

Multiple Sclerosis Detection With Convolutional Neural Networks

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ABSTRACT

Introduction: Multiple sclerosis (MS) is characterized by increased neurodegeneration and inflammation, leading to long-term damage to the brainstem and central nervous system (CNS) and impairing neurological development. Magnetic Resonance Imaging (MRI) plays a crucial role in diagnosing and monitoring MS, as it reveals significant aspects of the disease's pathology. However, challenges remain regarding prognosis, tracking disease progression, assessing CNS damage, and establishing differential diagnoses.

Objectives: The objective of this study is to explore machine learning (ML) techniques to address persistent challenges in MS diagnosis and monitoring. Specifically, we aim to enhance neurodegenerative characterization, improve prognostic subtyping, optimize imaging of critical brain pathology, and develop better lesion segmentation and diagnostic classification tools.

Methods: We conducted a thorough review and application of various machine learning approaches to the study of MS. Techniques were evaluated for their ability to support neurodegenerative assessment, differentiate MS from similar conditions, and improve lesion detection and segmentation. Emphasis was placed on enhancing model generalizability across different MRI scanners and patient populations. We also explored the development of user-friendly interfaces to ensure clinical applicability and precision validation by radiologists.

Results: Machine learning models demonstrated potential in aiding differential diagnosis, especially for radiologists without specialized neuroradiology expertise. While several models focus on distinguishing MS from non-muscular obstructive sleep disorder (NMO), broader clinical diagnostic challenges remain, particularly differentiating demyelinating lesions from vascular lesions. Limitations identified include the models' generalizability to different MRI scanners and broader populations, as well as potential diagnostic tunnel vision due to narrow differential focus.

Conclusions: Although the use of machine learning tools for MS diagnosis is still in its early stages, they hold promise for aiding clinical practice. Future work must prioritize the robustness of ML models across varied MRI scanners, ensure broader applicability to diverse populations, and establish clear clinical thresholds for diagnostic outputs. Development of accessible interfaces that allow easy verification of results will be crucial for integrating these technologies into routine clinical workflows.

Keywords: deep learning, artificial intelligence, machine learning, autoimmune diseases, and tomography.

INTRODUCTION

CNS is impacted by progressive, chronic disease known as multiple sclerosis (M-S), which can cause crippling symptoms and disability. The breakdown is the outcome of several scleroses (the condition), a protracted autoimmune neurological disorder. Autoreactive lymphocytes have the ability to penetrate The brain-blood barrier, the brain's central nervous system as their targets. Once these lymphocytes have penetrated the central nervous system, they produce local inflammation that eventually leads to demyelination and axon loss. The condition is thought to afflict 2.5 million people globally. Youths aged between 20 and 40 are the main target

population. The rate at which women are afflicted by multiple sclerosis is double that of males. Treatment options for multiple sclerosis and its symptoms are many and include both pharmaceutical and non-pharmacological methods. With the advent of disease-modifying medications, illness treatment has greatly improved, especially for recurrent infection types. In this article, we'll go over M-S symptoms, diagnosis, and therapy. Most people with M-S who get a diagnosis eventually suffer disease progression. Nonetheless, there can be significant individual variations in the rate and pattern of multiple sclerosis development, which can cause disagreements about terminology and treatment modalities in addition to uncertainty over the prognosis. When referring to deterioration in individuals with recurrent M-S, researchers like Lublin et al. suggest using the word "worsening". However, while this approach has been approved in this context, the word "progression" is only used for people who have received a clinical diagnosis of progressive multiple sclerosis. As a result, people with multiple sclerosis (also known as PW M-S) may have to face an uncertain future as their condition progresses and gets worse. This might occasionally be accompanied with a greater load of symptoms and impairment. In addition, the difficulties brought on by the illness are made worse by the need for constant monitoring, the potential for side effects from pharmacological therapies, and their use. The fact that advancing multiple sclerosis and its exacerbations may both seriously interfere with many facets of a person's daily life should not be surprising. The aforementioned factors encompass employment, customary pursuits, interpersonal connections, family structuring, and individuals' self-concept. These difficulties may be exacerbated by the persistent stigma associated with multiple sclerosis (M-S), which can exacerbate the illness and set off a loop that is ultimately harmful. Working together, individuals with multiple sclerosis and healthcare professionals (HCPs) demonstrate how important it is for patients to be informed about the course of the disease and to actively participate in their own care. Benign and malignant are phrases that are commonly used to assess the severity of multiple sclerosis (M-S) at different times, despite the fact that there are no set categories for the disease's progression. In contrast to malignant multiple sclerosis, which progresses rapidly and causes several severe episodes, benign multiple sclerosis often leads to a few relapses and mild impairment after twenty years. Although specialists employ a range of factors to identify these categories, they frequently rely on the disability EDS-S, which assesses them with MS neurological status during the course of their therapy. More severe neurological illnesses are indicated by bigger scores on the EDS-S, which evaluates eight functioning systems. There are ten potential ratings, ranging from normal (0) to multiple sclerosis death (10). While scores between 5.0 and 9.5 suggest that the patient has a significant ambulatory impairment, those with EDS-S scores between 1.0 and 4.5 are thought to have excellent ambulatory competence. The outcome of the research is greatly impacted by the concept of benign multiple sclerosis as the percentage of benign and malignant patients differs greatly between studies. Research not only tries to anticipate the course of the disease but also looks for predictors; a high recurrence frequency and increased EDS-S scores during the early stages of the disease are typical signs of a bad outcome. Prediction models use genetic data, clinical study data, and information from magnetic resonance imaging (MRI) scans. Researchers have connected early illness start, brain parenchymal fraction, female gender, ethnicity, family history of multiple sclerosis, optic neuritis, and sensory symptoms to a better disease course. However, brain T2 lesion magnitude and pyramidal involvement are linked to a more severe progression. Furthermore, compared to conventional onset predictors, predictors that are revealed later in the course of the illness may be more accurate, according to the results of Bengt Skoog and colleagues. As a result, only few viable predictors remain. On the other hand, different studies reached different results on the key elements. For example, despite the EDS-S connection to motor processes, Reynders et al. claimed that other aspects like its impact on mental and cognitive functions are hardly assessed. This suggests a connection between the EDS-S and motor processes. Another research indicated that age and gender did not affect the course of multiple sclerosis; instead, they interacted with the clinical disease phenotype. A seemingly benign course can often turn out to be malignant, despite the fact that the EDS-S may be able to offer useful prognostic information, according to Hawkins and colleagues. Early studies on machine learning models relied on correlations and statistical testing, but subsequent work has shown that these models might potentially treat a variety of illnesses, including multiple sclerosis. In the present research, we describe a new machine learning architecture that uses clinical data gathered during the first five years of the illness to forecast how M-S will progress. Our prediction model is based on two primary parameters: the initial diagnosis, the progression of M-S (i.e., whether it progresses to secondary progressive or not), and the severity of the disease (varying from benign to malignant forms) in them with the RRM-S. By creating machine learning

models that use progression data across multiple years, we may gain understanding of how forecast accuracy varies over time. This offers us a certain level of confidence. By employing this technique, scientists can also look into the relationship between significant predictors and the sickness, as well as how they change over time. This makes it simpler for medical professionals to decide which therapeutic choice is ideal for a given patient and to comprehend how each patient's condition develops. Females are more prone to neuro inflammation of brain nervous-system (CN-S), then males. First manifesting in adult time, this syndrome is more widespread and on the rise in the Western world. MRI scans of the brain or spinal cord can identify the emergence of localized inflammatory lesions in the CN-S. The degree and location of damaged nerve tissue can determine whether these injuries cause a somewhat treatable reduction in motor, sensory, or cognitive functioning. Although a percentage of people's limitations may be explained by localized inflammation, this explanation is insufficient to explain the entire spectrum of impairments. It is acknowledged that extensive neurodegeneration throughout the entire CN-S has important role in progressive accumulation of impairment, particularly in the latter stages of the illness. This is on top of the localized swelling that already exists. The progressive loss of function is thought to be caused by neurodegeneration rather than localized inflammation. Both standard and advanced magnetic resonance imaging (MRI) examinations that evaluate the structural integrity of brain tissue can show it. Medical professionals distinguish between three subtypes of M-S: relapsing-remitting (RRM-S), secondary progressive (SPM-S), and primary progressing numerous (PPM-S) sclerosis. One common subtype for relapsing-remitted RRM-S is can be characterised as periods of alternating symptom worsening and remission, with only mild disability. There's a possibility that RRM-S will eventually move to SPM-S, which is distinguished by a gradual rise in disability over time. On the other hand, impairment in progressive multiple sclerosis (PPM-S) worsens gradually and begins as soon as the illness does. It is more prevalent in people who were older when the illness first started, particularly in men.

OBJECTIVES

The primary objective of this study is to utilize early clinical, imaging, and demographic data to predict the progression and severity of multiple sclerosis (MS). We aim to develop and validate machine learning models capable of forecasting disease trajectories, particularly the transition from relapsing-remitting MS (RRMS) to secondary progressive MS (SPMS), and distinguishing between benign and malignant courses of the disease. By integrating various predictors such as early Expanded Disability Status Scale (EDSS) scores, recurrence rates, MRI findings, genetic markers, and clinical symptoms, we intend to enhance prognostic accuracy and guide timely therapeutic interventions. In addition, this research seeks to address the limitations of existing prognostic models that primarily focus on motor function while overlooking cognitive and psychological impacts. By creating more holistic and dynamic prediction tools, we aim to provide healthcare professionals with better resources for patient counseling and treatment planning. Our work aspires to offer a deeper understanding of MS heterogeneity, improve individualized care strategies, and support patients in actively managing their disease trajectory through early, informed clinical decisions.

RELATED WORKS

Fiorini et al. employed machine learning approaches to identify unique courses of M-S by analysing clinical data. Their objective was to distinguish between benign and rapidly advancing forms of the illness. A range of classifiers were employed, such as logistic regression (L-R), K-nearest neighbours (KN-N), regularized least squares (RLS), ordinary least squares-OLS, linear vector machines-SVM. First, they took clinical data from 457 individuals and identified 91 characteristics. They made use of the median to handle missing data. They then used minimum-maximum scaling technique to normalize the attributes between 0 and 1. The algorithm that produced the best accuracy of 78.32% was the ordinary square algorithm using L1, L2 feature selection. Maximum F1 score of 70.2% is achieved by RLS technique with L1, L2 feature selection. Using a straightforward and non-invasive technique, a decision support system (DSS) was able to identify MS patients based on balance problems. For three minutes, the study's twenty healthy participants and fourteen MS patients stood in front of a dark background with markers positioned precisely between their brows. These markers' motions were examined using an image processing method. The 'tan-sigmoid' transfer function was used to train an artificial neural network (ANN). By identifying significant differences between MS sufferers and healthy individuals, features

were retrieved. Neural network- ANN's remarkable 92.35% accuracy rate was attained. Furthermore, with an accuracy rate of 84.8%, the researchers created a second DSS with the goal of identifying people who may acquire MS in the future. Those who were diagnosed with this intermediate state were counselled to prevent the disease from progressing by keeping their vitamin D levels up to date, limiting their exposure to pollutants, and learning how to manage their stress. Ettema et al. looked at how well an electronic nose (eNose) worked using exhaled air analysis to identify multiple sclerosis (M-S). There were 129 healthy controls and 124 verified M-S patients in the study. For five minutes, participants exhaled into the TM gadget. The tool distinguished between M-S patients and healthy people by identifying volatile organic molecules in exhaled breath. To train the AN-N Sample data was used. An additional prognostic model was created with untreated M-S patients in mind. With 75% sensitivity and 60% specificity. Model's results on healthy people and M-S patients who did not seek any medical help showed 80% accuracy, 93% sensitivity, and 74% specificity. Lotsch et al. created a detailed blueprint for utilizing supervised machine learning methods like Random Forest (R-F) to create a blood lipid-biomarker classifier for M-S diagnosis. Using information from 403 patients, a biomarker based on Bayesian statistics was developed to distinguish M-S sufferers from healthy people. After the data was meticulously gathered and pre-processed, RF was used to pinpoint important characteristics. After training with all available features, the RF classifier obtained 100% accuracy, specificity, and sensitivity. Nonetheless, difficulties emerged since the data distribution was unequal between the groups M-S patients varied in age and controls were healthy people. To identify putative markers of multiple sclerosis (M-S) in blood and cerebrospinal fluid (C-SF), Martynova et al. examined a panel of 45 cytokines. They examined CSF samples from 25 healthy controls and 101 M-S patients using a multiplex immunoassay. With the use of cytokine data, five machine learning models were created to diagnose M-S, distinguish between three subgroups of patients namely: RR(M-S), secondary Progressive SP(M-S), and Primary Progressive PP(M-S). These models are K-Nearest Neighbours (KN-N), Decision Trees (DT), X-G-Boost (XG-B), Gaussian Naive Bayes-GNB, RF. Based on the findings of A-NOVA and Pearson correlation coefficient, features were chosen, resulting in the identification of 20 significant serum cytokines and 22 significant CS-F cytokines. The diagnosis of MS obtained 99% accuracy rate across all models using randomly selected biomarkers, such as CCL27, IFN- γ , and IL-4, suggesting its potential for MS prediction. Based on serum and CSF, the XGB model was able to classify MS subtypes with 78% and 69% accuracy, respectively. Ali et al. presented a technique for using next-generation sequencing (NGS) to analyse transcriptome microRNA data in order to uncover MS biomarkers. This method allowed for early MS identification by combining machine learning and text mining. The National Centre for Biotechnology Information (NCBI) provided 54 RRMS patients' NGS microRNA data, which were used in the study. Transcriptome data were analysed both pre- and post-administration of the immune-modulating medication fingolimod. KmerFIDF was employed in the feature extraction process, while linear discriminant analysis (L-DA) was used to reduce dimensionality. Vector Machines, random forest formation, and logistic Regression technique were models used for classification; RF performed better than the other two, with 96.4% sensitivity, 96.47% specificity, 95.6% F1-score, and 97% average accuracy. Using layered cross-validation and peripheral blood mononuclear cells (PBMCs), Acquaviva et al. created an unbiased machine learning system. They contrasted three machine learning techniques: ADA boost-FT, FT, and RF. Blood transcriptomes from 313 patients with different neurological disorders and MS subtypes were included in the study. To accomplish several classification tasks, including differentiating between MS patients and non-MS individuals, CIS from healthy controls, and MS subtypes, models were developed. ADA boost-FT demonstrated great sensitivity, specificity, precision, and total accuracy, consistently outperforming other algorithms. Based on blood cytokine levels (IFN- receptors TNF- α , IL-1 beta, IL-2 in combination cytokines like inflammatory mediator-8, the hormone IL-10 and IL-13 antibodies), Goyal et al. created an MS diagnosis model. 910 MS patients and 199 healthy controls from American and Russian datasets were included in the study. Thorough planning and cross-validation made guaranteed that the outcomes were objective. The RF classifier was able to distinguish between MS patients who were in remission and those who were not, demonstrating superior sensitivity, specificity, and accuracy. Blood cytokines and clinical information including age, gender, disease duration, EDS-S, and MS severity score were added in the predictive model. A method for identifying multiple system dysfunction (MS) utilizing serum levels of vitamin D3, B12, and selenium was presented by Sharifmousavi and Borhani. Using a chemical auto-analyser and atomic absorption spectroscopy, they assessed the vitamin and selenium levels in 81 healthy people and 99 M-S patients. The S-VM-based diagnostic model outperformed the

other machine learning models (D-T and S-VM), with a sensitivity of 98.98%, accuracy 98.89%, 99.9% genuine positive rate with 98.98% predicted success. For MS detection and classification, Pinto et al. evaluated four machine learning models: S-VM, LR, KN-N, T. This relationship will ultimately lead to improved disease management and an overall improvement in standards of living. Peoples in Large number suffer from multiple-sclerosis, a neurological disease that primarily affects women over males. The majority of instances of M-S occur in adults between the ages of 20 and 45. In the end, this causes problems for society, such as discrimination and stigmatization. The symptoms of M-S can vary greatly, and the illness's trajectory is not always known. Conversely, the disease typically begins with transient neurological episodes known as relapses, which are succeeded by a steady deterioration in neurological function. Symptoms associated with this disorder include abnormal optic nerves, sensory deficiencies, discomfort, fatigue, weaker muscles, cognitive issues, and depressive symptoms. This event might serve as a precursor to the development of M-S such as clinical relapses or MRI activity, should be considered when diagnosing relapsing-remitting sclerosis. A reduction in disability is the hallmark of secondary progressive- sclerosis, which follows an initial phase of relapsing-remitting- sclerosis. The hallmark- primary progressive sclerosis a progressive increase in disability from the outset. There are differences between the two types of M-S. SPM-S can occur in people with RRMS who are diagnosed but do not receive the appropriate therapy. The hallmark of SPM-S is a persistent deterioration in neurological function, either with or without periods of recovery. In order to predict the change from relapsing-remitting to secondary progressive M-S, a research examined professional characteristics collected throughout the initial five years of the illness. Two further models were developed to predict the severity of the condition after six and 10 years. Data on 187 respondents for the M-S conversion model & 145 for the sixth-year forecast was sent to the neuroscience Department via Centro hospitalar universitário de coimbra (CHU-C), situated in Portugal as well as 67 for an extreme forecast for the tenth year. Clinical information from patients with SPMS and RRMS is included in the research. For every 5-year simulations were employed for feature extraction. Normalization, feature selection, and missing value imputation were all part of the data pre-treatment procedure. Each training and testing set had a k value of ten and was subjected to 100 repetitions with ten-fold cross-validation. The sets were selected from distinct patients. The average of the results from every execution was used to gauge performance. Among the models, SVM consistently gave the best results. For M-S transition estimation, it had an area under the curve of 0.862 ± 0.071 , sensitivity equal to 0.761 ± 0.141 , and the specificity of 0.771 ± 0.051 , the two-year model proved to be the most accurate predictor. Similarly, with an area under the curve of 0.89 ± 0.03 , sensitivity of 0.84 ± 0.11 , and specificity of 0.81 ± 0.05 , the two-year model fared better than the sixth-year severity prediction. In Ashtiani et al.'s (ML) technique, graph characteristics gathered during a cognitive task are combined with statistical tests and a linear support vector machine classifier to discriminate between M-S patients and healthy persons [26]. Twelve healthy individuals and eight early-stage M-S patients participated in the study. Combining many local metrics, including Rank centralities, K-Coreiness, cluster level, and segment precedence within specific brain areas (left fusiform, hippocampus, and parahippocampal gyri), resulted in an accuracy of 85%. Additionally, by utilizing individual in between centrality and two ideal global metrics- modularity and small-world index, it was possible to identify M-S patients more accurately, yielding an 81.25% sensitivity. In general, there are still problems with stability across images acquired from different MRI scanners, generalizability to a larger population, and confirmation that the machine learning method produces data relevant to biology and medicine [27].

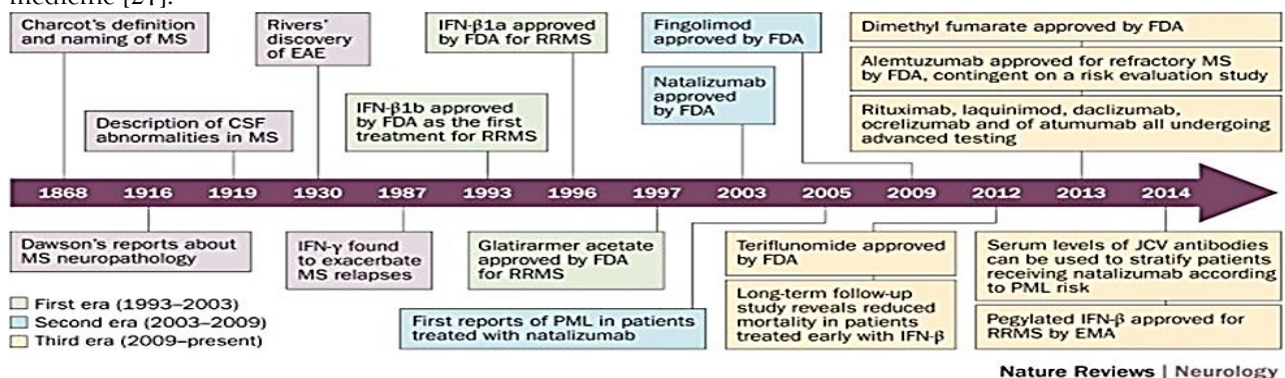


Fig 1: A chronology of multiple sclerosis detection and classification techniques

Figure-2 top row shows proton density (PD)-weighted magnetic resonance (MR) images of typical T2/PD hyperintense lesions in multiple sclerosis. These images were captured at a variety of different times. These images demonstrate the dynamic nature of lesion creation and the progression of multiple sclerosis by showing onsets, lesions accumulation that are specific to the illness.

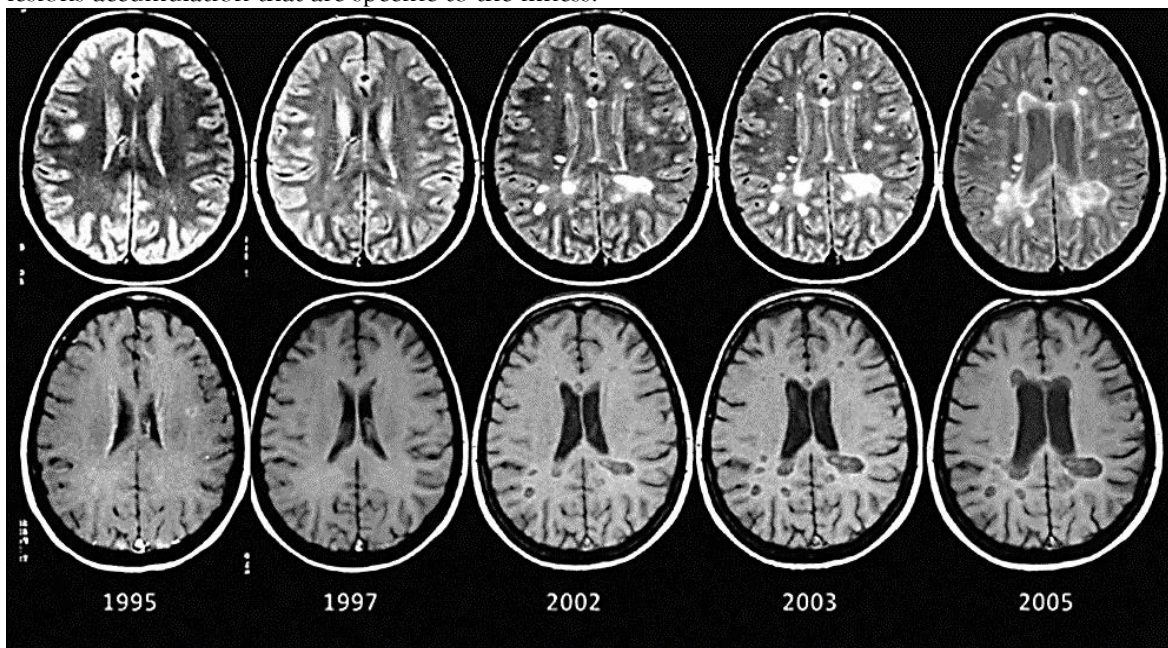


Fig 2: hyperintense lesions in multiple sclerosis

METHODS

An examination of research on multiple sclerosis diagnosis was done using machine learning. Because convolutional neural networks (CNN-s) are capable of understanding minute patterns in data, especially photographs, using machine learning to detect M-S is a potential approach. Below is a potential approach for utilizing a CN-N model to identify multiple sclerosis. Get a selection of brain MRI pictures from both healthy people and those who have multiple sclerosis. A wide range of demographics, disease stages, and imaging conditions must be included in this collection. The MRI pictures are normalized and their quality is raised by pre-processing, preparing them for input into the CN-N model. Pre-processing techniques that could be used include noise reduction, scaling, intensity levelling, and skull stripping. Using the validation dataset, the hyper parameters of the CN-N model may be adjusted. If you want to improve the model's performance, you might have to change the learning rates, batch sizes, dropout rates, and possibly other factors. The pre-processed dataset must be split into three separate sets: the testing, training, validation. Basically, 70-80% is used for training, 10-15% is used for validation (to adjust the hyper parameters), and the remaining 10-15% can be used for testing the final version of the model. Construct a CN-N architecture that may be applied to photo categorization applications. Convolutional layers should be the first in this architecture, followed extraction of features from pooling layers and categorization using fully connected layers come next. Investigate utilizing multiple Network designs including VGG, Res-Net, and bespoke architectures, is required to determine which CN-N design provides the best performance. Convolutional Neural Network (CN-N) model implementation: Train the model with the given training dataset. The model's parameters should be optimized during training by using a suitable strategy, such Adam or stochastic gradient descent, in combination with a respectable loss function, like categorical cross-entropy. Data augmentation methods like flipping, rotating, and zooming can boost the model's ability to generalize and diversify the training dataset. The accuracy, precision, recall, and F1 score of the CNN model that was trained using the testing dataset must all be taken into account when assessing the model's efficacy. It is advised to assess the model's performance and identify possible areas for improvement using methods like ROC curves and confusion matrices. Make use of all available strategies to raise the model's longevity and forecast accuracy. Morphological procedures and thresh-holding could be used as image processing tools in these techniques. When the model's functionality is shown to be adequate, (M-S) should be identified

with it in practical settings. Other ways to achieve this include developing an application exclusively for use by medical professionals or integrating the model into an already-in-place healthcare system. It is recommended to combine ongoing assessment of the deployed model's effectiveness with active user feedback in order to establish continuous monitoring and improvement. To take into consideration any changes that might take place in the dataset or in the advancements of imaging technology, the model must be regularly retrained and fresh data added. By using the suggested method for multiple sclerosis diagnosis, an efficient Convolutional Neural Network (CN-N) model might be created using brain MRI data. This would lead to faster diagnosis and better disease control.

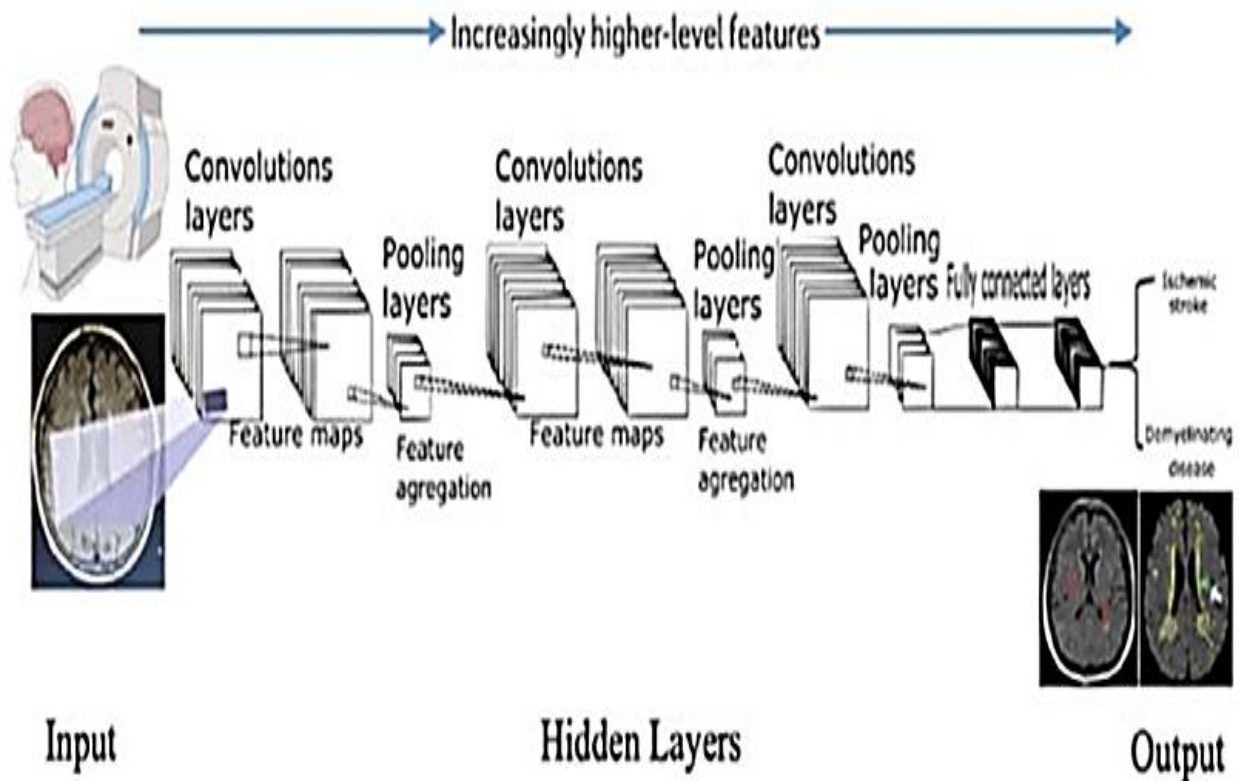


Fig 3. Architecture- convolutional layers

First Phase

The development of localized lesions in the brain and spine which are inflammatory is a prominent attribute, which can be detected using MRI examinations of the brain or the spine (Fig. 4). Depending on where the lesion is and how much of the central nervous system's nerve tissue is damaged, these lesions may result in a partial loss of motor, sensory, and cognitive function. Irreversible incapacity develops as a result of both the disease's progression and the central nervous system's damage getting worse. Even with their attractive appearance, the individual inflammatory lesions cannot fully explain the whole accumulated harm. Diffuse neurodegeneration in the central nervous system is another histological characteristic that is thought to be accountable for the slow accumulation of impairment. It is proposed that a pathway that is not entirely dependent on localized inflammation is responsible for mediating this neurodegeneration. When using enhanced MRI methods that identify brain tissue integrity, or traditional magnetic resonance imaging, this neurodegeneration can be seen as mild progressive brain shrinkage (Fig. 5). Multiple sclerosis may be divided into three main categories based on its clinical history (Fig. 3). remitting multiple sclerosis is prevalent MS kind, marked by intermittent episodes of symptoms sometimes accompanied by mild disability. One of the features that sets apart the secondary progressive subtype, which progresses from the RRMS subtype, is a progressive rise in disability. Primary progressive, a subtype of multiple sclerosis that often affects older male patients at the onset of symptoms. It is distinguished by the progressive accumulation of handicap beginning at the moment the sickness first appears.

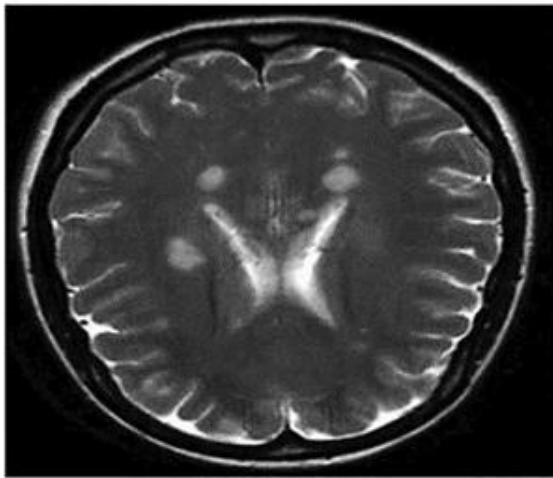


Figure 4: MS disease lesions in the brain.

The goal of M-S treatment is to reduce the inflammation in the CN-S. The majority of previous therapies (immunomodulation) involved the use of medications that interfere with the molecules that signal cells and regulate the immunological response. The CNS in-inflammatory response is suppressed by these drugs. In the tenth decade of the 20th century, interferon was the initial immune-modulating drug which can be authorised for the treatment of RRM-S. This medication was able to reduce the inflammatory lesions on M-RI by around thirty percent. Since the year 2000, many immunomodulatory medications have been developed and authorized for the management of multiple sclerosis with remission, including teriflunomide, dimethyl fumarate, and glutaraldehyde. These medications work about the same way. These drugs are generally well tolerated, and there is little chance that they will have significant side effects. More modern medications like fin-golimod, alemtuzumab, ocrelizumab, natalizumab, and sip-nimod are based on monoclonal antibodies. These antibodies have an immunosuppressive impact because they can directly inhibit immune cell receptors. This stops the central nervous system from being inflamed due to immune cells. Compared to the immunomodulatory medications that were previously mentioned, these therapies are typically more successful. They successfully reduce the amount of new active lesions on (M-RI) and cut frequency relapses by fifty to eighty percent. The latter therapies are linked to an increased risk of more significant adverse effects, including but not limited to cardiovascular disease, autoimmune sickness, most notably advanced multi-focal leuko-encephalopathy (PM-L) which is a problem with the more recent therapies. The most severe and potentially fatal side effect linked to natali-zumab, fingo-limod, in very rare cases, di-methyl fu-marate usage is P-M-L. It is brought on by a JC virus infection of the central nervous system (CNS). Despite being less effective than other forms of therapy, "immunomodulatory" medications are advised as "first-line" therapy because they have a lower risk of major side effects. The search continues for M-S therapies that are not only more effective and comfortable, but also appropriate for those with progressive M-S. Tole-bruti-nib, which is a inhibitor of the enzyme "Burtons' tyrosine kinase," which causes in-flammation in the CNS, and vido-fludimus calcium the IMU-838, a di-hydroorotate dehydrating enzymes inhibitor that ceases B, T-cells that from releasing cytokines that are pro-in-flammatory, are two novel treatments that are presently being tested. The development of in-flammatory activity in the CN-S throughout time and space is used to diagnose M-S. This progresses following the typical episodes of localized inflammation in different parts of the central nervous system that are indicative of the illness. These two requirements were first satisfied by the clinical history, which showed that there were at least two distinct episodes of clinical impairment connected to different regions of the CN-S. Clinically isolated syndrome, or CIS, is defined by one or more episodes of symptoms or signs in a single central nervous system (CN-S) region. A second episode that takes place in a different part of the CN-S could be a sign of a type of M-S that is clinically distinct (called CDM-S). It may take years to make an accurate diagnosis of M-S with the current medical diagnosis method. It's an unacceptable amount of time in today's world, where efficient treatments have to be explored at the beginning in the disease. As a result, similar guidelines have been applied, and MRI of the brain data has been included into the diagnostic standards. In order to detect and localize inflammation-related lesions in the diagnostic scenario, the MR imaging method should ideally include a FLAIR and T2 brain scan. In addition, a T1-weighted scan of the brain should be performed after intravenous gadolinium contrast administration in

order to detect any active inflammatory lesions with contrast material seeping into the surrounding brain parenchyma. In order to do a differential diagnosis, a T-1 without contrast and D-W-I sequence imaging of the brain are often included. When brain imaging is not enough to do a diagnosis, T-2-P-D and T-1 spinal cord are not required. MR-I process for M-S spread in a space necessitate the presence of several inflammatory lesions in brain or spinal-cord. These lesions must be present in two of the four usual regions of the C-N-S, an juxta-intra-co-rtical, peri-ventricular, in-fratentorial, and spinal-cord. For more information, see Table 1. The condition for spread in time is satisfied when one or more additional lesions appear on subsequent M-R-I pictures. Moreover, lesions that both grow and do not increase after the gadolinium therapy must be observed concurrently on each specific scan. Further improvements in the diagnostic requirements have allowed for a diagnosis of between three and twelve months after the first sign of symptoms in most cases of suspected typical neurological disease.

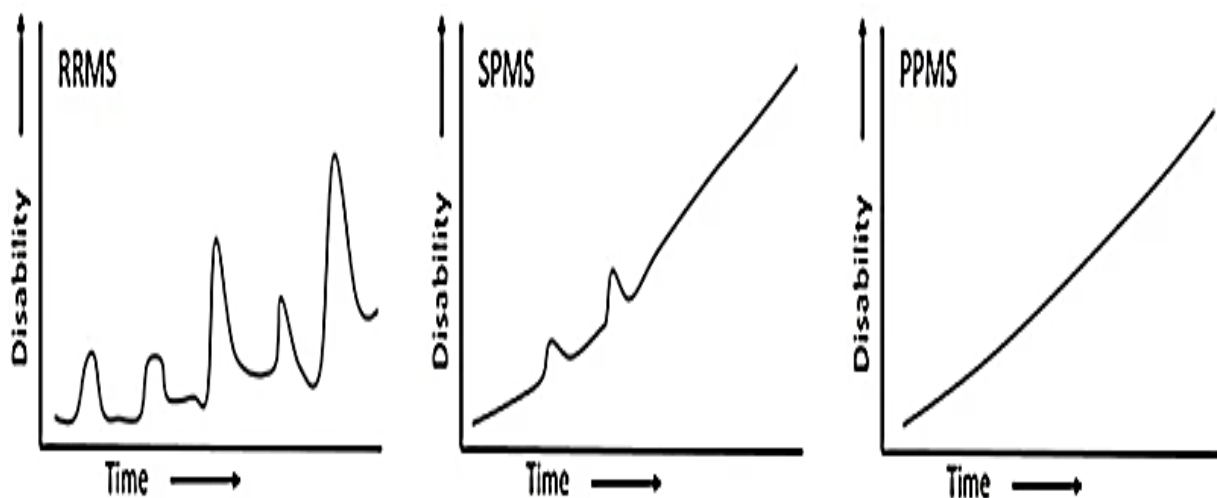


Fig 5: M-S subtypes - the progression of disability over time.

Second Phase

Neurology examinations are done to check for indications of the neurological condition multiple sclerosis (MS), fresh lesions found on brain or spinal column M-R-I are used to see the course of disease, and those with M-S self-report their symptoms. A yearly brain M-R-I is usually performed, using the FLAIR method plus T-2/P-D sequence to detect any recently developed lesions. Additionally, the D-W-I series on brain tissue is performed in order to differentiate lesions classified as likely P-M-L by the first course of treatment from lesions classified as MS. Depending on the clinical indications and complaints before therapy is started, T-1-weighted post-contrast brain patterns, spinal cord scans, and more frequent magnetic resonance (M-R) scans are all entirely optional. An overview of the common M-R-I sequences used to assess the progression of the illness is given in Table 1.

In real-life situations, more advanced M-R-I includes magnetic-transfer-ratio, diffusion-tensor-imaging, resting-state-functional M-R-I are rarely used to detect, monitor ones with M-S. Under carefully regulated experimental settings, these intricate sequences have proven to be useful in illuminating the structural, functional dynamics of M-S. M-T-R and D-T-I are typically employed to examine spinning breakdown periods or protons migration within white matter routes, accordingly, in order to assess the microstructural quality of the brain. At rest brain-response to certain activities is measured using the bold effect in the repetitive functional magnetic resonance imaging (RS-FMR-I). Unusual radiological anomalies lead to diagnostic problems. These may indicate other diseases that mimic multiple sclerosis. This is true even though the majority of people with suspected multiple sclerosis may be effectively diagnosed with the disease using the highly precise and useful current diagnostic criteria. Machine-learning techniques have been used to differentiate multiple sclerosis from other disorders in order to aid with these diagnostic challenges. Because of the clinical connections between M-S as well as neuromyelitis eye problem range sickness (NM-OSD), as well as the presence of bulky patches in optical-nerve, spinal-cord, and later-brain, it was once thought that NM-OSD was an example of M-S. This is since clinical signs for the two illnesses are same. RNM-OSD has been accepted as a different illness due to the active antibodies

against myelin-oligodendrocyte glycoprotein (MOG), a component of the myelin, aquaporin-4, which is a water channel involved in maintaining the water balance in CNS. It is difficult to achieve a diagnosis since there is significant overlap with multiple sclerosis, despite the known clinical and radiological distinctions. To differentiate between non-muscular organization of the spine (NM-OSD) and MS, numerous ML methods are created. These models employ a range of techniques, such as CNN on brain MRI, random-forest on radiomic features of brain lesions, decision-tree based on findings of MRI of brain, spine, LASSO binary-logistic-regression on the combination of radiological-features. The areas under the curve (AUC) of these models varied from 0.712 to 0.935 degrees. How to Tell Multiple Sclerosis Apart from Other Illnesses: Brain MRI results identical to MS can be seen in a wide-range of other inflammatory, immunological, and vascular-disorders. Nonetheless, it is typically simple to differentiate these illnesses from multiple sclerosis using clinical criteria, such as age and the onset of the condition. However, if radiologists are not knowledgeable with illnesses involving the brain and spinal cord, they may find it difficult to interpret these data from an MRI. Luo et al. developed a model with AUC-0.967 that could distinguish between brain lesions among individuals with systemic lupus erythematosus, and those in patients with R-R-MS using S-V-M of MRI-based lesions of brain. As part of a larger effort to give a neuro radiological differential diagnosis for MS and other brain illnesses, Rauschecker and colleagues developed a machine learning model. The initial phase in their research was to discover and classify brain lesions using brain magnetic resonance imaging. Afterwards, they used a large number of pulse sequences extracted from the segmented lesions to identify eighteen quantitative imaging parameters based on position, spatiality, and signal. The underlying brain disorder was then predicted by combining these 18 imaging features with five clinical criteria and utilizing a Bayesian classifier. Our classifier correctly identified the top-3 diagnoses in 91% cases, its performance is identical to that of academic neuro radiologists (86%, $p=0.20$) who specialize in this area. We found that our classifier performed better than Gen-radiologists (57%, $p<0.001$), neuroscience fellowships (77%, $p=0.003$), radiography-residents (56%, the $p<0.001$). limited number of the data-sets used (86 for training and ninety-two for evaluation, with about five for every diagnosis class.

MS Detection Phase

For Lesion Quantification and Segmentation Precise lesion segmentation ML is necessary because lesion volume remains a crucial outcome indicator in multiple sclerosis research and therapeutic trials, even if lesions may not perfectly match the build-up of clinical impairment over time. This is due to the fact that manual lesion segmentation on magnetic resonance imaging requires a great deal of time and labour; thus, automated segmentation is the obvious choice, particularly for three-dimensional scans. Among these strategies are unsupervised K-means clustering and semi-automated seed growing. In recent years, it has been shown that convolutional neural networks do exceptionally well when it comes to lesion segmentation. Lesion Division Through Cross-Sectional Examination: Using a broad spectrum of machine learning architectural designs, several ML models are constructed to enable cross sectional lesion segmentation in MS. Previous MS-lesion-segmentation challenges showed that for cross-sectional pictures in MICCAI- 2016 challenge, segmentation-algorithms were able to get a mean-surface-distance of 0.91, mean-dice-score of 0.59. Furthermore, segmentation-algorithms were able to get a mean-symmetric-surface-distance of 2.16, mean-dice-score of 0.670 for Longitudinal-MRI in ISBI-2015. While many methods need sequences as input, just three of these techniques required a single FLAIR sequence. T1, T2, PD, FLAIR sequences were among these. These techniques must be tested in real-world scenarios, where individuals are scanned using MRI machines that are not the same as the dataset used for the first training. Apart from the segmentation performance assessments, this is also done. To get this desired outcome, it is sometimes required to undertake some tuning and optimization before to deployment on a specific dataset. Several techniques for cross-sectional segmentation of lesions from multiple sclerosis were investigated by Jasperse, B. et al. and Weeda et al., with and without local optimization. They used a wide range of openly accessible programs, such as BIANCA, Nic-MS-lesions, and LST (Fig. 4). All of these techniques performed better when the local dataset was refined.

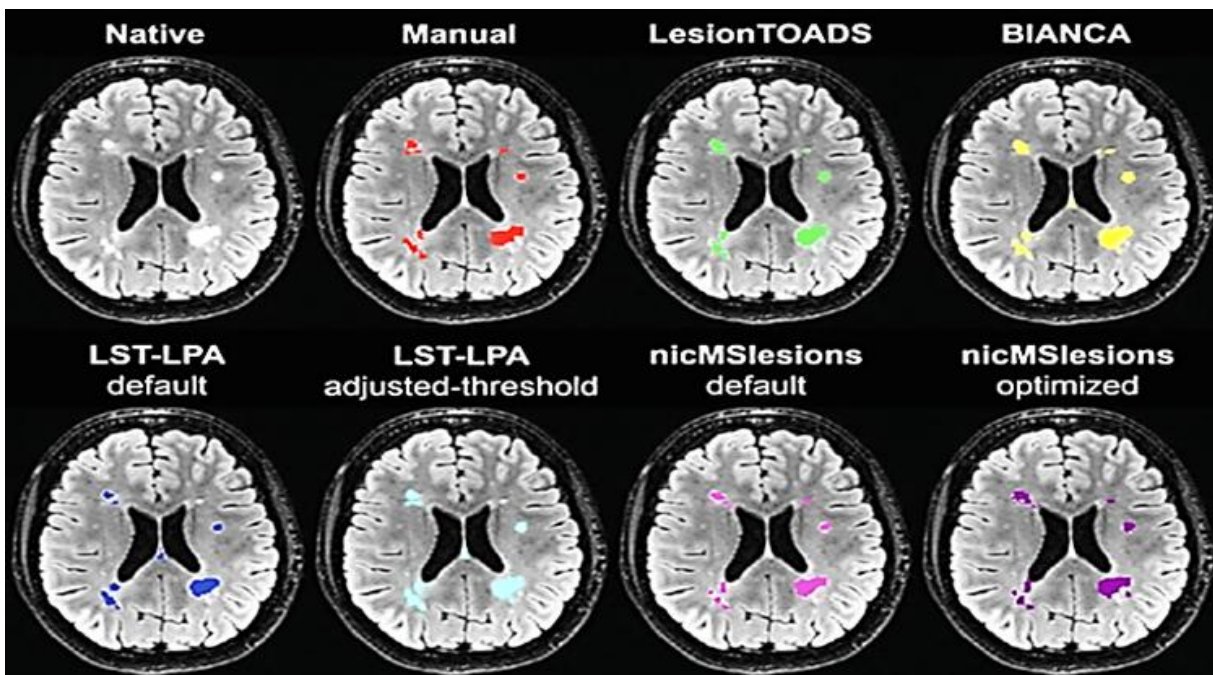


Fig 6. Four lesion segmentation algorithms-samples are displayed with manual segmentation on FLAIR brain images. (first published by Weeda et al.)

A critical component of clinical monitoring choreography is the longitudinal identification of new M-S lesions, which can reveal fresh inflammatory activity in the nervous system- central, informed initiation or adjustment of treatment for a particular M-S patient. Visual examination of FLAIR pictures is tedious and time-consuming, especially in patients with several confluent lesions. The primary goal of each therapy was to remove any signs of disease activity (NEDA). This was not feasible since patients receiving various modalities throughout time demonstrated a minimal number of new lesions. A single-centre cohort of hundred people with M-S was examined to figure out the number of fresh spots noticed by visual inspection (sensitivity-69/accuracy-67), automated evaluation (sensitivity-84/accuracy-64), visual verification assessments (sensitivity-86). By applying automated procedures, there were more atypical M-S marks discovered in comparison to optical-techniques. Visual inspection alone has detected a number of improperly allocated new M-S patches, whilst automatic evaluations alone have identified a number of incorrectly identified new areas. This study revealed that vision based trials can lead to detect new M-S patches. The following norms, must be used to objectively assess efficacy: (1) Determine lesion-segmentation-algorithm effectiveness to inter-scanner-variability, various M-R things. (2) Established medically meaningful threshold for the provided measurements that are related to significant future disability-progression. (3) Putting a mandate into place. Because MR imaging is readily available. It is the method of choice for MS patient diagnosis and follow-up in clinical trials as well as routine clinical practice. Scan systems, when used in routine clinical practice, serve to lessen patient burden and associated costs. Typically, they are restricted to the most essential standard sequences. With machine learning, these traditional sequences can be improved and previously hidden significant tissue features displayed. artificial D-I-R Sequences-Cortical-scars are an essential part of M-S pathology since they are unique to the illness and associated with its progression. They are now included in the criteria for radiological diagnosis. Cortical lesions are typically undetectable on conventional FLAIR and T2-P-D-weighted M-R-I. The ability to visualize these cortical scars is made possible by the double-inversion-recovery M-R-I sequence, which reduces the M-R signal from both white matter and cerebrospinal-fluid. D-I-R sequences are rarely employed in routine clinical practice or clinical research because to their lengthy acquisition periods and unavailability on the majority of MR equipment. Synthetic DIR pictures have been generated by teaching models based on generative adversarial networks with conventionally acquired T-1, T-2, FLAIR as well as T-1 and P-D-T-2m Synthetic D-I-R images outperformed conventional M-R-I sequences in detecting cortical-scars ($N = 626.v.s.696$) and juxta-cortical scars (12.3 ± 10.8 against 7.2 ± 5.6 , $p < 0.001$). Even though synthetic D-I-R pictures are not as sensitive as natural D-I-R images, they are nevertheless sufficient

to improve diagnosis and prognosis in typical clinical settings. Damage detection using contrast-enhancement: Apart from a very minimal risk of nephrogenic-systemic-fibrosis, gado-linim-based contrast chemicals are usually harmless for imaging. However, it has been demonstrated that following many I-V gado-linim treatments, gado-linim accumulates in the brain. Even though there have been no reported adverse effects, the medical community is nonetheless concerned since it is unclear what the long-term effects will be. It is therefore desirable to predict the existence of active inflammatory-contrast-enhancing lesions without the need for contrast agents. Narayana et al. used a sizable multicentre dataset to create a deep learning model that, when applied to T-1, T-2, and FLAIR images, could detect contrast-enhancing lesions with a sensitivity and specificity of 78% and 73%, respectively, for patient-specific enhancement identification using fivefold cross-validation. Visualizing tissue myelin content using M-R-I: De-myelination is a pathogenic feature of M-S that is not well seen with M-R-I. In-vivo-testing is useful in finding damage caused by inflammation, and the efficacy of my-Elin repair the pathways. Using the radio-tracer [11-C] P-I-B, P-E-T imaging can observe and quantify my-elin, despite being uncommon, expensive, and invasive. C-F-SAG-AN-based model was successfully trained using recent work's [11-C] P-I-B, P-E-T scans from M-S patients to observe changes in my-elin from M-T-R, D-T-I, T-2, and T-1 M-R-I (Fig. 7).

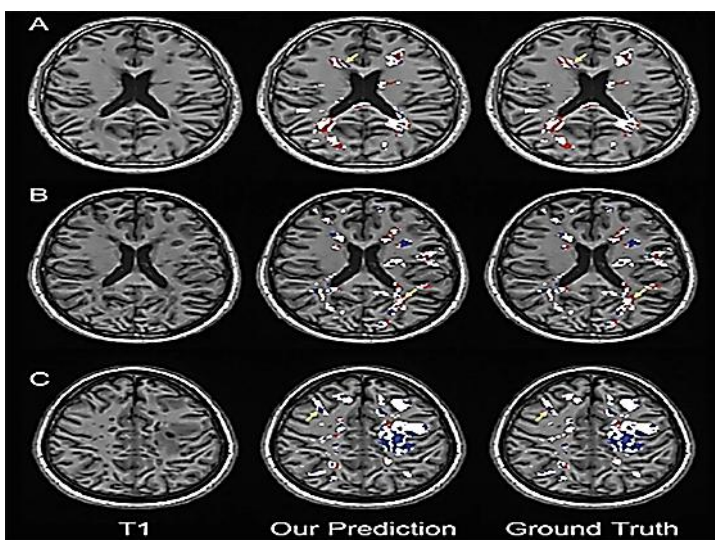


Fig.7: alteration in my-elin stuff using [11-C] P-I-B, P-E-T image (right col), the predicted change in myelin content using Wei et al.'s M-R-based model (middle col), and instances of lesion my-elin stuff changes using T-1-weighted images (left col). On top of the lesion mask (white), demyelinating (red) and demyelinating (blue) voxels.

With the help of benchmark age, M-R-I, CN-N analysis of injury maps, M-L method have effectively developed to forecast the growth of disabilities. Additionally, S-V-M classifiers have been used to integrate medical damage score, M-R-I-derived tumour volume and dementia. The subsequent investigation showed that including MRI measurement changes over the first year improved the prediction capabilities of the S-V-M model. In order to predict a second-relapse or conversion from C-I-S to C-D-M-S, a variety of studies made use of S-V-M to calculate health and socioeconomic factors, tumour-specific qualitative properties to whole brain area proportions. As per Pareto et al this shift from C-I-S to C-D-M-S could not be predicted reliably, despite developing a model based on regional grey matter volume and T-1-hypo intensities taken from T-1-Weighted M-R-I. Recognizing Patients at risk for the disease growth, even-though the above outline algorithms have more understanding of the predictive-capabilities of medical and radiological factors, their application to specific patients in routine medical practice is still very limited. These models have a major drawback in that they make the assumption that baseline variables' predictive characteristics are constant for all patients, even though these characteristics might change over time and within individuals. Based up-on medical as-well-as radiological features, Su-Sta-In model has been utilized in recent research to determine M-S subtypes, assuming that these factors vary over time. In order to explain cortex-led, normal-appearing white matter-led, and lesion-led M-S sub-types at early stages of the disease, Eshaghi et al., used this technique on M-R-I derived G-M volumes in brain areas, white-matter-volume, total-brain-scar number,

T-1/T-2 ratio inside brain structures of six thousand, three hundred twenty-two- 6322 M-S patients (Fig. 6). The scar sub-type was found to have a greater risk of disability, relapse-rate, treatment-response in the next 24-weeks compared to the other two groups after additional analysis of the validation dataset (N = 3068). A different study using Su-Sta-In in order to analyse the G-W figures in different brain areas and T-2 scar numbers in 425 M-S patients identified two sub-types that remained un-changed over period of time. Compared to the sub-type with early de-menia, the sub-type with early deep G-M atrophy was associated with faster disability-progression as-well-as cognitive-impairment. When combined, these findings show that physiologically and medically relevant M-S sub-types that have already been identified via Su-Sta-In modelling. After being modified to include strong metrics that can be produced from M-R-I scans obtained in routine medical practice, the Su-Sta-In models have the potential to be employed in everyday medical practices since they can be used to stratify specific patients. M-R-imaging is the recommended modality for M-S patient diagnosis and follow-up in routine medical practice due to its accessibility. In everyday medical practice, scan is usually limited to the most necessary standard sequences to reduce patient burden and financial expenses. These conventional-methods can be enhanced by M-L.

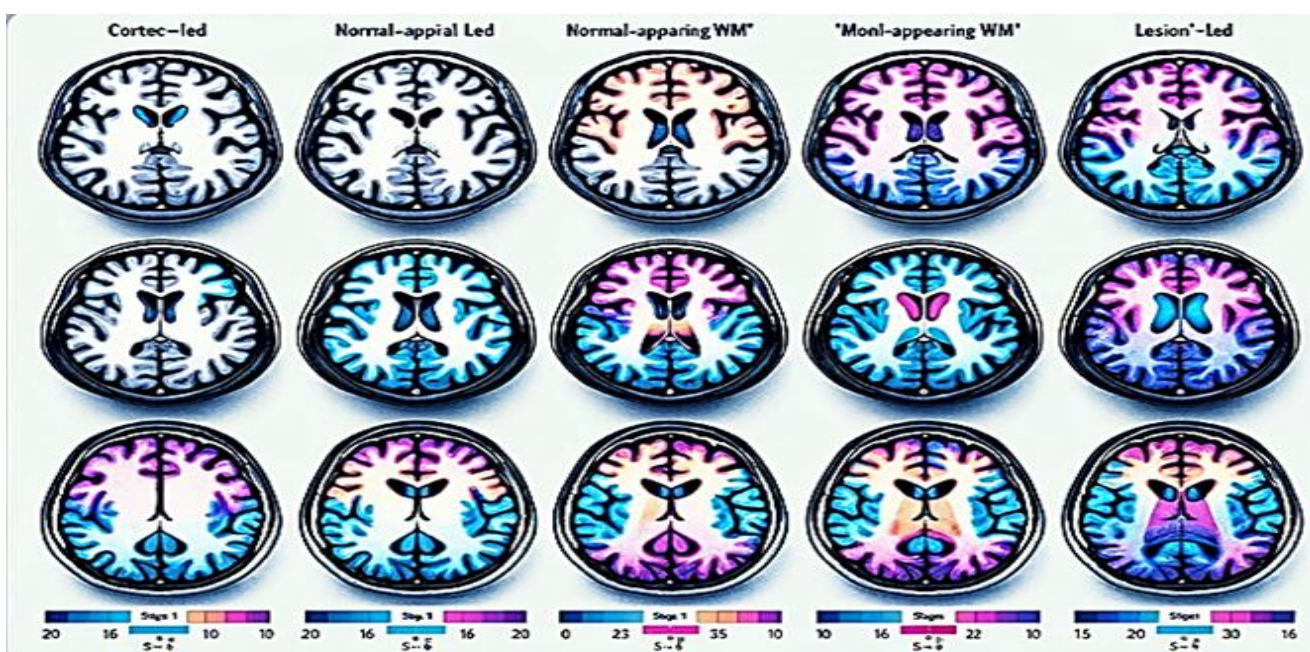


Fig.8: The Su-Sta-In research conducted by Eshaghi et al. shows the changes in M-R-I defects across three M-R-I-based categories. chance of lesion occurrence at each stage of the development of an M-R-I defects is displayed in the right col, whereas the left two col for each sub-type shows the likelihood of regional brain atrophy.

RESULTS AND DISCUSSION

Therapy modifications along the illness's progression are mostly in contrast to newly identified Degenerative or swelling action on brain MRI scans, which are shown as new or enhancing lesions. It is like this in routine clinical practice. However, when clinical decisions regarding therapy and monitoring are being made, the component of the M-S illness which is highly cytotoxic can be fundamentally unrelated but clinically significant is often overlooked. This is because there aren't enough clear-cut, accurate, and clearly interpretable indicators to pinpoint the exact level of neurodegeneration that a certain patient is experiencing. The primary method for measuring neurodegeneration in M-S is now brain volume measurements using magnetic resonance imaging. These metrics haven't yet been used in standard clinical care, though. This is due to the significant variations in age-related factors, biological parameters, and technology that have so far made it impossible to identify broadly applicable and clinically significant the threshold values for the decrease in brain volume. dependable among patients, even if their prognostic attributes may vary over time and within individuals. Based on clinical and radiological criteria, the SuStaIn model has been used in recent research to identify the sub-types of M-S. The basic purpose of this study is that these variables evolve with time. This approach was used by Eshaghi et al., to

identify cortex-led, normal-appearing white matter-led, lesion-led M-S (different kinds) in the initial phases of the illness by analysing M-R-I derived G-M numbers in various parts of the brain, white-matter-volume, total-brain-scar-numbers, and T-1/T-2 ratio within the brain areas of 6,322 M-S patients (Fig. 6). Compared to the other two treatment groups, the scar-led group had a considerably higher risk of disability advancement, relapse-rate, and treatment response in the next 24-weeks, according to additional analysis of the validation data-set, which included 3068 persons. An independent investigation that employed Su-Sta-In to quantify the volume of T-2 lesions and G-W matter in multiple brain areas identified a subset of 425 M-S patients. Early profound G-M atrophy and the development of scars were characteristics of this group. Likewise, a sub-group with an early cortical G-M volume reduction was seen; both of these groups showed stability across time. The sub-type with early G-M reduction was shown to be linked to an earlier onset of mental problems and disabilities than the variant having earlier cortex volume loss.

RESULTS

Magnetic-resonance-imaging (M-R-I) scans were used to compare the brain imaging of participants who were in great health (control group) with those who had M-S. The scans are shown in two different orientations: sagittal, which shows the brain in vertical side views, and axial, which shows the brain in horizontal slices. The brain architecture of healthy control subjects shows no appreciable variations from the norm, indicating normalcy. The ventricles, which are fluid-filled chambers found inside the brain, exhibit typical proportions and shape, and the brain tissue itself possesses symmetrical characteristics. This suggests that the brain is free of pathological or trauma-related issues. When persons with multiple sclerosis M-R-I, a variety of abnormalities are visible. In the brain's white matter, hyper intense, dazzling patch are clearly visible. These represent brain lesions. Demyelination is the loss of the myelin coating that encases nerve fibres for protection. Demyelination is the cause of these lesions. Such damage, which impairs normal brain function, is one of the fundamental features of multiple sclerosis. The corpus callosum, a large bundle of nerve fibres linking the two hemispheres of the brain, is a typical site of injury. Multiple-sclerosis patients often experience symptoms in this area. What essentially distinguishes the two sets of images is the presence and pattern of these anomalies in the M-S patient's photos. The absence of these anomalies in the control participants, or those who are not unwell, is the main distinction between the two sets of photos. Moreover, those with M-S may have bigger ventricles or greater gaps between brain regions, both of which suggest a reduction in the overall size of the brain. The equilibrium and regularity of the brain can be disrupted by these irregularities, which explains why multiple sclerosis patients' images differ greatly from those of healthy individuals. These M-R-I images clearly show how the structure of the brain is significantly altered in multiple sclerosis as compared to more typical, healthy brains. These results show an example of the accuracy of a machine learning model over thirty epochs, as well as the loss in training and validation. The accuracy and loss curves show a clear increasing trend during the first training session, indicating that the learning process is going well. It begins to do so quickly after the first few epochs, at which point the training loss starts to gradually decrease. This suggests that the model is doing a good job of fitting the training set. Simultaneously, throughout the training stage, the accuracy of the training dataset exhibits exceptional performance, quickly advancing, and ultimately surpassing 99%. Nevertheless, a notable divergence between the validation loss curve and the training loss curve is observed after around 10 epochs. Although the validation loss first decreases gradually, it ultimately rises in subsequent epochs, indicating the existence of overfitting. When a model performs exceptionally well on training data but struggles to effectively generalize to validation data, it is said to be over fitted. The observed divergence suggests that the model is becoming too fixated on the training set, collecting stochastic fluctuations instead of the main pattern. The little increase in validation loss that was noted serves as proof of this. However, the validation accuracy constantly hovers around 95%, which is little lower than the training accuracy and suggests a generally satisfactory performance. It is possible to conclude that the model can consistently perform well on fresh data based on the fact that the difference in the model's accuracy between the training and validation datasets has been comparatively steady. However, there is a small problem with overfitting that has to be fixed. By employing regularization, dropout, and cross-validation strategies, overfitting can be less common and the model's capacity for generalization can be enhanced. In summary, the model performs exceptionally well with room for growth in terms of generalization, as evidenced by its outstanding precision on both the training and validation sets.

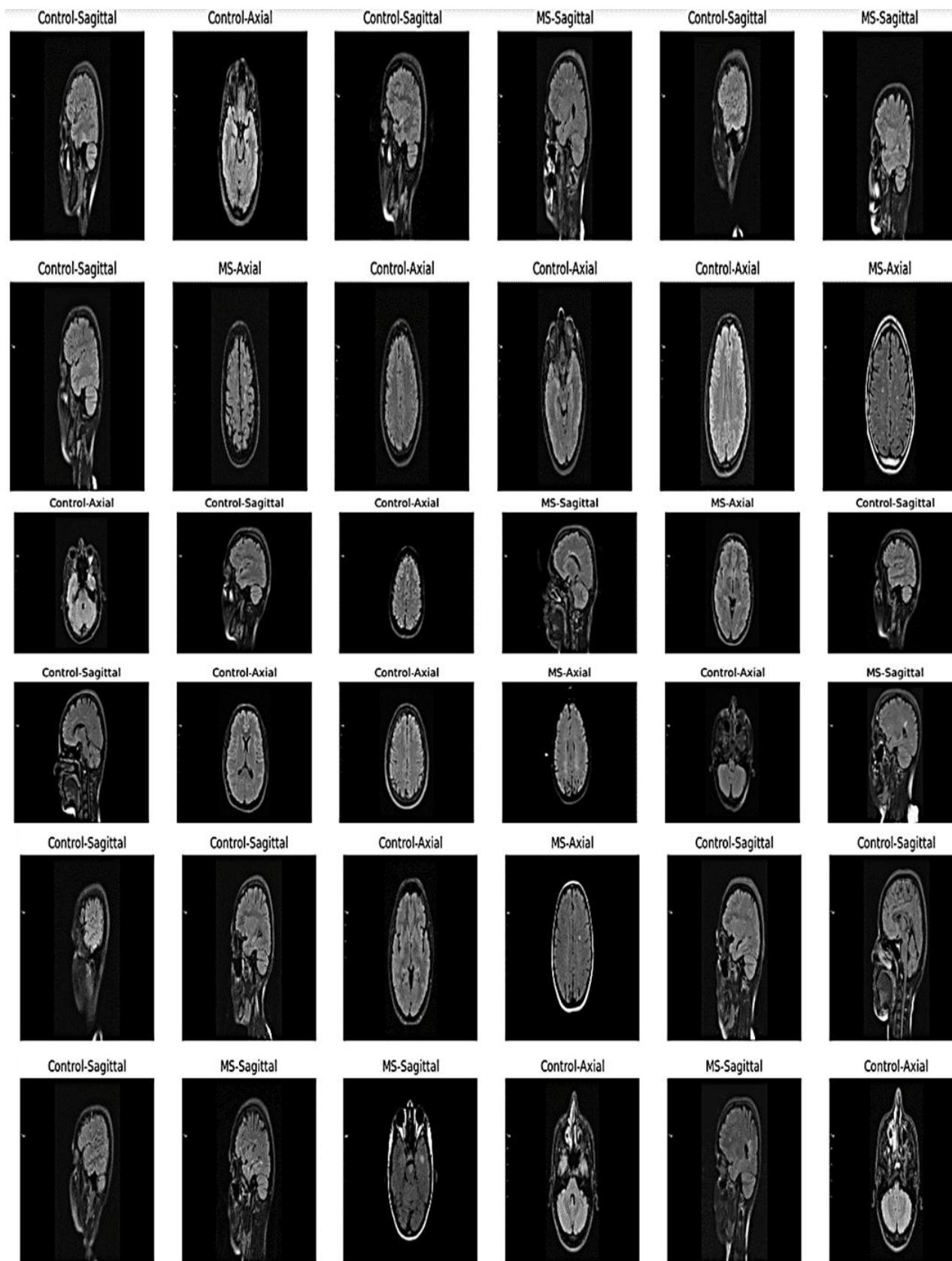


Fig 10. Magnetic resonance imaging (MRI) scans of participants who were in great health (control group) with those who had multiple sclerosis (MS). The scans are shown in two different orientations: sagittal, which shows the brain in vertical side views, and axial

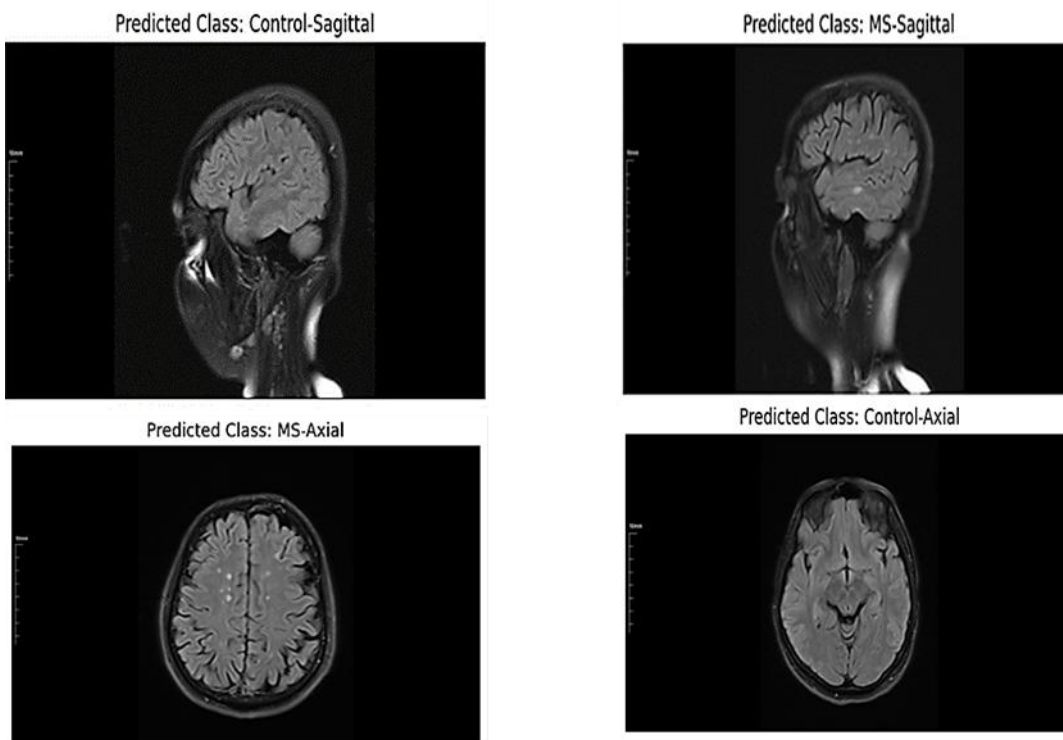


Fig 12. Output of the MS Detection: (a) MS-Axial (b) MS-Sagittal (c)Control-Sagittal (d) Control-Axial

CONCLUSIONS AND FUTURE SCOPE

Taking into account all of these data, it is evident that machine learning can help with the multiple sclerosis (MS) differential diagnosis. Radiologists who are not neuroradiology experts may find this very helpful. While there are machine learning models that can help with differential diagnosis, the majority of them have focused on distinguishing between multiple sclerosis and non-muscular obstructive sleep disorder (NMOSD). Although this distinction was intriguing from a scientific perspective, it is not the only diagnostic problem from a clinical standpoint. For radiologists unfamiliar with these kinds of disorders, the most challenging task is differentiating demyelinating lesions from lesions in the veins, that need to be the focus of next studies. The biggest barrier preventing the use of these models in clinical practice is their ability to be generalized to both MRI scanners and the general population. The use of these instruments in clinical practice may result in a scenario where individuals have tunnel vision since these investigations are frequently limited to a particular group of differential diagnoses. In summary, there are still problems that need to be fixed with regard to robustness among images obtained from different MRI scanners, generalizability to the broader population, and validation demonstrating that the M The application of various machine learning tools in clinical practice is still in its early stages, but it should offer information about how well-suited these tools are to different types of scanners, as well as provide precisely every result presented is offered has clearly defined clinically important limit points, and a simple interface enables the user to confirm the precision of the analysis anytime necessary.

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