# MAGNETIC RESONANCE SPECTROSCOPY IN EVALUATION OF MULTIPLE SCLEROSIS

**Essay**

**Submitted for partial fulfillment**

**Of master degree in radio diagnosis**

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2017

# Acknowledgement

First of all, all gratitude is due to Allah almighty for blessing this work, until it has reached its end as a part of his generous help throughout my life.

Really I can hardly find the words to express my gratitude to Prof. Dr. Eman Soliman Metwally; professor of Radio-diagnosis, faculty of medicine, Ain Shams University for her supervision, continuous help, & encouragement throughout this work and the tremendous effort she has done in the meticulous revision of the whole work. It is a great honor to work under her supervision and guidance.

I would like also to express my sincere appreciation and gratitude to Prof. Dr. Togan Taha, Assistant Professor of Radio-diagnosis, faculty of medicine, Ain Shams University for her continuous directions and support throughout the whole work.

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward; this work would not have ever been completed.

Mustafa Heidar

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# LIST OF ABBREVIATIONS

- $^{1}H$ MRS: proton Magnetic Resonance Spectroscopy
- CHESS: CHEmical shift Selective imaging Sequence
- CIS: Clinically Isolated Syndrome
- cMRI: Conventional Magnetic Resonance Imaging
- CSI: Chemical Shift Imaging
- DAWM: Dirty Appearing White Matter
- DTI: Diffusion Tensor Imaging
- ECC: Eddy Current Correction
- EPI: Echo-Planar Imaging.
- EPSI: Echo-Planar Spectroscopic imaging.
- FID: Free Induction Decay
- FOV: Field Of View
- FWHM: Full Width At Half Maximum
- FWTM: Full Width At Tenth Maximum
- GF: Frequency-encoding Gradient.
- GP: Phase-encoding Gradient
- GRAPPA: Generalized auto-calibrating partial parallel acquisition.
- GRE: Gradient Echo.
- MRSI: magnetic resonance spectroscopic imaging
- MTI: Magnetization Transfer Imaging
- NABT: Normal Appearing Brain Tissue
- NAGM: Normal Appearing Gray Matter
- NAWM: Normal Appearing White Matter
- NMO: NeuroMyelitis Optica
- OVS: Outer Volume Suppression
- PPM: Parts Per Million
- PPMS: Primary Progressive Multiple Sclerosis
- PRESS: Point RESolved Spectrsocopy
- PRMS: Primary Relapsing Multiple Sclerosis
- QC: Quality Control
- QUALITY: QUAntification by converting to the LorentzIan TYpe
- RF: Radio-Frequency
- RIS: Radiologically Isolated Syndrome

- RRMS: Relapsing Remitting Multiple Sclerosis
- S/N: single to noise ratio
- SE: Spin Echo.
- SENSE: Sensitivity Encoding,
- SMASH:  Simultaneous Acquisition of Spatial Harmonics
- SPMS: Secondary Progressive Multiple Sclerosis
- STEAM: STimulated Echo Aquistation Mode
- STIR: Short TI Inversion Recovery
- SVA: Single Voxel Aquistation
- SVS: Single Voxel Spectroscopy.
- SWI: Susceptibility Weighted Images.
- TDE: Turbo Spin Echo
- TDL: Tumefactive Demyelinating Lesion.
- TE: Echo Time.
- TR: Repetition Time.
- VOI: Voxel Of Interest.
- WMH: White Matter Hyperintensities.

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# INTRODUCTION

Multiple sclerosis (MS) is a complex autoimmune disease with a heterogeneous presentation and diverse disease course.

Recent studies indicate a rising prevalence of MS in the Middle East, MS affects individuals during the most productive time of their lives, and directly limits their work capacity, leading to major social and economic consequences; The mean age at MS onset is 26.61±7.82 years, With female dominance. With (female: Male) ratios of (2.14:1).

*(Hamdy et al., 2017)*

MS is a chronic inflammatory disorder of the central nervous system. There are multiple plaques of demyelination within the brain and spinal cord. Plaques are 'disseminated in time and place, hence the old name disseminated sclerosis.

*(Clarke, 2009)*

Multiple sclerosis (MS) is characterized by loss of motor and sensory function that results from immune-mediated inflammation, demyelination and subsequent axonal damage. MS is one of the most common causes of neurological disability in young adults.

*(Karussis, 2014)*

Magnetic resonance imaging (MRI) has revolutionized the diagnosis and management of patients with multiple sclerosis (MS). Data derived from conventional MRI are now routinely used to detect therapeutic effects and extend clinical observations. Conventional MRI measures have insufficient sensitivity and specificity to reveal the true degree of pathologic changes occurring in MS. T2-weighted and T1-weighted imaging cannot distinguish between inflammation, edema, demyelination, Wallerian degeneration, and axonal loss. Nonconventional MRI techniques are now emerging and proving to be more related with the most disabling features of MS.

Advanced MRI techniques provide a better understanding of the pathologic processes that most likely are related to disease activity and clinical progression. Such metrics are able to reveal a range of tissue changes that include demyelination, axonal loss, iron deposition, and neurodegeneration and they provide the evidence that important occult pathology is occurring in the normal appearing white and gray matter.

*(Poloni G et al., 2011)*

Proton magnetic resonance spectroscopy ($^{1}$H-MRS) permits the invivo study of certain cerebral metabolites thus it offers the possibility of greater pathological specificity in lesional areas of MS as well as in normal appearing white matter and even in the gray matter.

*(Narayana P.A., 2005)*

$^{1}$H-MRSI sequence allows an in vivo evaluation of different cerebral metabolites associated with cellular and functional processes. Among the metabolites determined with this technique are the following: (1)N-acetylaspartate (NAA), which is synthesized in the neuronal mitochondria and is considered a marker of neuronal body and axonal integrity depending on transient (mitochondrial dysfunction) or permanent reduction of NAA (irreversible neuronal and/or axonal injury)

*(Ciccarelli O, et al., 2014) and (Bertholdo D, et al., 2013)*

The extended use of $^{1}$H-MRS in clinical settings has been hampered by its technical demands. However, because of its ability to assist in simultaneous evaluation of different events involved in MS pathogenesis that cannot be determined by conventional magnetic resonance imaging (cMRI), $^{1}$H-MRS could become an important tool to decipher the sequence of the immunologic cascade and to evaluate the response to new disease-modifying agents, including neuroprotectants.

The use of the above mentioned nonconventional MRI biomarkers could lead to a better understanding of different aspects of the disease process and play a key role in early diagnosis and prognosis of the disease, assessment of therapeutic response, and the understanding of different MS phenotypes

*(Rovira A, & Alonso J, 2013) (Comabella M,& Montalban X, 2014)*

# Aim of the work

**To highlight the value of MR spectroscopy in evaluation & monitoring patients with multiple sclerosis and how MR spectroscopy can add valuable information to conventional MR**

# ANATOMICAL BACKGROUND

The white matter in the CNS is composed of a vast number of axons, which are ensheathed with myelin, which is responsible for the white color. Besides myelinated axons, white matter contains many cells of the neuroglia type, but no cell bodies of neurons. The axons it contains originate from neuronal cell bodies in gray matter structures.

Gray matter contains the nerve cell bodies with their extensive dendritic arborization. The myelin content of gray matter structures is much lower, but some myelin is present around intracortical and intranuclear fibers. The myelin content of the thalamus and the globus pallidus is relatively high.

The white matter of the brain is located in the central and subcortical regions of the cerebral and cerebellar hemispheres and accounts for about 60 % of the total brain volume. Histologically, the white matter contains nerve fibers, supporting cells, interstitial space and vascular structures.

White matter consists mostly of axons with their envelope of myelin, along with two types of neuroglia-oligodendrocytes and astrocytes. Axons are extensions of neurons that reside within the gray matter of the brain, spinal cord and ganglia. The myelin is produced and maintained by oligodendrocytes. Myelin functions as an insulator of axons, and its structure facilitates rapid transmission of impulses

*(Valk J. and Van der Knapp, 2005).*

The interchange of information involving the cerebral cortex is mediated largely by collections of vertical and horizontal axonal fibers. Vertical connections consist of ascending and descending pathways between cortical and subcortical, brain stem, or spinal nuclei, while horizontal communications are represented by either intrahemispheric or interhemispheric connections.

The white matter tracts are broadly classified into 3 groups according to their connectivity:

1. **Projection fibers:** These fibers connect the cortical areas with the deep gray nuclei, brainstem, cerebellum, and spinal cord or vice versa. Corticospinal fibers, corticobulbar fibers, corticopontine fibers, thalamic radiations, and geniculocalcarine fibers (optic radiations) are tracts identifiable on DTI.
2. **Association fibers:** These fibers connect different cortical areas within the same hemisphere. The fibers can be long range or short range, the latter including subcortical U fibers. The major long tracts include cingulum, superior and inferior occipitofrontal fasciculus; uncinated fasciculus; superior longitudinal fasciculus (SLF), including arcuate fasciculus; and inferior longitudinal fasciculus (occipitotemporal).
3. **Commissural fibers:** These fibers connect similar cortical areas in the 2 hemispheres, including the corpus callosum and the anterior commissure.

*(Wycoco V. et al., 2013)*

**1) Projection Fibers:**

Trajectories of the main projection fibers are shown in Figure 2. It can be seen that the corticobulbar tract collects projections from many areas of the cortex to the brainstem. The projection from pre and postcentral gyri (corticospinal tract) reaches the pyramidal tract at the pons.

All thalamic radiations converged into the internal capsule, located between the putamen and the thalamus–caudate nucleus regions. Among other types of sensory connections between the thalamus and cortex, the posterior thalamic radiation includes the optic radiation.

The corticobulbar and corticospinal tracts and the thalamic fibers all penetrate the internal capsule, where the cortex-brainstem connection occupies the more lateral regions. This type of preservation of topology seen in the internal capsule (i.e., anterior part projecting to frontal lobe; posterior part, to occipital lobe; lateral part, to cortex; and medial part, to thalamus) may be due in part to the limitation of the tract-tracking technique, which generally does not allow tracing of crossing configurations.

Therefore, although the 3D reconstruction results can provide macroscopic views of the tracts, they cannot be directly interpreted in terms of detailed connectivity information. It is noteworthy; however, that the topologic preservation seen in the internal capsule actually agrees well with what has been postulated by neuroanatomists on the basis of postmortem results.

*(Nieuwenhuys, et al., 2008)*

- **Internal capsule:** This contains sensory fibers from the thalamus to the sensory cortex and motor fibers from the motor cortex to motor nuclei in the brainstem, corticobulbar tracts and, in the spinal cord, the corticospinal (pyramidal) tracts In cross-section, the internal capsule has an anterior limb between the caudate and lentiform nuclei and a posterior limb between the lentiform nucleus and the thalamus.

  Both limbs meet at a right-angle called the genu The anterior limb is composed mainly of frontopontine fibers The genu and the anterior two-thirds of the posterior limb contain motor fibers The most anterior fibers at the genu are those of the head Fibers to the arm, hand, trunk, leg and perineum lie progressively more posteriorly Hemorrhage or thrombosis of thalamostriate arteries supplying this area leads to paralysis of these muscles Behind these fibers on the posterior limb and on the retro-lentiform part of the internal capsule are parietopontine and occipitopontine fibers and the sensory fibers More posteriorly are the visual fibers that extend towards the occipital pole as the optic radiation Most posterior of all are the auditory fibers.

*(Ryan et al., 2011)*

**2) Association (Arcuate) Pathways (Fibers):**

Association (arcuate) fibers, confined to one hemisphere and are grouped as short, connecting adjacent gyri, or long, connecting more widely separated gyri *(fig 1)*.

A) **Short arcuate fibers:** may be entirely intracortical but many pass subcortically between adjacent gyri, some merely from one wall of a sulcus to the other.

B) **Long arcuate fibers:** The following large fasciculi can usually be distinguished: the uncinate fasciculus, the cingulum, the superior longitudinal fasciculus, the inferior longitudinal fasciculus, the frontooccipital fasciculus.

- **The uncinate fasciculus:** connects the motor speech area and orbital gyri of the frontal lobe with the cortex in the temporal pole; the fibers follow a sharply curved course across the stem of the lateral sulcus. .
- **The cingulum:** a long, curved fasciculus starting in the medial cortex below the rostrum, then lies in the gyrus cinguli and follows its curve. Inferiorly it enters the parahippocampal gyrus and spreads into the adjoining temporal lobe. From its convexity fibers enter and leave in groups, giving it a spiked irregular appearance when dissected.
- **The superior longitudinal fasciculus:** largest of the arcuate bundles, commences in the anterior frontal region and arches back above the insular area and lateral to the massive cortical projection fibers of the internal capsule (corona radiate). Contributing fibers to the occipital