A Study On MRI-Based Early Alzheimer’s Detection and 3D Analysis

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***Abstract:*** ***Our work investigates two imaging methods to study brain pathology in neurodegenerative diseases. The first approach uses MRI-FLAIR images to generate clear 3D models that show abnormal tissue. By concentrating on key slices, we captured the most important features and applied an intensity bar to compare pixel brightness across the white matter lesions region. This method provides a reliable way to detect and visualize white matter lesions structures, making it a strong tool for early diagnosis. The detailed 3D views also help track how the white matter lesions evolve over time, and the clear visual output lays the groundwork for incorporating these images into larger diagnostic systems. The second approach uses MRI-MPRAGE images to measure brain volume changes over time. However, the results from this method were not as expected, as the volume measurements fluctuated widely instead of showing a steady decline. These inconsistencies indicate possible issues with image alignment and segmentation, suggesting the need for further refinement. Although some trends in brain shrinkage can be seen, the variability highlights the challenges in capturing subtle anatomical changes. This observation points to important areas for improvement in the image processing pipeline. Overall, while the 3D white matter lesions scanning technique delivers strong visual insights, the brain shrinkage method requires additional optimization for reliable results****.*

***Keywords: Alzheimer’s Disease, Early Diagnosis, 3D Brain Imaging, Brain Shrinkage, Corpus Callosum, Neuroimaging.***

# **INTRODUCTION**

Alzheimer's Disease (AD) is a progressive brain disorder that affects older adults, causing memory loss, thinking problems, and daily life challenges. It is the most common cause of dementia, accounting for about 60–80% of cases [1]. Dr. Alois Alzheimer discovered the disease in 1906 while studying a 51-year-old woman named Auguste D., who showed memory loss, confusion, and hallucinations [2]. These symptoms were later linked to brain changes, including amyloid plaques and neurofibrillary tangles [1] [2]. His use of silver staining to identify these features started the study of AD.

After this discovery, AD became a major research focus. Early in the 20th century, doctors observed brain changes like plaques and tangles but did not understand their molecular causes [1]. Later, studies showed that genetic and environmental factors, especially the buildup of amyloid-beta (Aβ) [3], play a key role. Advances in MRI [3] along with the discovery of biomarkers like elevated tau protein and amyloid-beta in cerebrospinal fluid, have made diagnosis more accurate [3]. These improvements have deepened our understanding of AD and continue to shape research and medical practice.

Alzheimer's symptoms develop gradually, starting with mild memory loss and difficulty with everyday tasks. Early signs include forgetfulness and trouble recalling recent events or names. As the disease progresses, memory loss deepens, and individuals become disoriented and have trouble recognizing familiar faces or places [4]. In later stages, patients often become very confused, struggle to communicate, and lose the ability to perform basic tasks. Physical issues like difficulty walking, swallowing, and controlling bodily functions appear due to widespread brain damage, especially in the hippocampus [1] [5]. Behavioral changes, including depression, agitation, aggression, and hallucinations, are also common in the middle to late stages [1].

AD is diagnosed using clinical evaluations, brain imaging, and biomarker tests. The process starts with a thorough assessment where healthcare providers review the patient’s medical history, cognitive function, and behavior with input from family members. Standard tests like the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) help check memory, attention, and language skills [6]. If cognitive issues are suspected, MRI and PET scans are used to spot brain shrinkage and detect amyloid plaques or tau tangles, which are typical signs of AD [1] [7]. In addition, tests for cerebrospinal fluid (CSF) biomarkers such as amyloid-beta and tau proteins confirm the diagnosis and help track the disease’s progress [5].

AD progresses through stages of increasing cognitive decline. It begins with Mild Cognitive Impairment (MCI), where memory issues are noticeable but daily tasks can still be managed [1]. MCI often leads to Early Mild Cognitive Impairment (EMCI), marked by more noticeable memory deficits and difficulties with complex tasks, though independence remains [8]. As the disease advances to Late Mild Cognitive Impairment (LMCI), memory loss worsens, and individuals may need help with daily activities, experiencing confusion about time, place, and people [1] [9]. In later stages, significant cognitive impairments make patients fully dependent on caregivers, a progression that can be tracked using MRI scans showing hippocampal shrinkage and the buildup of amyloid plaques and tau tangles [4].

AD often goes unnoticed for years because its symptoms start slowly and are very subtle. In the initial stages, individuals may show mild forgetfulness or have trouble with complex tasks, which are often seen as normal signs of aging or stress, so neither patients nor doctors recognize the seriousness [1] [7]. These early symptoms do not significantly affect daily life, allowing individuals to remain independent despite the gradual decline [4]. Early diagnosis is also challenging since no single test can definitively identify AD and tools like imaging and biomarker analysis can be costly and hard to access [3] [5]. Additionally, stigma or denial often delays seeking help, so the disease is usually diagnosed only when symptoms have significantly progressed, limiting treatment effectiveness [5].

Over the years, treating AD has focused on managing symptoms rather than slowing or reversing the disease. Early treatments aimed to improve memory and cognitive function without addressing the underlying causes. In the 1990s, medications like cholinesterase inhibitors (Donepezil, Rivastigmine, and Galantamine) were introduced to boost acetylcholine levels in the brain, offering modest improvements [4]. Later, Memantine was approved to regulate glutamate activity and help reduce neuronal damage [5]. More recent research has shifted toward disease-modifying therapies targeting amyloid-beta plaques and tau tangles, the major features of AD. However, progress has been slow, and while Aducanumab, approved in 2021, targets amyloid plaques, its clinical benefits remain debated [3].

Today's treatment of AD includes both medications and non-drug approaches. Medications focus on easing symptoms. Cholinesterase inhibitors are used in mild to moderate AD to improve memory and thinking, while Memantine is typically prescribed for moderate to severe cases, often alongside cholinesterase inhibitors [4]. More recently, anti-amyloid therapies like Aducanumab have been developed to target amyloid plaques, aiming to slow disease progression, though their benefits are still debated [1] [3]. Non-pharmacological approaches also play a key role. Cognitive stimulation therapies, such as memory exercises and structured activities, can modestly improve cognitive function and delay decline [1]. Additionally, physical exercise, a healthy diet, and social engagement are recommended to support brain health and potentially reduce the risk of AD progression [5]. While these methods do not cure AD, they help maintain cognitive function and improve quality of life.

Despite progress in understanding AD, significant gaps remain in treatment and detection. Current medications like cholinesterase inhibitors and Memantine offer only modest relief from symptoms and do not slow the underlying disease, losing effectiveness as the disease advances [5]. New therapies, such as Aducanumab, aim to target amyloid plaques, but their ability to slow cognitive decline is still debated [3].

On the diagnostic front, advanced neuroimaging and biomarker tests have improved our ability to identify AD. However, methods like MRI, PET scans, and cerebrospinal fluid tests are expensive and complex, limiting their routine use [4]. Early detection is further complicated because AD symptoms often overlap with normal aging or other conditions, and no single test can definitively diagnose the disease at its initial stages [1].

Moreover, treating AD on a personalized level is challenging due to the disease's varied progression among patients, influenced by genetic, environmental, and lifestyle factors [5]. Biomarkers that could help identify individuals likely to respond to specific treatments are still under research and not widely used in clinical practice [3]. Overall, there is an urgent need for more effective disease-modifying treatments and improved diagnostic tools for earlier and more accurate detection of AD.

We have enhanced the analysis of MRI FLAIR [3] scans by converting axial 3D MRI data into detailed 2D slices. Our focus has primarily been on areas critical for clinical evaluations, such as the corpus callosum, white matter, and regions surrounding fluid-filled spaces. FLAIR (Fluid-Attenuated Inversion Recovery) imaging specifically reduces signals from cerebrospinal fluid, helping to highlight subtle lesions or abnormalities in brain tissue, particularly those associated with white matter changes or early demyelination. We applied methods including skull stripping, normalization, and intensity-based segmentation to extract precise grayscale pixel values and MinMax coordinates from each of these slices. These processed data were then reconstructed into comprehensive 3D visualizations, making subtle pathological features more visible, which are generally difficult to detect in routine clinical reviews.

Additionally, we have integrated MRI MPRAGE [3] (Magnetization Prepared Rapid Acquisition Gradient Echo) imaging into the workflow to perform volumetric analyses. MPRAGE is a high-resolution T1-weighted MRI technique known for providing clear structural differentiation and accurate anatomical boundaries, essential for assessing structural changes in the brain. Using K-Means clustering for segmenting important brain structures, along with rigid registration across different imaging time points, we were unable track down shrinkage of brain volume as the known fact due to some difficulties with segmentation, registration or flow of algorithm. The strength of FLAIR for lesion visibility analysis has successfully identified subtle morphological changes and hidden pathological signs typically missed during standard clinical assessments.

# **RELATED WORK**

Magnetic Resonance Imaging (MRI) has emerged as an invaluable tool in the early diagnosis and monitoring of Alzheimer's Disease because it effectively captures subtle anatomical and pathological brain changes, including white matter lesions, hippocampal shrinkage, and cortical atrophy. To fully leverage the diagnostic capabilities of MRI, extensive research has focused on applying various machine learning and deep learning methodologies to enhance the accuracy and precision of detecting early pathological changes. Previous studies have employed diverse strategies, ranging from deep convolutional neural networks (CNN) to classical machine learning algorithms, each offering distinct strengths and limitations. Transfer learning, structural MRI analyses, and hybrid models incorporating multimodal data have also been extensively explored. Reviewing these different approaches collectively provides critical insights into the strengths, current limitations, and gaps in existing diagnostic techniques, thereby highlighting opportunities for innovation and improvement in early AD detection.

1. **Transfer Learning and CNN Approaches**

In the study conducted by Marcia Hon and Naimul Mefraz Khan [11], the authors explored transfer learning as a method to address the common problem of small sample sizes in medical imaging. They fine-tuned a VGG16 model originally trained on ImageNet to classify Alzheimer’s Disease from brain MRI slices. Recognizing that not all MRI slices contribute equally to the classification task, they proposed an entropy-based slice selection approach, where slices with higher entropy indicating richer information were selected for training and evaluation. This strategy helped reduce noise and redundancy in the dataset while still preserving critical features necessary for the model to learn meaningful representations. Their results confirmed that transfer learning could be adapted to medical contexts effectively. However, their work mainly focused on 2D imaging, which naturally limits the ability to analyze the full spatial structures of the brain, a factor that becomes especially important when tracking the progression of subtle early-stage abnormalities.

W. Salehi, P. Baglat, A. Upadhya, and B. Sharma [12] proposed a deep learning model built specifically for early detection and classification of Alzheimer’s Disease using MRI data. Their custom CNN architecture was designed to automatically learn hierarchical spatial features from 2D slices without requiring manual feature extraction. The model performed well, demonstrating the strength of convolutional networks in picking up on complex brain patterns those traditional statistical methods often missed. However, like other 2D-based models, their approach focused largely on classification outputs without explicitly analyzing regional variations or abnormality patterns within the brain slices themselves. By limiting the spatial context to isolated 2D planes, important three-dimensional relationships between brain regions could be overlooked, which might delay the detection of very early structural deformities.

Expanding the analysis to a volumetric context, G. Praveena and G. Ramesh [13] introduced a 3D convolutional neural network designed for the multi-class classification of dementia stages. Their model utilized full 3D MRI scans, allowing it to retain spatial continuity across slices, a crucial factor when studying progressive diseases like Alzheimer’s. They categorized subjects into four groups Normal cognitive, Very Mild Dementia (VMD), Mild Dementia (MD), and Moderate Dementia (MoD), achieving an impressive classification accuracy of 99.94%. By capturing volumetric features, their model proved that 3D architectures could greatly improve detection performance compared to 2D slice-based approaches. However, despite the high accuracy, the study focused more on overall stage classification and did not specifically attempt to highlight or visualize the anatomical changes such as local white matter disruptions or early atrophy patterns.

While CNNs improve classification, they often miss visualizing early brain changes. Our work focuses on reconstructing subtle abnormalities from FLAIR and MPRAGE slices to aid early clinical assessment.

1. **Structural MRI Analysis**

Understanding subtle structural changes in the brain has been a key research direction for improving early Alzheimer's detection.

Gokce Uysal and Mahmut Ozturk [9] focused on classifying Early Mild Cognitive Impairment (EMCI) and Late Mild Cognitive Impairment (LMCI) stages by analyzing volumetric features from multiple brain regions. They extracted 13 different regional brain atrophy values including left and right hippocampus, cerebral gray matter, white matter, and supratentorial volumes using FreeSurfer tools. Their study highlighted how early atrophy patterns differ subtly between EMCI and LMCI patients. Although they achieved a notable classification accuracy of around 75%, their approach mainly centered on pre-defined structural areas and might have missed hidden abnormalities present outside these regions.

Kapil Kumar Et al [12] performed a comparative study of multiple machine learning techniques based on structural MRI data. They focused on gray matter density and cortical thickness measurements, employing Support Vector Machines (SVM) and K-Nearest Neighbors (KNN) classifiers to differentiate between AD and control groups. Their work showed that structural features, particularly cortical thickness and gray matter shrinkage, were highly informative for early diagnosis, achieving a remarkable classification accuracy of 99.76% with KNN. However, like earlier studies, their pipeline depended heavily on feature extraction from known brain areas without fully exploring subtle pixel-level intensity changes across the brain.

While structural MRI often depends on fixed regions, we focus on extracting pixel intensities to reveal hidden early abnormalities.

1. **Classical Machine Learning Techniques**

Before deep learning became dominant, classical machine learning methods were widely used for analyzing MRI datasets and detecting early signs of Alzheimer's Disease. Techniques like Support Vector Machines (SVM), Random Forests (RF), and Feed-Forward Neural Networks (FNN) have shown strong performance, particularly when applied to carefully extracted structural features.

Aunsia Khan and Muhammad Usman [15] conducted a broad review of classical ML algorithms applied for early Alzheimer’s diagnosis. They discussed how traditional models such as SVM, Decision Trees, Random Forests, and Naïve Bayes classifiers had been adapted for MRI-based studies and clinical datasets. Their review highlighted key challenges including imbalanced datasets, irrelevant features reducing model efficiency, and the risk of overfitting with limited data samples. To address feature selection issues, they proposed using association rule mining as an effective way to reduce feature dimensionality while maintaining diagnostic accuracy. Although their survey showed that classical ML methods could still perform well, it also emphasized that these techniques heavily depend on manually extracted and pre-processed features, which can limit their ability to detect subtle or unexpected pathological variations.

Shanmukha Sai Varma Et al [16] specifically applied classical ML models such as SVM, Random Forest, and Feed-Forward Neural Networks to early Alzheimer’s diagnosis tasks. They constructed classification experiments using clinical and structural features from MRI datasets and compared model performances. Among the models tested, Random Forest delivered the highest classification accuracy at 93.69%, outperforming both SVM and FNN in their experiments. Their study showed that Random Forest’s ensemble approach provided better generalization by handling non-linear relationships between features. However, their pipeline, like many classical frameworks, relied mainly on structured tabular features derived from manual measurements or clinical scoring systems, which may miss finer, pixel-level spatial patterns within MRI scans that often signal early disease progression.

Aditya Shrivastava [17] also explored the application of the Random Forest algorithm, focusing exclusively on MRI-based Alzheimer’s detection. They emphasized Random Forest’s strengths in handling large numbers of input features without requiring significant feature scaling or heavy pre-processing. Their work reported an impressive classification accuracy of 93.69%, validating Random Forest as a competitive method even against more complex models. Nonetheless, their analysis also pointed out a common limitation, the trust on already extracted features, such as hippocampal volume or gray matter density measurements, without engaging in direct imaging intensity analysis or spatial feature extraction from raw MRI volumes. This trust may prevent the discovery of subtle abnormalities that appear outside the traditionally studied regions.

While classical ML relies on manual features, our work extracts pixel intensities directly to uncover hidden early abnormalities without fixed assumptions.

1. **Hybrid and Ensemble Models**

As researchers tried to push the boundaries of Alzheimer's detection, many moved beyond single network models and started combining different deep learning approaches to improve prediction stability and accuracy. Some studies explored hybrid architectures to capture both spatial and sequential changes in brain structures, while others built ensemble models that could learn from multiple viewpoints and reduce prediction errors.

In one such effort, Chiyu Feng Et al [18] designed a hybrid model that connected the strengths of two powerful architectures 3D Convolutional Neural Networks (3D-CNN) and Fully Stacked Bidirectional LSTM (FSBi-LSTM). They used 3D-CNN layers to first grab the spatial patterns hidden across the 3D MRI volumes, learning how different regions of the brain are affected in Alzheimer's Disease. After that, they passed these spatial features into the FSBi-LSTM, which helped capture how structures change slice-by-slice, almost like understanding the sequence of brain deterioration. Their hybrid method showed strong results, reaching 94.82% accuracy in distinguishing Alzheimer's patients from healthy individuals. But even with all these strengths, the focus remained on boosting classification scores they didn’t really dig into explaining what exact changes in the brain were driving their predictions.

A different approach was taken by S. Fathi, A. Ahmadi, A. Dehnad, M. Almasi Dooghaee, and M. Sadegh [19], who proposed building an ensemble model by stacking multiple CNN classifiers together. Instead of depending on a single model’s opinion, their system combined the “votes” of different CNNs, making the final prediction more stable and resistant to errors. Their ensemble method delivered impressive results, achieving 98.57% accuracy in differentiating normal cognitive function from Alzheimer’s, and 99.83% accuracy when separating LMCI from AD. While their work clearly showed that combining models could produce more reliable predictions, like many other deep learning studies, it mainly focused on performance numbers rather than exploring what subtle brain changes were responsible for those differences.

While hybrid and ensemble models improved accuracy, they often hid the reasons behind predictions. Our work focuses on extracting intensity and volume changes to build 3D visualizations, making early abnormalities easier to detect.

1. **Multi-Modal and Deep Learning Techniques**

As Alzheimer's research kept evolving, it became clear that relying on a single type of scan or a single imaging modality might not always capture the full complexity of how the disease affects the brain. Researchers started exploring multi-modal approaches combining MRI, PET scans, and other clinical data and built deeper neural networks to piece together a more complete story about disease progression.

Narges Khanmohammadi and Niloofar Ghassemi [17] explored the power of combining FDG-PET imaging with deep learning models for diagnosing Alzheimer’s Disease. FDG-PET captures glucose metabolism levels across the brain, offering insights into functional impairments that often show up before major anatomical damage occurs. Their deep neural network was trained to differentiate between cognitively normal (CN), Mild Cognitive Impairment (MCI), and Alzheimer’s Disease (AD) subjects, achieving exceptionally high accuracy 99.31% for CN vs. AD and 99.88% for CN vs. MCI. Their approach showed that functional brain imaging could reveal very early disease markers even before MRI visible atrophy sets in. However, although their system achieved impressive predictive performance, it mostly focused on classification outputs without mapping these metabolic changes back to specific anatomical structures or visually explaining the early-stage alterations in brain regions.

M. Bagheri and B. Pooya [18] shifted focus back to structural MRI, using deep Convolutional Neural Networks (CNNs) to automatically learn critical features for early Alzheimer’s detection. Instead of manually selecting features like hippocampal volume or cortical thickness, their model learned subtle gray matter shrinkage, white matter loss, and brain atrophy patterns directly from imaging data. Their study showed that CNNs could outperform traditional methods by discovering hidden imaging biomarkers that hand-crafted features might miss. However, while they successfully improved detection accuracy, their system also acted like a black box it was difficult to trace which areas or intensity variations influenced the decisions, which limited its clinical interpretability for early-stage diagnosis.

S. Fathi, A. Ahmadi, A. Dehnad, M. Almasi Dooghaee, and M. Sadegh [19] took the ensemble route by merging the outputs of several CNN models to create a stronger, more stable Alzheimer’s detection framework. Their ensemble method aggregated predictions from multiple models trained on different MRI representations, achieving very high classification results across various stages of Alzheimer’s Disease. By combining several perspectives, they reduced model variance and improved generalization across datasets. However, like many ensemble-based studies, their work emphasized boosting classification accuracy and robustness, while offering little focus on directly visualizing or interpreting the subtle anatomical changes that might explain why one brain was classified differently from another.

# **Our Contribution**

In this work we investigated 2 different ways to visualize and assess the presence of brain white matter lesions. In the first approach we extracted the white matter lesions from FLAIR MRI images to render a 3D scan of foreign brain matter questionably a white matter lesion. In the second approach we use K-Mean clustering with MRI MPRAGE images to predict the volume of brain matter. In the following subsections we present these two approaches and our findings.

## *Background*

MRI is widely used to detect AD by capturing clear brain images. It identifies key changes like hippocampal shrinkage, cortical thinning, and corpus callosum damage, which disrupt brain communication and contribute to memory loss. Additionally, MRI is safe, non-invasive, and suitable for repeated scans, making it valuable for machine learning models that predict disease progression.

The MRI data used in this study were collected from the Alzheimer’s Disease Neuroimaging Initiative (ADNI), a widely used resource that offers a variety of scan types across different stages of Alzheimer's. The scans were provided in DICOM (.dcm) format, which not only preserved the imaging details but also included rich metadata like subject identifiers, scan dates, and acquisition parameters. These files supported both structural analysis and longitudinal tracking by offering consistent formatting across modalities such as FLAIR and MPRAGE [3].

FLAIR is often preferred over other MRI techniques for detecting AD because it is particularly good at showing changes in white matter and areas near fluid-filled spaces in the brain. It is highly effective at detecting small lesions, signs of blood vessel damage, and early degeneration in the corpus callosum, which are key indicators of AD. FLAIR works by suppressing signals from fluid, making abnormalities in the brain easier to see. This makes it especially useful for identifying early disease changes that might not be visible with other MRI techniques.

Using an axial MRI FLAIR 3-D image from Alzheimer’s Disease Neuroimaging Initiative (ADNI) website, we extracted 2-D slices to facilitate clearer observation during extracted 3D visualization. The original 3D image contained unrelated data that could interfere with the analysis, so we applied skull stripping to remove unwanted portions, such as the skull, which might also affect the gray matter regions of interest.

We selected slices 16 through 24 because these slices provide the clearest view of the corpus callosum as we can see in fig 1 and fig 2. This specific range captures the full extent of the brain, including regions prone to abnormalities such as white matter damage, lesions, and atrophy in the corpus callosum. As a result, these slices reveal essential features, including early signs of Alzheimer’s disease, enabling more accurate diagnosis and progression tracking as shown in fig 1 and fig 2.

A close-up of a brain scan

Description automatically generated  
Fig. 1. Images with skull of selected slices (slice# 14, 15, 23, 24)

A collage of images of a brain

Description automatically generated  
Fig. 2. Images without skull of selected slices(slice#14,15,23,24)

1. *3D White matter lesions scanning*

Our approach focused on white matter lesions, we specifically worked with FLAIR images obtained from the ADNI dataset. Each FLAIR scan came as a series of DICOM files, where each slice represented a portion of the full brain volume. These files were organized by subject and then merged into complete 3D volumes. To make the data usable for visualization and pixel-level intensity analysis, we converted these volumes into NIfTI (.nii) format. This step was essential, as it allowed us to apply skull stripping, slice extraction, and 3D reconstruction techniques for isolating regions affected by white matter abnormalities.

The next step involves preprocessing the images through skull scripting [19], a critical process that removes non-brain structures, such as the skull, which may otherwise interfere with the accurate measurement of pixel intensities. Skull stripping not only eliminates unwanted tissues but also improves the overall quality of the image by reducing noise and focusing the analysis on the regions that contain relevant clinical information. This sanitization step is evident when comparing the original images Fig. 1 with the processed images Fig. 2, where the removal of unnecessary tissues results in a clearer focus on the brain matter and a more uniform intensity distribution.

Following skull stripping, the sanitized images are input into our automated processing code. The first operation performed by the code is normalization. Given that the original images exhibit intensity values that are not directly compatible with our analysis framework, they are converted to the uint16 data type, thereby standardizing them into a 16-bit format. This conversion is indispensable as it ensures consistency across the dataset, facilitating more accurate comparative analysis and reducing the potential for errors during subsequent processing steps. Furthermore, normalization aids in minimizing the effects of variability inherent in raw imaging data, thus enhancing the robustness of the automated pipeline. Subsequently, the normalized 3D images are segmented into 2D slices. This approach simplifies the analysis by allowing us to process individual slices rather than the complete 3D dataset, thereby reducing computational complexity and enhancing the clarity of the features under investigation. The extracted slices are saved in both TIFF and PNG formats, ensuring that they are easily accessible for both visual inspection and automated processing. Particularly, only a subset of slices (specifically slices 16 through 25) is selected for further analysis which covers the complete corpus colosseum of the brain. This careful selection is based on careful observation is done manually by checking with expert as the original set of 35 slices including the top and bottom portions of the brain which tends to contain extraneous information that may confuse the interpretation of the 3D reconstruction as seen in Fig. 1.

The subsequent phase of the workflow involves detailed pixel intensity extraction from the selected 2D images. As the MRI images are rendered in grayscale, our focus is on extracting gray pixel intensity values that reflect the subtle variations in tissue density. This is accomplished using a specialized tool available online known as PixSpy application which quantifies the grayscale values on a 0–255 scale. Through careful observation and analysis across multiple images, we determined that the intensity range of 23170 to 30840 is most indicative of the features of interest which is taken from 16-bit (0-65535). The automated code systematically extracts these intensity values along with associated metadata, including the filename, slice number, X and Y coordinates, cluster numbers (which denote the number of distinct clusters in each image), and cluster sizes. The inclusion of cluster size data is instrumental in filtering out insignificant clusters, thereby ensuring that the analysis remains focused on clinically relevant regions. All extracted information is meticulously organized and saved in an Excel file within corresponding folders, which facilitates subsequent data management and further analysis.

Once the X and Y coordinates have been extracted from the individual slices, they are aggregated across adjacent slices. This step ensures that only consistent, contiguous regions are considered, thereby facilitating the formation of a comprehensive 3D reconstruction of the ROI. By correlating adjacent slices and combining the extracted pixel data, the algorithm can form a detailed three-dimensional representation that mirrors the spatial continuity of the brain tissue. This is crucial in ensuring that the final 3D model accurately reflects the true anatomical structure and any associated pathological changes. The collated pixel intensity data is then used to generate a 3D visualization of the white matter lesions region, as shown in Fig. 3.

A screenshot of a computer

Description automatically generated

Fig. 3. 3D extracted image

The creation of the 3D model is further enhanced by the inclusion of an intensity bar, which serves as a quantitative reference for the pixel values across the reconstructed volume. This bar enables precise examination of pixel intensities, where higher values are represented in a high-contrast manner in Fig. 4 and lower values are depicted towards black or zero as we can see in Fig. 5. In these 3D visualizations, the z-axis corresponds to the slice number, while the x and y axes hold the original coordinate values extracted from the 2D images. This multidimensional approach ensures that the spatial and intensity information is accurately represented, thereby aiding in the detailed analysis of white matter lesions morphology.

Local (x, y, z) coordinates represent the positions of the extracted data within the processed images, while the actual values reflect the original spatial dimensions as captured during the MRI scan. As shown in Fig. 3, the x and y ranges are derived from the Excel dataset, and the z-axis represents the number of slices, with an additional padding of 20 pixels on each side to enhance the outlining of the white matter lesions boundaries. This padding not only improves the visual clarity of the white matter lesions but also ensures that peripheral regions, which may be of diagnostic importance, are adequately represented. Also, the original pixel dimension (PixDim), defined by a 5mm slice thickness, is used to accurately calculate the ROI, thereby ensuring that the 3D reconstruction is both spatially and dimensionally accurate.

For instance, Cluster 6 is one of several clusters identified within the 3D visualization, representing a separate segment of the white matter lesions that has been quantitatively analyzed. Each cluster is carefully evaluated based on its size, location, and intensity characteristics, which enables the differentiation between caring variations and clinically significant abnormalities. The detailed analysis of these clusters provides invaluable insights into the white matter lesion’s heterogeneity, a factor that is critical in understanding disease progression and in planning subsequent treatment strategies. By visualizing the 3D reconstruction from a single sample, our method enables the detection of white matter lesions regions ranging from minute clusters to larger conglomerates. This comprehensive 3D analytical approach not only enhances diagnostic accuracy but also provides a richer, more fine understanding of white matter lesions morphology. Detailed visualization allows clinicians and researchers to identify subtle patterns and irregularities that may not be freely visible through traditional 2D imaging techniques slice by slice or in complete 3D image.

A screen shot of a computer generated image

Description automatically generated

Fig 4: The pixel intensity with high contrast

A screen shot of a computer

Description automatically generated

Fig 5: pixel Intensity with low contrast

1. *Brain matter volume predictions*

We first obtained the MRI-MPRAGE images in the DICOM (.dcm) format, where each file represents a segmented portion of the overall imaging dataset and includes essential metadata. This metadata, which details the imaging parameters and patient information, is crucial for ensuring the proper alignment and scaling of the images. For each subject, we then systematically combined these individual DICOM files to construct a complete 3D volume. Following this, we converted the aggregated data into the NIfTI (.nii) format. This conversion is a key step in the process, as the NIfTI format is widely recognized and used in the field of neuroimaging. The computational pipeline begins with comprehensive data collection and systematic organization. Multiple MRI-MPRAGE scans are taken which are AD, MCI, LMCI, and EMCI. Each scan’s filename is embedded with crucial metadata, such as the acquisition date, a unique subject identifier, and the diagnostic label. The pipeline leverages regular expressions to automatically extract the date formatted as “YYYY-MM-DD”, isolate the subject ID based on a predefined pattern, and determine the category from the filename prefix. Once these attributes are parsed, the scans are grouped according to the subject identifier. The grouped files are then sorted chronologically, designating the earliest scan for each subject as the baseline against which all future scans will be compared. This organization is fundamental because accurate temporal analysis requires a reliable reference point to evaluate subsequent changes in brain anatomy.

A diagram of a software process

Description automatically generated

Fig 6: Flow chart of brain volume prediction

Following file organization, the next phase involves difficult image preprocessing and normalization. Each MRI scan is first rescaled so that its intensity values lie within the range [0, 1]. This normalization step reduces potential variability across different scans that may have resulted from variations in acquisition settings or scanner performance. Subsequently, a Gaussian smoothing filter is applied during preprocessing to reduce high-frequency noise. This filtering reduces minor intensity fluctuations that might interfere with accurate segmentation. By smoothing the images, the pipeline improves the fidelity of subsequent tissue differentiation and enhances the overall robustness of the segmentation outcome as shown above in fig 6. For segmenting the brain tissue from the rest of the image, the preprocessed data is reshaped into a one-dimensional array, thus enabling the application of a clustering algorithm. K-Means clustering is chosen due to its simplicity and effectiveness in distinguishing areas of high and low intensity. The algorithm is set to identify two distinct clusters, one that represents brain tissue, which is assumed to exhibit higher intensity values and another representing the background. After clustering the segmentation result in the form of a binary mask undergoes refinement through morphological operations. A binary closing operation is first performed to close small holes and eliminate minor discontinuities in the mask. The connected component analysis is implying, so that only the largest connected region assumed to be the brain is retained. Finally, by calculating the number of voxels within this refined mask and multiplying by the volume of a single voxel (derived from the image's spatial resolution) the method computes an absolute measure of brain volume in cubic millimeters (mm³) as shown in fig 7 and fig 8.

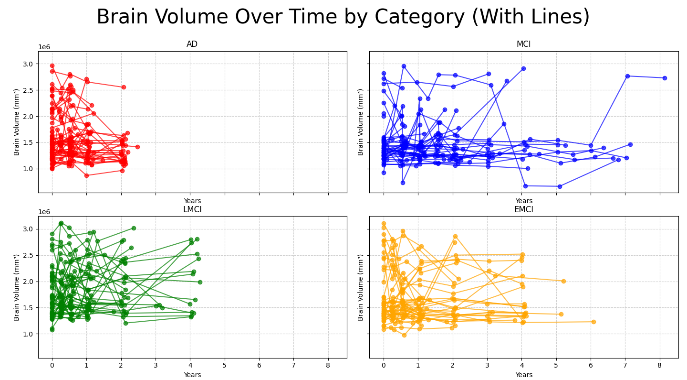


Fig 7: connected points with same subject over the time vs volume

The methodology focuses on aligning the scans temporally through image registration. Accurate registration is essential because minor differences in patient positioning or slight variations in imaging protocols can significantly impact volume measurements. To address this, the earliest scan (baseline) serves as the reference image, and subsequent scans are registered to this baseline using a rigid registration method based on Euler 3D transforms. The registration process is used by a Mean Squares similarity metric, with a gradient descent optimizer ensuring iterative minimization of errors. The use of a centered transform initializer further enhances the registration by aligning the centers of the moving and baseline images. This careful alignment ensures that any measured differences in the segmented brain volumes are more likely to reflect true anatomical changes rather than pieces arising from misregistration or patient movement.

Once the scans are registered and the brain volumes calculated, the temporal evolution of brain volume is analyzed. For each subject, the time difference between each scan and the baseline (expressed in days and converted to years) is computed. This measurement provides a consistent temporal axis for subsequent analysis.

Volume (mm³) = Number of voxels in the brain mask Volume of a single voxel (mm³)

Therefore, Single voxel volume=1.0 1.0 1.2=1.2 mm3

1. **RESULTS AND ASSESSMENTS**

In the first part of our study, we worked on creating clear 3D visualizations of white matter lesions using MRI-FLAIR scans. Our main goal was to capture very small changes in the brain, especially around the corpus callosum and nearby white matter areas, because these can be early signs of Alzheimer’s disease.

We looked at a few important points. initially, for visual clarity and anatomical accuracy, we built 3D models by combining slices 16 to 24, where the corpus callosum shows up clearly. The 3D models we created matched well with what we expect to see in standard brain atlases. When we compared our processed images with known brain structures, we found that the areas we extracted made sense and were likely related to early disease changes.

Next, we analyzed the pixel intensity from the grayscale MRI images. We focused on a specific range of intensity values (between 23170 and 30840 on a 16-bit scale), which usually points to bright spots that can represent lesions or damaged tissue. By using this range, we were able to highlight clusters of higher intensity that likely represented abnormal regions, rather than just picking up normal or random brain tissue. we also made sure that the changes we saw were continuous across multiple slices. This spatial continuity helped show that the lesions weren’t random but extended through the brain in a meaningful way. This made our 3D reconstructions even stronger and more trustworthy. To make it easier to understand the intensity variations, we included an intensity bar alongside the 3D models (shown in Figures 3, 4, and 5). This bar helped quickly point out the high-intensity regions, making it easier to spot subtle abnormalities briefly. Although picking slices manually helped us focus better on important regions, it also introduced a small risk of human bias. In the future, we plan to use automated methods, like entropy-based slice selection, to make the process more objective and reliable across different scans.

Overall, our 3D visualization method for white matter lesions worked very well. It produced high-quality, anatomically correct, and intensity-validated models. This approach shows a lot of promise as an extra tool to help detect Alzheimer’s disease at an early stage.

In the second part of our project, we focused on tracking changes in brain volume over time using MRI-MPRAGE scans. Our main goal was to detect signs of brain shrinkage, also known as atrophy, which is a key marker of Alzheimer’s disease. We aimed to monitor how brain volume decreased across different scan sessions for the same individuals. We looked at several important points. First, we expected to see a slow and steady decline in brain volume as time went on. Ideally, if we plotted brain volume against years, we should have seen a smooth downward line.

Another important step was to make sure that the different scans were properly aligned. We used a rigid Euler-based registration method to line up follow-up scans with each subject’s baseline scan. We also wanted brain volume measurements to stay consistent between scans, without a lot of random jumps up or down. However, when we looked at the actual results shown in Fig 7, we found a lot of inconsistencies. Instead of a smooth downward trend, brain volumes jumped around irregularly for most subjects and sometimes even showed increases instead of decreases between scans. This unexpected pattern made it hard to trust the method for tracking disease progression based on brain volume alone. Fig 7 shows each subject’s brain volume changes over time, separated into groups like AD, MCI, LMCI, and EMCI. Ideally, the lines for each subject should have sloped steadily downward. Instead, the lines went up and down in unpredictable ways, showing that the volume measurements were unstable.

This inconsistency could be because of:

* The inaccuracies of the volume measurement module
* The faulty image acquisition and processing module
* The low accuracy of the segmentation module in addition to the noise

1. **FUTURE WORK**

Based on the limitations encountered, several improvements are planned for future development of this research. Firstly, addressing the volume measurement inaccuracies is critical. The current method calculates brain volume solely based on segmented voxel counts, which makes it highly sensitive to even minor segmentation errors. Future work will involve incorporating more robust volume estimation strategies that account for anatomical landmarks and cross-verify brain region boundaries to reduce such discrepancies. Secondly, improvements in image acquisition and processing standardization are necessary. Image quality variability caused by scanner differences, protocol variations, and patient movement significantly impacts downstream analysis. We propose to introduce intensity normalization pipelines and pre-scan quality control checks to standardize datasets before processing. Additionally, introducing session-to-session bias correction techniques may stabilize longitudinal comparisons. Thirdly, and most importantly, enhancing segmentation quality is crucial. While K-Means clustering provided a simple starting point, it lacks the refinement needed for reliable anatomical segmentation.

Moreover, future work should include extending the study to a larger cohort to validate findings statistically and understand subject-specific variations better. Subject-specific longitudinal brain volume plots, as suggested in fig 7, will become standard to monitor and quantify individual progression patterns. In summary, enhancing measurement precision, stabilizing image quality and applying more advanced segmentation methods will be the main pillars of future improvements. These refinements are expected to provide more consistent and reliable longitudinal tracking of brain atrophy, thereby increasing the clinical relevance of MRI-based Alzheimer’s detection methodologies.

1. **CONCLUSION**

In this study, we explored two parallel approaches to enhance the early detection and analysis of Alzheimer’s Disease using MRI imaging. The goal was to design practical methods that reveal hidden brain abnormalities either through detailed lesion visualization using MRI-FLAIR and by measuring brain volume changes over time using MRI-MPRAGE scans.

The first approach focused on visualizing 3D white matter lesions. This method worked well and allowed us to generate high-quality anatomical views of subtle white matter disruptions, especially around the corpus callosum. By selecting relevant axial slices and applying steps like skull stripping, normalization, and pixel intensity extraction, we could reconstruct detailed 3D models that clearly highlighted abnormal tissue zones. We also added intensity bars to aid interpretation, helping to visualize pixel value variations and confirm the presence of bright lesion regions. This technique adds an extra layer of clarity and could support traditional diagnoses by making early-stage abnormalities more visible particularly those that may go unnoticed in routine clinical scans.

The second approach, tracking brain volume changes across time using MPRAGE scans came with more difficulties. Although we followed a structured pipeline involving intensity normalization, segmentation, and registration, the expected downward trend in brain volume was not consistently observed. Instead, we saw random fluctuations, including some cases where volumes increased unexpectedly between sessions. These inconsistencies likely resulted from segmentation inaccuracies, rigid registration limitations, and noise in image acquisition. Still, this part of the study was crucial in pointing out where the method needs refinement and what future improvements should focus on.

From both approaches, we learned that working with MRI data especially for Alzheimer’s detection requires balancing technical accuracy with biological variability. The white matter lesion visualizations showed promise and offered stable, interpretable outputs. However, the brain volume tracking method highlighted the need for stronger segmentation models, improved registration techniques, and better handling of scan-to-scan variability. This work serves as a solid foundation for future progress. We now see the importance of adopting more advanced segmentation methods, such as deep learning or atlas-based models, and using non-rigid registration to account for anatomical changes more effectively. Standardizing preprocessing across subjects and expanding to larger datasets will also play a key role. Adding longitudinal tracking plots for individual subjects could provide deeper insight and stronger statistical evidence.

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