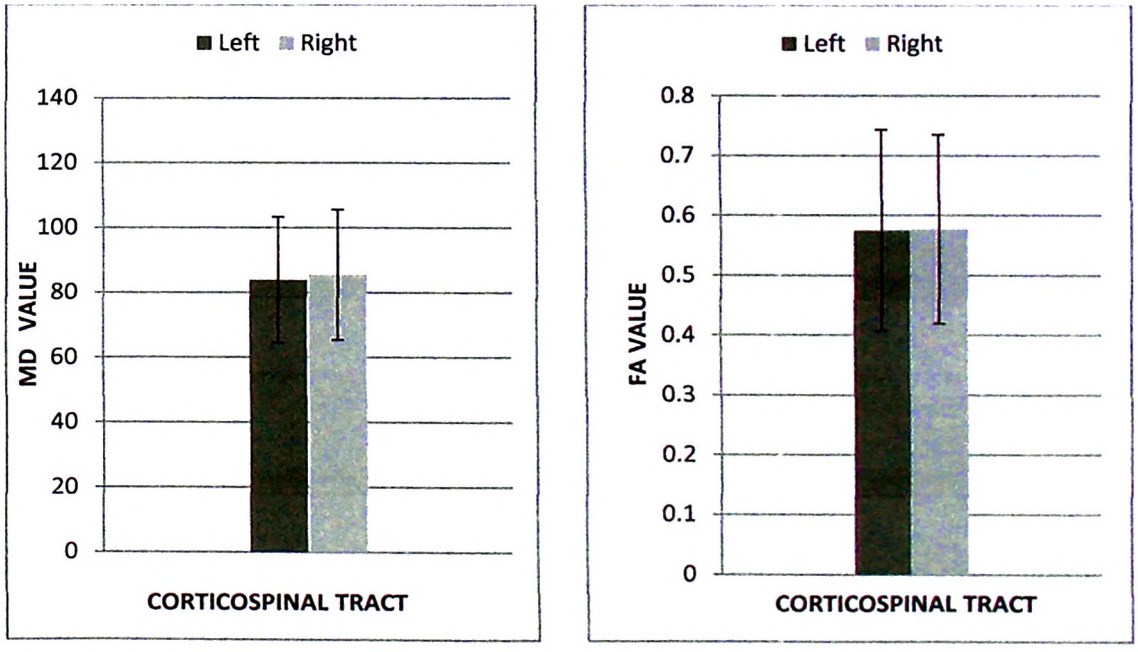
4.3.1 Comparison of DTI values

Comparison of MD and FA values was made between right and left corticospinal tract and the result was shown in Table 4.1.

Region of interest(ROI)		MD ($\times 10^{-5}$ mm²/s)	FA
Corticospinal tract (CST)	Right	85.45 ± 20.08	0.58 ± 0.16
	Left	83.91 ± 19.39	0.57 ± 0.16

Table 4.1 MD and FA values of right and left CST

Based on the previous study (Mohd Taib et.al,2012),supposely for leukoaraiosis it have higher MD and reduced FA compared in normal area. In this study,there is no significant difference in MD and FA values between right and left CST.



(a) (b)

Figure 4.5 (a) MD and (b) FA values at left and right CST that show no significant difference

4.3.2 Comparison of fibre tractography obtained in right and left corticospinal tract

The fibre tractography of CST is shown in Fig 4.6. There was a slight difference in number of fibres found between right and left cst, that is 17.4%. Less number of fibre bundle was found at right side compare to left side of CST. Fiber direction was indicated as follows; red: right-left, green: anterior-posterior, and blue: superior-inferior.

ROI		Number of fibres
Corticospinal tract (CST)	Right	443
	Left	520

Table 4.2 Number of fibres for right and left CST

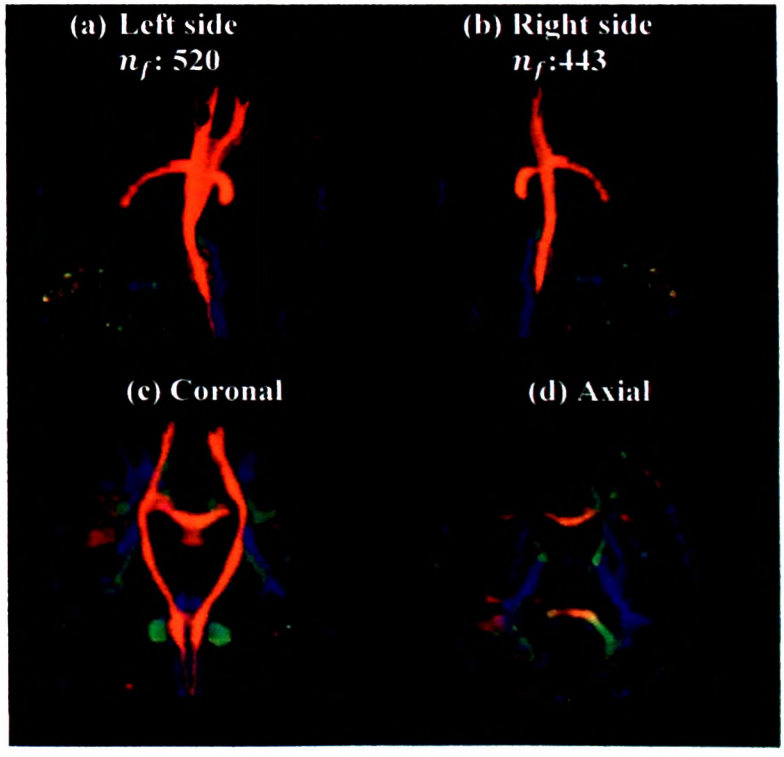


Figure 4.6 (a)left sagittal view, (b)right sagittal view, (c)coronal view and (d) axial view of corticospinal tract

There is 17.4% of reduction fibre's number between right and left side of corticospinal tract as in Figure 4.7.

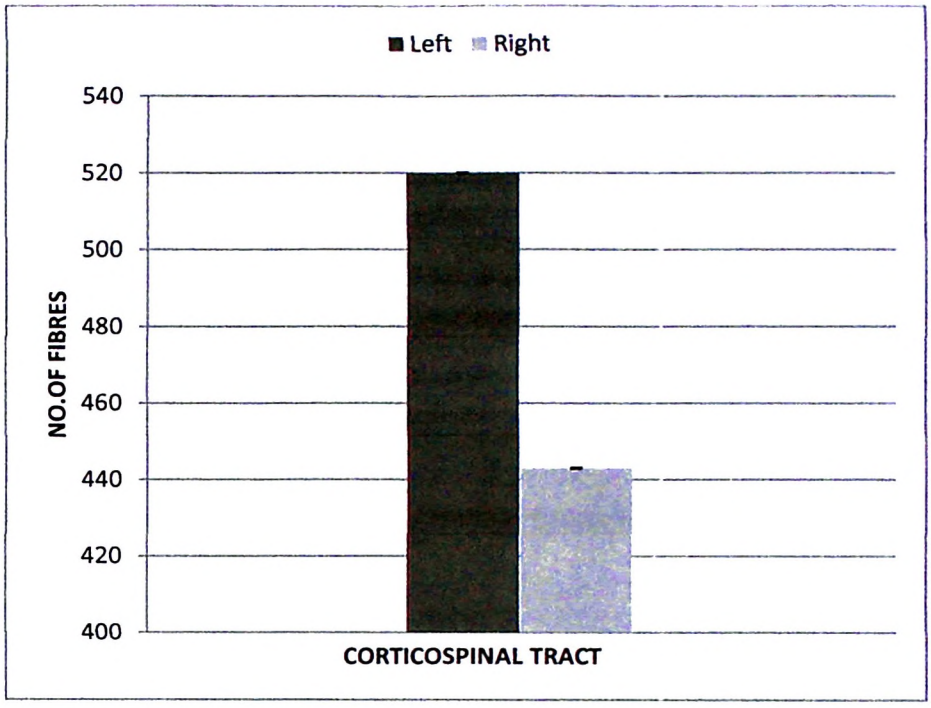


Figure 4.7 Number of fibres for right and left side of corticospinal tract

4.4 DTI Values and Fibre Tractography of Corpus Callosum

For corpus callosum, the MD value is 96.52 ± 30.34 and FA is 0.56 ± 0.19 with 11451 number of fibres as shown in Table 4.3.

ROI	Number of fibres	MD ($\times 10^{-5}$ mm²/s)	FA
Corpus callosum	11451	96.52 ± 30.34	0.56 ± 0.19

Table 4.3 DTI values and fibre tractography for CC

This is an images acquired after fibre tracking which show the corpus callosum from sagittal an axial view. Fiber direction was indicated as follows; red: right-left, green: anterior-posterior, and blue: superior-inferior as shown in Figure 4.9.

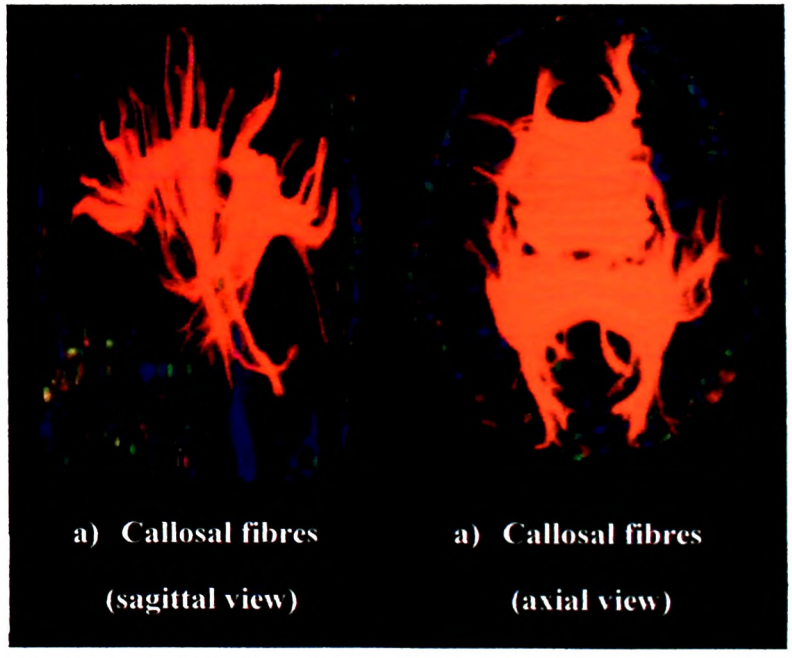


Figure 4.8 Images of Callosal fibre from a) sagittal view and b) axial view

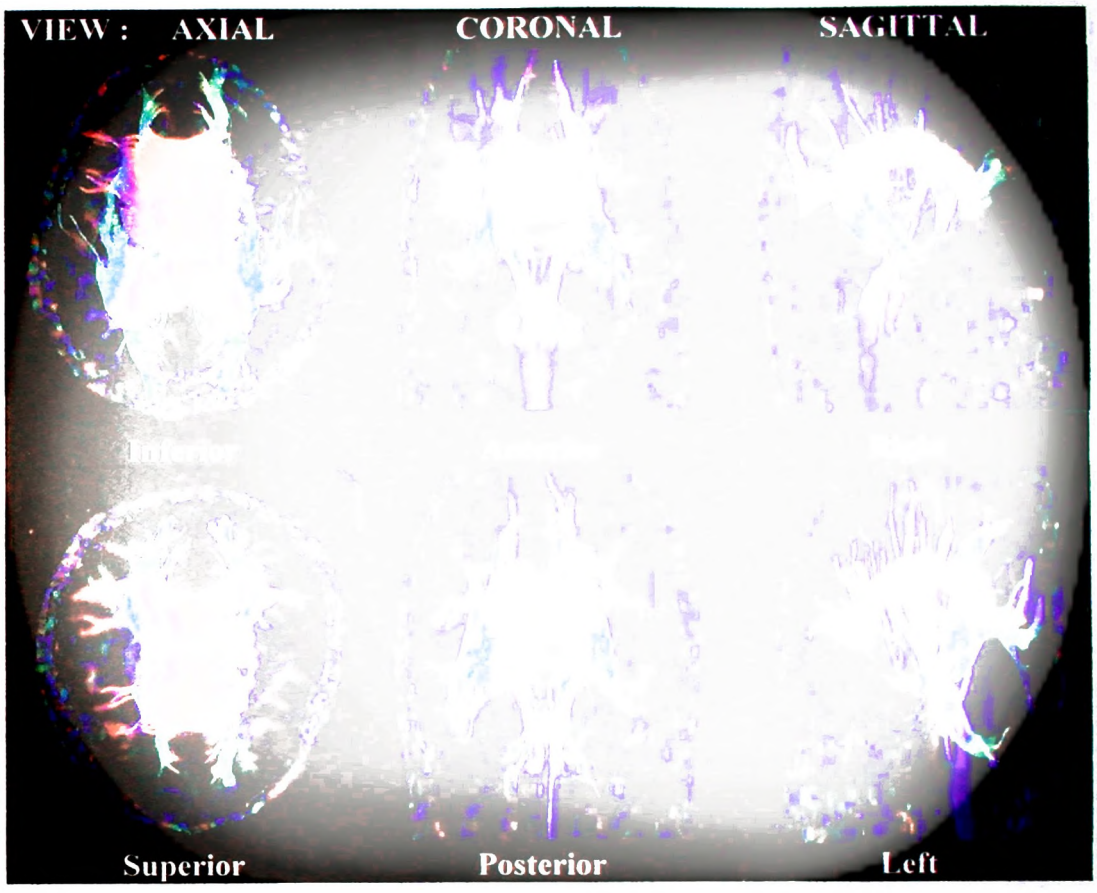


Figure 4.9 Images of CC in axial, coronal and sagittal view.

CHAPTER 5

DISCUSSION

A few study have done to measure and compare quantitative parameters of DTI for subject which have leukoaraiosis by comparing MD and FA values of grey matter, CSF, LA and NABT area. Specifically, this study are more focus to corpus callosum and corticospinal tract. In this study, an evaluation was made on MD and FA values and fibre tractrography at for both corpus callosum and corticospinal tract.

First region of interest was drawn at area of corpus callosum followed with second ROI for CST at posterior limbs of the internal capsule (PLIC) up to the parietal lobe. The comparison was made between right and left CST and the result was normal and not impressed with leukoaraiosis

Based on the result, MD values found in right CST is slightly higher than left CST. Unfortunately, FA value in right CST is same with left CST which is contrast with findings from previous reported studies which supposely, FA should have lower value due to less manner of specific direction of water molecules. (Mohd Taib et.al, 2015). However, there is only small differences of FA value for both region.It may lead to early signs of tissue damaged at that right CST. According to (Heiervang et.al,2006), his study revealed that FA is more variable among normal subjects than MD.

Fibre tractography clearly demonstrates fibre tracts on condition of white matter with and without leukoaraiosis. Fibre tractography at corticospinal tract (CST) shows significantly reduced number of fibres on the right side of CST which better demonstrated on cDTI colour maps. Percentage difference is 17.38% between right and left CST. The difference number of fibres detected at right CST can be area of leukoaraiosis.