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# Main methods to detect multiple sclerosis (MS) lesions in patients with MS

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## Abstract

The aim of the study is to investigate the main methods to detect Multiple Sclerosis (MS) Lesions in patients with MS. This study was a systematic review to detect main methods to detect of MS lesion in patients with MS. As a result, we found that MRI is the most accuracy and powerful tool for diagnosing a MS especially in early phase. In conclusion, the McDonald criteria is the best criteria that it has been proposed and revised in recently years to diagnose of MS based on clinical presentation and MRI.

**Keyword:** Magnetic, Resonance, Imaging, Multiple, Sclerosis.

## Principales métodos para detectar lesiones de esclerosis múltiple (EM) en pacientes con EM

### Resumen

El objetivo del estudio es investigar los principales métodos para detectar lesiones de esclerosis múltiple (EM) en pacientes con EM. Este estudio fue una revisión sistemática para detectar los métodos principales para detectar la lesión de la EM en pacientes con EM. Como resultado, descubrimos que la RM es la herramienta más precisa y potente para diagnosticar una EM, especialmente en la fase inicial. En conclusión, los criterios de McDonald son los mejores criterios que se han propuesto y revisado en los últimos años para diagnosticar la EM según la presentación clínica y la RM.

**Palabra clave:** Magnética, Resonancia, Imagenología, Múltiple, Esclerosis.

## 1. INTRODUCTION

Multiple sclerosis (MS) is a one of the common central nervous system disease that characterized by inflammatory demyelinating in white matter in the brain, spinal cord, and optic nerves and cerebral cortex and variable degrees of axonal loss. It is kind of autoimmune that immune system including T cells with B cells attack against CNS antigens (Holmøy & Hestvik, 2008). This disease almost effect on young people in 20 -40 years old. As well as it is more common in females than males (Garg & Smith, 2015). Unfortunately, the etiology of MS is unknown and it seems that the environment and genetic factors both of them have effect on the creation of MS (Kargarfard et al., 2017). Although MS is not an inherited but the studies have shown that the prevalence of MS in first degree relatives of patients with MS is 10–50 times higher than the other individuals (Garg & Smith, 2015). (Ascherio & Munger, 2007; Yang et al., 2019; Soo et al., 2019; Fitriani & Suryadi, 2019).

MS has a various sign and symptoms and it can effect on sensory, motor, visual, and brainstem pathways and makes a various disability including numbness, weakness, imbalance, vision dysfunction, vertigo, and bladder or bowel dysfunction (Berger, 2011). Since, this disease approximately involves young people and has

serious outcomes, it is important to diagnosis it in early phases. In recently decades, neurologists and radiologists have used several methods to diagnose this disease including clinical presentation, neuroimaging including MRI, CSF analysis (to elevate IgG index) and evoked potential studies (to look for the lesion in the visual, brainstem, or spinal cord pathways) (Link & Huang, 2006). Finally, the calculated that there is no single test or methods to diagnose of MS. As well as, there is no evidence about the best method to diagnose it in early phases. The aim of this study was to review the methods to use for diagnosing of MS and answer to this question that which methods is the best way to diagnose MS in early phase?

### *1.1. Objective*

The aim of this review was to assess and detect of the main methods that use for detecting MS Lesions in the patient with MS. Answer to this question that which methods are the best way to diagnose MS in early phase?

### *1.2. Materials and methods*

This study was a systematic review to detect main methods to detect MS lesion in patients with MS. The protocol of this study was as follows, at first two researchers reviewed database and journal websites, including PubMed, web of science, Scopus, Google Scholar

by keywords including multiple sclerosis, Lesions, MS, detect, diagnosis. Then all of the studies entered in endnote folder and the duplicate was removed, after that two researchers separately checked the title and abstract of articles, in next step, the full text of related articles was checked. Finally, the studies that related to the aim of this study and had inclusion criteria, entered in this study. Inclusion criteria were: original English article, articles published from December 2010 to December 2018. As well as exclusion criteria were: articles that were not focused on the method of detecting MS lesions and articles published before the 2010 year.

Totally 11 articles were entered in this study. Figure 1 show detail of the protocol of selecting studies.

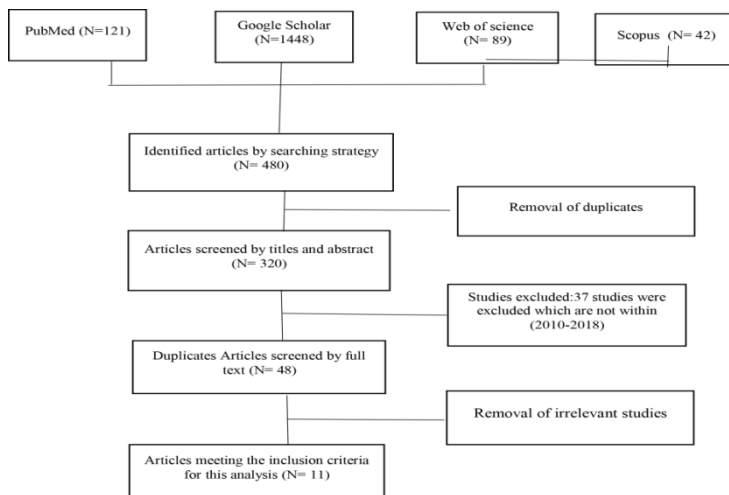


Figure 1: Flow diagram of the selection process of the study for systematic review on detect main method to diagnosis Multiple Sclerosis (MS) Lesions in patient with MS 2010- 2018

## **2. RESULTS**

After searching databases and journal website by related keywords, totally 11 studies were selected in this review and researchers screened them. Details of these studies explained below. Paul Schmidt et al. (2012) performed a study to detect the ability of the automated tool to detect FLAIR-hyperintense white-matter lesions in patients with Multiple Sclerosis in the 2011 year. Total their participants were 53 patients with MS with a lesion in different lesion volumes and area. After intervention, they found that this tools were useful to detect a FLAIR sequence and a 3D GRE T1-weighted sequence in patient with MS. Kilsdonk et al. (2016) performed a study to determine the sensitivity of 7 T versus 3 T magnetic resonance imaging pulse sequences to detect cortical grey matter lesion in patients with MS.

They entered 23 patients in their study that 19 patients were intervention group and 4 patients were a control group. After the intervention, they found that 7 T magnetic resonance imaging can detect more cortical lesions than 3 T. so they concluded that 7 T magnetic resonance imaging is more useful than 3 T for detecting a lesion in patients with MS (Kilsdonk et al., 2016). Furthermore, Datta et al. (2017) year performed a study to assess the ability of PET to detect lesions microglial activation in normal-appearing white matter. 64 patients with MS entered in this study. They used from the different approach of MRI in their study. After the intervention, they realized

that the SPMS can detect more lesion inactive than RRMS, but both of them can detect an active lesion in all patients (Datta et al., 2017).

Bitirgen et al. (2017) performed the study to assess the features of corneal subbasal nerve plexus morphologic, corneal dendritic cell (DC) density, and par-papillary retinal nerve fiber layer (RNFL) thickness. Their study was cross-sectional. 87 patients entered in their study and they were divided into two groups. Their finding showed that corneal confocal microscopy can detect an axonal loss in patients with MS (Bitirgen et al., 2017). As well as, Brownlee et al. (2015) performed a study to assess the accuracy of McDonald criteria by using MRI to detect MS in patients. For this, they recruited 178 patients and they used MRI with McDonald criteria for them. They found that the McDonald criteria could identify a significant number of patients with CIS with MRI evidence of dissemination of time and space without clinical events (Indriastuti, 2019; Kosari, 2018; Sears, 2018).

Ertan et al. (2018) performed the study to assess the efficiency of Double Inversion Recovery (DIR) to detect lesion of MS in patients in the 2018 year. Total of their sample size was 24 patients with MS. Also, they assessed the relationship between the number of lesions and type of MS, patient age, gender, duration of the disease, disability, and the mean number of attacks per year. Finally, they found that the DIR sequence compared to the FLAIR sequence can detect more lesion in patients. Wang et al. (2018) performed the study in 2018 to compare the accuracy of T2-weighted spin-echo, 2D-FLAIR, and 3D-FLAIR

sequences to detect lesions in MS patients. 85 patients entered this study. After the intervention, they found that 3D fluid-attenuated inversion recovery could detect more lesions than those on 2D and T2-weighted spin echo.

Yeliz et al performed a study in the 2017 year to assess the accuracy of MRI and Expanded Disability Status Scale (EDSS) to detect lesion of MS in patients. 120 patients and 19 healthy individuals were entered into this study. Their conclusion showed that their proposed model with MRI and EDSS had significant effect on detect lesion of MS. Furthermore, Becker et al. (2016) performed a study to assess the effect of D313Y mutation in the differential diagnosis of white matter lesions in patients with MS. Two female patients and one son presenting with WML and atypical clinical features for MS were assessed by mutation D313Y. Their results were that rare mutations could not only be a neglected differential diagnosis explaining the clinical picture but also a co-morbidity with or without relevance (Becker et al., 2016).

Zhang et al. (2015) in the 2015 year performed a study to provide evidence in patients with MS. In this study, they calculated a clinical data OF 527 patients with MS. the main methods that had been used for detecting MS in those patients was MRI, optical coherence tomography (OCT) and blood sample to detect of autoimmune antibodies and aquaporin (AQP-4). Finally, they calculated that MRI scanning was a useful method to detect of a lesion in patients with MS. Finally, we assessed the study of Böttcher et al. They performed a



study in the 2013 year to determine the effect of MRI to detect MS in patients with Fabry disease. 11 patients with Fabry disease that initially diagnosed as MS entered in this study. Their finding was that MRI showed white matter lesion in all of them (Böttcher et al., 2013).

Table 1

N O	Authors & Years	Size	Region	Finding	Summary
1	Schmidt et al (2012)	53 MS patients with different lesion volumes	Germany	They found good agreement with lesions determined by manual tracing (R2 values of over 0.93 independent of FLAIR slice thickness up to 6 mm).	This tool allows fast and reliable segmentation of FLAIR-hyperintense lesions, which might simplify the quantification of lesions in basic research and even clinical trials.
2	Kilsdonk et al (2016)	19 patients with multiple sclerosis and four control subjects	Netherlands	7 T magnetic resonance imaging detected more cortical lesions than 3 T. Fluid attenuated inversion	ultra-high field 7 T magnetic resonance imaging more than doubles detection of cortical multiple sclerosis lesions,

				recovery	compared to 3 T magnetic resonance imaging
3	Datta et al (2017)	Thirty-four MS patients (7 with secondary progressive MS [SPMS], 27 with relapsing remitting MS [RRMS]) and 30 healthy volunteers	United Kingdom	The mean DVR in NAWM of patients was greater than that of the healthy volunteer white matter for both radioligands	TSPO radioligand uptake was increased in the brains of MS patients relative to healthy controls with 2 TSPO radiotracers. WML showed heterogeneous patterns of uptake. Active lesions were found in patients with both RRMS and SPMS
4	Bitirgen et al (2017)	Fifty-seven consecutive patients with relapsing remitting MS and 30 healthy, age-matched control participants were enrolled in	Turkey	Corneal nerve fiber density, nerve branch density, nerve fiber length, and the mean parapapillary RNFL thickness were reduced in	These data suggest that corneal confocal microscopy demonstrates axonal loss and increased DC density in patients with MS

		the study		patients with MS compared with healthy controls. The	
5	Yeliz et al (2017)	120 patients and 19 healthy individuals were entered to this study	Turkey	the Convex Combination of Infinite Kernels model was developed to measure the health status of patients based on features gathered from MRI and EDSS	Proposed model classifies the multiple sclerosis (MS) diagnosis level with better accuracy than single kernel, artificial neural network and other machine learning methods, and it can also be used as a decision support system for identifying MS health status of patients.
6	Brownlee et al (2015)	We recruited 178 patients with CIS presenting	UK	McDonald criteria could identify a significant	the McDonald criteria allow MS to be diagnosed

				number of patients with CIS with MRI evidence of dissemination of time and space without clinical events	sooner and more often in patients with CIS
7	Ertan et al, (2018)	24 patients (9 males, 15 females; mean age 34.4±12.0 (16-69) were retrospectively evaluated	Istanbul Turkey	More lesions were detected by the DIR sequence compared to the FLAIR sequence in all regions except for thalamus	The DIR sequence is superior to the FLAIR sequence in the detection of intracortical and GM lesions. Also, the mixed lesion load on the DIR sequence is correlated with cerebral atrophy.
8	Wang et al (2018)	85 brain MRIs in patients with clinically definite multiple sclerosis	United state	The number of lesions on 3D fluid-attenuated inversion recovery was significantly higher than those	The 3D fluid-attenuated inversion recovery sequence addresses the disadvantage of poor infratentorial lesion detection on

				on 2D ( $p < 0.001$ ) and T2-weighted spin echo ( $p < 0.001$ )	2D, while still maintaining the advantage over T2-weighted spin echo in the detection of lesions adjacent to the cerebrospinal fluid
9	Bo'ttcher et al (2013)	Eleven Fabry patients (one male, ten females) initially diagnosed with multiple sclerosis were entered	Germany	All patients revealed white matter lesions on MRI. The lesion pattern and results of cerebrospinal fluid examination were inconsistent and non-specific.	: There are several anamnestic and clinical hints indicating when Fabry disease should be considered a relevant differential diagnosis of multiple sclerosis, e.g. female patients with asymmetric, confluent white matter lesions on MRI, normal spinal MR imaging, ectatic vertebrobasil

					ar arteries, proteinuria, or lack of intrathecally derived immunoglobulin synthesis.
10	Zhang et al (2015)	527 patients entered in this study. 123 males and 404 females	China	MRI scanning was useful method to detect of lesion in patients with MS	MS is more commonly misdiagnosed with NMO-ON and sjogren syndrome, when compared to optic neuropathy, tumor and ischemic optic neuropathy
11	Becker et al (2016)	Two female patients and one son entered in this study	Germany	rare mutations could not only be a neglected differential diagnosis explaining the clinical picture but also a co-morbidity with or without relevance	Fabry mutation D313Y may be involved in neural damage resulting in WML

### 3. CONCLUSION

Since MS is a common inflammatory central nervous disorder that can effect on individuals in every age and every situation and it makes severe symptom and disrupts normal life of patients, it is important to find the most accurate method to the diagnosis of this disease in early stage. After reviewing the current study about methods to detect MS in a patient, we found that MRI is the most accuracy and powerful tool for diagnosing an MS, especially in the early phase. Furthermore, it is a popular method these years between neurologists and radiologists. It is noteworthy that in addition to diagnosis, MRI is the best method to evaluate prognostic as well as the efficacy of treatment and safety monitoring for MS patients. Furthermore, The McDonald criteria are the best criteria that it has been proposed and revised in recent years to diagnose MS based on clinical presentation and MRI.

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