

Role of Diffusion Tensor Imaging in evaluation of Alzheimer's Disease

Essay

Submitted for partial fulfillment of Master's degree
in
Radiodiagnosis

By

Shereif Ahmed Momtaz Mostafa Haykal
M.B., B.Ch.

Supervised by

Dr. Lobna Abdelmoneim Habib

*Assistant Professor of Radio diagnosis
Faculty of medicine, Ain-shams University*

Dr. Yosra Abdelzaher Abdualлах

*Lecturer of Radio diagnosis
Faculty of medicine, Ain-shams University*

Faculty of medicine
Ain-shams University
2013

دور الرنين المغناطيسي باستخدام الانتشار ممتد الكمية في تقييم مرض الزهايمر

رسالة تمهيداً للحصول علي درجة الماجستير في الاشعة التشخيصية

مقدمة من

طبيب / شريف أحمد ممتاز مصطفى هيكل
بكالوريوس الطب و الجراحة العامة

تحت إشراف

أ.د/ لبنى عبد المنعم حبيب

أستاذ مساعد الاشعة التشخيصية
كلية الطب- جامعة عين شمس

د/ يسرا عبدالظاهر عبدالله

مدرس الاشعة التشخيصية
كلية الطب- جامعة عين شمس

كلية الطب

جامعة عين شمس

2013

بسم الله الرحمن الرحيم



(سورة الرحمن: الآية 1 و2)

Acknowledgments

First and foremost I would like to thank God for all of His blessings, for guiding me throughout my life and for giving me the patience and wisdom to undertake this endeavor.

I would like to express my deep appreciation to Dr. Lobna Abdelmoneim Habib, Assistant Professor of Radiodiagnosis, Faculty of Medicine, Ain Shams University, for her support and guidance throughout the whole work. It is a great honor to have worked under her supervision.

I would also like to thank Dr. Yosra Abdelzaher Abdullah, Lecturer of Radiodiagnosis, Faculty of Medicine, Ain Shams University, for her continuous help and the tremendous effort that she has put forth in the meticulous revision of this work.

To my family, I'm forever grateful for your support and encouragement and for always putting my needs before yours.

Shereif Ahmed Momtaz Haykal

Contents

List of Abbreviations	I
List of Figures.....	III
List of Tables.....	VI
Introduction and Aim of the Work.....	1
Chapter 1 – Anatomy of Brain White Matter Tracts.....	4
Chapter 2 – Pathology of Alzheimer’s Disease.....	33
Chapter 3 – Physical principles and Technique of Diffusion Tensor Imaging.....	41
Chapter 4 – Role of DTI in evaluation of Alzheimer's disease...	61
Summary and Conclusion.....	84
References.....	87
Arabic Summary	

List of Abbreviations

3 D	Three dimensional
A β	Amyloid- β
AD	Alzheimer's Disease
ADC	Apparent Diffusion Coefficient
aMCI	Amnesic Mild Cognitive Impairment
COH	Mean regional intervoxel coherences
CP	Cerebral Peduncle
CSF	Cerebrospinal Fluid
CT	Computed Tomography
DT	Diffusion Tensor
DTI	Diffusion Tensor Imaging
DTT	Diffusion Tensor Tractography
DW	Diffusion Weighted
EC	Entorhinal Cortex
EEG	Electroencephalography
EPI	Echo Planar Imaging
FA	Fractional Anisotropy
FACT	Fiber Assignment by Continuous Tracking
FOV	Field Of View
GE	Gradient Echo
HF	Hippocampus
HPC	Hippocampus
ICp	Posterior limb of Internal Capsule
ILE	Inferior Longitudinal Fasciculus
MCI	Mild Cognitive Impairment
MD	Mean Diffusivity
MPRAGE	Magnetization Prepared RApid Gradient Echo
MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
NC	Normal Control

NCI	No Cognitive Impairment
NFTs	Neurofibrillary Tangles
NPs	Neuretic Plaques
OA	Non-demented older adult
PCC	Posterior Cingulate Cortex
PWM	Parahippocampal White Matter
RA	Relative Anisotropy
ROI	Region Of Interest
SLE	Superior Longitudinal Fasciculus
SPGR	Spoiled Gradient
T	Tesla
T1WIs	T1 Weighted Images
T2WIs	T2 Weighted Images
TBSS	Tract Based Spatial Statistics
TE	Echo Time
TI	Inversion Time
TR	Repetition Time
WB	Whole Brain
WM	White Matter

List of Figures

Fig. No.	Title	Page
1.1	Cingulum, sagittal view.	5
1.2	Superior occipitofrontal fasciculi, sagittal view.	6
1.3	Inferior Occipitofrontal Fasciculus, gross dissection, lateral view	7
1.4	Uncinate fasciculus, sagittal view.	8
1.5	Superior longitudinal fasciculus, gross dissection, lateral view.	9
1.6	Corpus callosum, axial view.	12
1.7	Anterior Commissure, gross dissection.	13
1.8	Corticospinal tract: Illustration.	15
1.9	The origin, course, and termination of the corticospinal tract.	16
1.10	Illustration and gross dissection, medial view of the corona radiata.	17
1.11	Internal capsule, axial view, illustration.	18
1.12	Geniculocalcarine tract (optic radiation), axial view.	19
1.13	Cingulum, sagittal view.	21
1.14	Superior occipitofrontal fasciculi, sagittal view, tractogram.	22
1.15	Inferior occipitofrontal fasciculus and inferior longitudinal fasciculus, axial directional map.	23
1.16	Tractogram of the inferior occipitofrontal fasciculus.	23
1.17	Uncinate fasciculus, sagittal view, tractogram.	24
1.18	Superior longitudinal fasciculus, sagittal view.	25
1.19	Inferior longitudinal (occipitotemporal) fasciculus.	26
1.20	Corpus callosum, axial view.	27
1.21	Sagittal directional map of the corpus callosum and tractogram.	28
1.22	Inter-subject track variability maps of the anterior commissure in standard space.	28
1.23	Corticospinal tract: Coronal directional map and Tractogram.	29
1.24	Directional map and Tractogram of Corona Radiata.	30
1.25	Internal capsule, axial view, directional map.	31
1.26	Geniculocalcarine tract (optic radiation), axial view.	32

2.1	Gross photograph of the brain of a patient with Alzheimer's disease.	35
3.1	Diffusion within a single voxel.	43-45
3.2	Diagram showing the cellular elements that contribute to diffusion anisotropy.	45
3.3	Multiple transverse DW images of same brain slice with diffusion gradients applied in different directions demonstrate anisotropic diffusion.	47
3.4	Common types of coronal DT images in a healthy subject.	49
3.5a	Abstract representation of tensors in a 5 x 5 grid, with two regions of interest.	52
3.5b	Streamline tractography propagates a fiber tract in the direction of principal eigenvector.	53
3.5c	Probabilistic tractography produces a likelihood map of the diffusion path between two ROIs.	53
3.5d	Coronal images of internal capsule in healthy adults demonstrate diffusion ellipsoid maps.	54
3.5e	Streamline tractography of corticospinal tract.	54
3.5f	Probabilistic tractography of corticospinal tract.	55
3.6a	Tractography of corticospinal tract performed by iteratively extending streamlines from a seed ROI in the direction of principal eigenvector by using the fiber assignment by continuous tracking, or FACT, algorithm .	56
3.6b	Volume-rendered probability map of corticospinal tract produced by generating several thousand tracts from each seed voxel.	56
4.1	Illustration of ROIs positioned on T2-weighted echoplanar images	63
4.2	Transverse MR images show ROIs at which ADC, FA, and RA values were determined	63
4.3	Illustration of a fractional anisotropy map.	66
4.4a	Fractional anisotropy color-coded map shows splenium of corpus callosum, right posterior cingulate gyrus, and left posterior cingulate gyrus.	67
4.4b	Fractional anisotropy color-coded map shows right superior longitudinal fascicle and left superior longitudinal fascicle.	67
4.4c	Fractional anisotropy color-coded map shows right hippocampus and left hippocampus.	67
4.5	Triplanar view of the hippocampus , entorhinal cortex, and perforant pathway region on a high-resolution 3D MPRAGE sequence.	69

4.6	Corresponding axial T1 image and interpolated DTI map.	70
4.7	Axial anisotropy map with a graphical illustration of the tensors in the hippocampus, entorhinal cortex, and perforant pathway zone.	70
4.8	A coronal slice illustrating the segmentation of the entorhinal cortex, hippocampus and parahippocampal white matter.	72
4.9	Example of tractography results for an older healthy control participant.	72
4.10	Average fractional anisotropy and mean diffusivity for participants with amnesic MCI and healthy controls with no cognitive impairment.	73
4.11	Top panel. Example of a mean FA map in nondemented older adults and patients with AD resulting from the spatial normalization of the FA volumes from tract based spatial statistics (TBSS). Bottom panel. Example of an individual FA map in a non-demented older adult and in a patient with AD.	74
4.12	TBSS-based statistical comparison of FA and diffusivity between OA and AD, regressing out T2 signal intensity.	75
4.13	TBSS-based statistical comparison of FA and diffusivity between OA (nondemented older adults) and AD.	76
4.14	DTT and voxelization along the posterior cingulum.	77-79
4.15	DTI–fiber tracts from ROI to the Whole Brain (WB). NC subject; MCI subject; AD subject.	80
4.16	Statistical analysis of fiber tracts shows mean and one standard deviation for three groups.	81
4.17	Regions of interest: posterior limb of the internal capsule, superior longitudinal fasciculus, cerebral peduncles, and inferior longitudinal fasciculus overlaid on mean FA skeleton.	82
4.18	Voxelwise group differences in the uncinate fasciculus, inferior longitudinal fasciculus, fornix, splenium, cingulum, forceps major and superior longitudinal fasciculus overlaid on mean FA skeleton.	82

List of Tables

Table no.	Title	Page
4.1	Mean diffusivity values of the selected white matter areas from Alzheimer patients and controls.	64
4.2	Fractional anisotropy values of the selected white matter areas from Alzheimer patients and controls.	66
4.3	Fractional Anisotropy Values in Regions of Interest.	67
4.4	Mean values and standard deviations for normalized ROI volumes and mean regional intervoxel coherences.	71
4.5	Average fractional anisotropy values for Alzheimer's disease patients and healthy normal control participants for each region of interest.	83

Introduction

Alzheimer disease (AD) is the most common neurodegenerative disease and the most common cause of dementia. The number of those affected by AD is rapidly increasing as the world's population ages. It is estimated that by the year 2050, the number of people with AD will increase threefold, to about 60 million worldwide (*Barakos and Purcell, 2012*).

AD is clinically characterized by cognitive impairment, including memory dysfunction, severe enough to interfere with activities of daily living. However, cognitive symptoms and brain abnormalities may be present many years before a clinical diagnosis of AD can be made. This preclinical phase of AD is the subject of intense investigation, since prompt diagnosis could allow early drug therapy, thereby improving the chances for a positive clinical response (*Ramani et al., 2006*).

Although the cause of AD is not clear, histopathologically the disease is characterized by two abnormal structures in the brain: neuritic plaques and neurofibrillary tangles. Both plaques and tangles seem to interfere with normal neuronal functioning (*Barakos and Purcell, 2012*).

The microscopic histological changes in the neurodegenerative diseases are inevitably associated with progressive regional and global brain atrophy, which could be assessed using conventional CT and MR imaging. However,

neuroanatomical changes over time may be too mild, diffuse, or topographically complex to be detected by simple visual inspection or even with manually traced measurements of regions of interest (*Barkhof et al., 2011*).

In addition to the examination of grey matter in AD, there is increased interest in white matter changes in these conditions. Reports of pathological white matter changes have been documented in at least 50% of patients with AD (*Stebbins and Murphy, 2009*).

MRI T2 signal decay rate has been used to document increased white matter damage in patients with AD. Although T2 weighted MRI scanning is sensitive to white matter damage, it does not provide information on the microstructural integrity of white matter (*Bartzokis et al., 2003*).

DTI is an MRI scanning technique that allows for the examination of white matter microstructural integrity based on the directionality of diffusion in the brain. DTI indices show a significant association with cognitive functions typically impaired in AD, including mental status (*Fellgiebel et al., 2008*).

Studies of DTI in dementia have consistently shown altered diffusion (tract) properties in accordance with the pattern of neurodegenerative pathology. By using DTI and fiber tracking, tract-specific pathology can be demonstrated, which may be specifically linked to the clinical syndrome at hand (*Barkhof et al., 2011*).

Aim of the work :

The aim of this study is to illustrate the role of diffusion tensor imaging (DTI) in the diagnosis and follow up of Alzheimer's dementia.

Chapter 1

Anatomy of Brain White Matter Tracts

The nerve fibers which make up the white matter of the cerebral hemispheres are categorized on the basis of their course and connections. They are either:

- **Association fibers**, which link different cortical areas in the same hemisphere
- **Commissural fibers**, which link corresponding cortical areas in the two hemispheres
- **Projection fibers**, which connect the cerebral cortex with the corpus striatum, diencephalon, brain stem and the spinal cord (*Standring et al., 2008*).

Gross Anatomy of White Matter Tracts:

Association Fibers:

Association fibers interconnect cortical areas in each hemisphere. They consist of axons arising from small pyramidal cells, primarily from cortical layers II and III. These fibers vary in length from short to long, and project in the ipsilateral hemisphere. Association fibers that connect various cortical areas make up most of the subcortical white matter. These fibers gather to form fasciculi that connect different lobes, but, like a two-way highway, fibers merge into and exit these fasciculi all along their course (*Patestas and Gartner, 2006*).