

Investigating the Extent to Standard Uptake Value Ratios Measure the Efficacy of Anatomically-Guided PET Reconstruction on the Diagnostic Quality of Florbetapir-F18 PET Scans for Alzheimers Disease

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Alzheimers Disease (AD) is a common neurological disorder that affects the nerve cells in the brain, and anatomically guided PET reconstruction (AGR) is an imaging reconstruction technique that has been a promising method to improve the quality of amyloid PET images. While previous studies investigated the AGR method on PET images, it is unclear whether the AGR method improves PET image quality in the context of Alzheimers Disease diagnosis. This study aimed to determine the influence of AGR on the diagnostic quality of Amyloid PET images for AD. The diagnostic quality of PET images for AD were quantified based on standard uptake value ratios (SUVrs) that were used in this study. A dataset of 76 volunteers aged 50-87 years old from imaging records from NYU Langone Radiology in Manhattan, NY was investigated. There were no statistically significant differences between the AGR and non-AGR standard uptake value ratios (SUVrs) (Whole Temporal Lobe: $p=0.94272$; Whole Superior Frontal: $p=0.91928$; Whole Precuneus: $p=0.98383$; Whole Hippocampus: $p=0.98383$; Whole Lateral Occipital Lobe: $p=0.98677$). These results suggest that the AGR method did not improve the diagnostic quality of the PET image for AD. These findings highlight a central challenge in applying AGR for AD diagnosis: while AGR may improve visual image quality, it does not appear to significantly affect quantitative diagnostic markers such as SUVrs, and contribute to the ongoing effort to enhance imaging techniques for more accurate and sustainable diagnostic practices. Future studies should focus on alternative PET image metrics when applying the AGR method to better understand how the AGR method affects the diagnostic quality of the PET image for AD.

Keywords: Alzheimers Disease (AD), PET imaging, neuroradiology, amyloid-beta protein, amyloid PET scan.

1 Introduction

1.1 Rationale

Alzheimers Disease (AD) is a prevalent neurological disorder that leads to the degeneration of nerve cells and is the primary cause of dementia^{1,2}, and amyloidosis, which is the process of amyloid-beta proteins building up in the brain, is thought to be the central cause of the pathogenesis of AD^{3,4}. Positron emission tomography (PET), a noninvasive imaging technique that can determine the quantification of changes in metabolic processes and other physiological activities in the body, is capable of detecting amyloid plaques associated with AD and is therefore a crucial imaging tool for the diagnosis of early onset AD^{5,6}. Amyloid PET is able to detect amyloid plaques associated with AD due to its utilization of Florbetapir-F18, a PET tracer that can measure the presence of A β aggregates in the white and gray matter of the brain⁷. Thus, the improvement of the spatial resolution of PET imaging is of significant interest, as it can ultimately enhance the diagnosis for neurological disorders such as Alzheimers Disease⁸. Anatomically Guided Reconstruction (AGR) is a promising method to improve the quality of PET im-

ages that has been implemented in previous studies^{8,9}. Although prior studies have investigated the effect of the AGR method in improving PET images, there has been a lack of evidence regarding whether or not the anatomically guided reconstruction method improves the contrast between white and gray matter in the brain^{8,9}. Additionally, there is a lack of evidence concerning whether the improvements seen in PET contrast are sufficient to improve the diagnostic quality of the PET images in the detection of Alzheimers Disease¹⁰. Therefore, the aim of this novel retrospective study is to determine the extent to which the anatomically guided reconstruction method enhances the quality of the PET image contrast of the Florbetapir-F18 tracer, and whether or not this potential improvement in tracer uptake is sufficient to improve the diagnostic quality of the PET images for Alzheimers Disease. These findings may have the potential to improve the diagnostic quality of PET images for Amyloid plaques, which allows for patients to begin treatment earlier to reduce the development of amyloid plaques that are linked to AD^{11,12}.

1.2 Background

1.2.1 Alzheimers Disease and the Amyloidosis Hypothesis for AD

Alzheimers Disease (AD) is a neurological disorder that causes the death of nerve cells and is the most common form of dementia, which is an umbrella term for neurological disorders characterized by cognitive impairments and difficulties in performing everyday activities^{13,14}. Amyloidosis is thought to be the central cause of the pathology of AD among neuroscientists and is therefore a promising target for AD treatment^{3,15}. Amyloidosis is the process of amyloid beta ($A\beta$) protein buildup in the brain, and is caused by the release of extracellular deposits of amyloid-beta protein, which form senile plaques in the brain¹. Since AD is an irreversible and progressive neurological disorder, early diagnosis is imperative for preventing further developments of amyloid plaques that are linked with AD^{1,11,16}.

1.2.2 Amyloid PET imaging

Positron emission tomography (PET) is a non-invasive imaging technique that may be used to determine the changes in metabolic processes in various organs of the human body⁵. Amyloid PET is a form of PET that is designed to detect amyloid plaques in the brain which are associated with the early onset of AD⁶. Amyloid PET may be conducted with several different radiotracers that used to detect amyloid plaques in the brain: these radiotracers include 18F-florbetaben, or Neuraq; 18F-flutemetamol, or Vizamy; and 18F-florbetapir, or Amyvid^{4,15}. Florbetapir F-18 has a high affinity for amyloid beta protein aggregates which allows for quantification of cerebral retention of amyloid beta proteins and may be important in the diagnosis of AD^{17,18}. Amyloid PET using 18F-florbetapir PET had a substantial clinical impact on AD and non-AD diagnosis by improving diagnostic confidence, which may play a crucial role in the early diagnosis and treatment of AD^{11,19,20}.

1.2.3 Gray Matter Regions of Interest for Amyloid β Plaque Formation

There are several regions in the brain that are susceptible to amyloid β plaque formation in the early onset of AD that may serve as a region of interest (ROI) for tracer activity²⁰⁻²².

One study implicated the temporobasal and frontomedial areas of the brain from where the plaques then progress into the rest of the neocortex until they finally reach the striatum²¹. Another study found that the precuneus, and the medial and lateral orbitofrontal cortices are the earliest brain regions that are susceptible to amyloid beta plaque formation in the onset of AD²². A recent study utilizing a Pearson correlation coefficient test found a significant relation between PET standard uptake value ratios (SUVr), which are quantitative mea-

surements that quantify tracer uptake in the brain, and white matter hyperintensity volumes in the precentral, caudal middle frontal, cuneus, fusiform, isthmus cingulate, lateral occipital, lingual, paracentral, pericalcarine, precuneus, superior parietal, and supramarginal regions²⁰. Investigating a specific region of interest (ROI) is imperative to analyzing differences in tracer uptake between the white and gray matter areas of the brain, as the selection of both a target ROI as well as a reference region directly influences Standard Uptake Value (SUV) sensitivity²³. A reference region is needed when investigating a brain ROI to determine the amount of tracer uptake in non-pathological tissue⁶. Therefore, the cerebellum is usually the brain structure that is used as a reference region when implementing SUV ratios due to the cerebellum being the last region where amyloid beta protein plaques develop⁶.

1.2.4 PET Reconstruction

1.2.4.1 PET Reconstructions Improvement in Signal-Noise Ratio

Despite the fact that positron emission tomography (PET) imaging is an important tool for AD diagnosis, there are several fundamental limits with the traditional PET scan^{19,24}. PET imaging has a low spatial resolution which results in a lower accuracy of identifying tracer uptake within small biological structures, such as small lymph nodi or gray matter nuclei, resulting in an increased misdiagnosis rate for Alzheimers Disease (AD)⁹. Additionally, the signal-to-noise ratio for the PET scan is a strong indicator of PET image quality, but there is a dearth of knowledge regarding how AGR may enhance PET image diagnostic quality by increasing the signal to noise ratio of the PET image. Therefore, by investigating the impact of AGR on SNR values, we get a better sense of the extent to which AGR may positively influence the diagnostic quality of the PET image. Additionally, PET image diagnostic quality for AD is heavily dependent on the differences in tracer uptake of white matter and gray matter areas in a given region of interest of the brain, as gray matter uptake increases in pathological amyloid-beta tissue associated with the onset of AD¹⁹ (Figure 1)

1.2.4.2 PET Reconstructions Improvement in White Matter and Gray Matter Delineation

White matter and gray matter barriers in the brain as seen under PET scans may be seen more clearly with a higher signal-to-noise ratio of the PET scan; therefore, if the anatomically guided PET-MR reconstructed image improves the signal-to-noise ratio of the scan, then the white and gray matter delineation may be more clear and therefore an improved diagnostic quality of the PET image may be achieved^{19,25}.

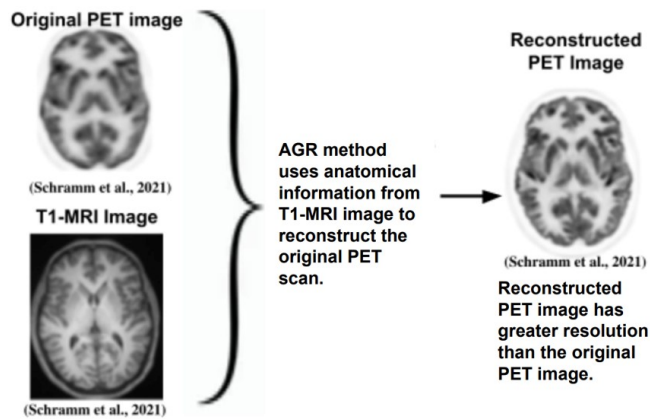


Fig. 1 This schematic portrays how the AGR method utilizes anatomical information from a T1-MRI image to correct and reconstruct the original PET scan, which renders an image with improved resolution. Images of scan from Schramm et al., 2021. (Figure created by Author).

1.2.5 Standard Uptake Value Ratios

Standard uptake values are quantitative measurements that quantify tracer uptake in the brain²³. Tracer uptake is more intense in gray matter areas of the brain when pathological brain tissue is present, resulting in higher SUVs to demonstrate an increased likelihood of the tissue being pathological AD tissue^{19,20}. The quantification of cortical amyloid burden that may be performed by SUV ratios (SUVrs) may improve the Florbetapir-F18-AV-45 PET imaging evaluations of the clinical diagnostic quality of the PET images²⁶. Standardized uptake value ratios are ratios that are made by extracting the standard uptake value of the pathological tissue and the standard uptake value of the cerebellum and creating a ratio with the two values²⁶.

1.2.6 Gap in the Literature and Objective

Despite its theoretical benefits, the efficacy of the AGR method in improving diagnostic quality for AD has not been validated in the context of diagnosing Alzheimers Disease.

Therefore, the aims of this study are to successfully determine the extent to which the Anatomically Guided Reconstruction Method may improve the image contrast of the PET scan by increasing the signal-to-noise ratio and enhancing the anatomical boundaries in the PET scan. Additionally, this study aims to determine if the potential improvements in the PET image quality from the implementation of the Anatomically Guided Reconstruction method may be significant and sufficient to suggest that an improvement in amyloid plaque detection has been achieved.

1.2.7 Hypothesis

The hypotheses set forth prior to this study include that the implementation of the Anatomically Guided Reconstruction method may significantly improve the SUV white-gray matter contrast of the Florbetapir-F18 tracer activity and improve the delineation of gray-white matter boundaries in the PET images. Additionally, the improvements in SUV Florbetapir-F18 PET image contrast with AGR may reduce uncertainty in amyloid plaque detection. Finally, the AGR method may significantly improve the diagnostic quality of the PET image for early onset AD.

2 Methods

*All methods were conducted by Author unless otherwise stated

2.1 Participants

This study utilized radiology imaging records from NYU Langone Health Radiology in Manhattan, New York to access a dataset that may be used for data analysis. This institution has collected >100 imaging studies of suspected Alzheimers Disease patients who have received Florbetapir-F18 Amyloid PET scans. The dataset used in the present study consists of 76 volunteers ages 50 to 87 years old (age = 74.5+7.7yo; bmi = 24.5+4.2; range 16.6324 - 35.6298; 44 female, 32 male).

2.2 Data Acquisition

The research was conducted retrospectively and the data was already acquired during the standard medical care that these patients received. I received and analyzed anonymized PET scans of patients who have received an Florbetapir-F18 PET scan for data investigation in this novel research study. The PET scans were both uncorrected, and modified with the Anatomically Guided Reconstruction method which combines PET scans with T1 weighted MRI images to improve PET scan resolution (7). The PET images were stored in nifti (.nii) format, and the summarized data of the PET scans were located in the summarize_MRI.m file, whereas the file utilized and adapted to create violin and scatter plot graphs along with line graphs were located in the sanitycheckgraphs.m file.

2.3 Selecting Brain ROIs

I investigated several regions of interest (ROI) within the brain to determine the gray matter to white matter standard uptake value ratios (SUVrs) in this study. I selected ROIs within the brain on the basis of vulnerability to amyloid beta plaque deposition as the focus of the study. The specific brain ROIs that were analyzed for this study included the frontal and temporal

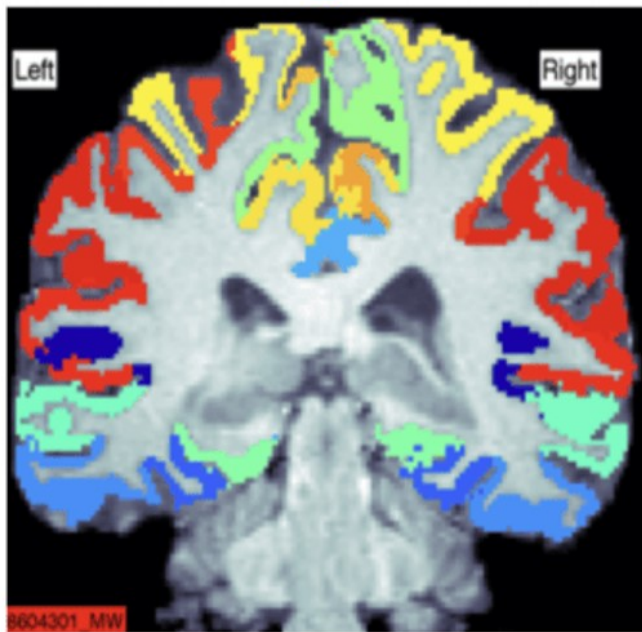


Fig. 2 Close up example of a good segmentation according to the Meld Protocol 3 FreeSurfer Quality Control webpage. The colors of the segmentation are largely symmetrical, the gray matter is mostly segmented, and no portion of the skull nor the cerebellum is wrongly segmented. These are the parameters that I utilized to perform FreeSurfer quality control.

lobes and the precuneus due to these brain regions typically being susceptible to early amyloid beta plaque deposition during AD pathology^{21,22}. The lateral inferior occipital lobe and the hippocampus were added as ROIs upon recommendation by principal investigator Dr. Timothy Shepherd. The cerebellum white matter was utilized as the reference region in this study due to this brain region being the last region of the brain where amyloid beta plaque formation typically forms¹⁵.

2.4 Image Processing

For each patient, FreeSurfer segmentation software on T1 weighted MRI images has been utilized to segment the different regions of the brain and perform a quality assessment over the gray matter segmentations created by FreeSurfer within the given images. This was done to ensure that the PET images that were investigated had no inaccuracies that altered the SUVs of the ROIs that were analyzed. The images were stored in a .html file and were opened via Google Chrome for investigation. The three parameters that I used to discern whether the FreeSurfer segmentation was of high quality were if the colors were symmetrical, the cerebellum was not wrongly segmented, and the gray matter has been segmented for the most part (Figure 2). I

specifically examined these images for Florbetapir-F18 binds to amyloid plaques in the brain in both the white matter and gray matter areas, but gray matter uptake increases in pathological tissue¹⁹. The detection of these plaques is the clinical application that the increased Florbetapir-F18 tracer activity indicates²⁷. The images from these scans have been compared to the PET images following Anatomically Guided Reconstruction to ascertain the extent to which the reconstructed image shows a difference in Florbetapir-F18 activity⁹.

```
283 % ratio GM/WM, variability
284 ratioLeftSuperiorTemporal_WM = dat.SUV_LEFTsuperiortemporalInid./dat.SUV_WMLEFTsuperiortemporal./dat.SUV_CerebellumWhiteMatter;
285 ratioLeftSuperiorTemporal_AGR_WM = dat.SUVAGR_LEFTsuperiortemporalInid./dat.SUVAGR_WMLEFTsuperiortemporal./dat.SUVAGR_CerebellumWhiteMatter;
```

Fig. 3 This is an example for the ratio I created between the gray matter and white matter SUV ratios for a given ROI, corrected by the cerebellum white matter reference region. The specific ROI in the example above is the left superior temporal lobe, although this same format of code has been utilized for all the examined brain ROIs in this study to create ratios and examine the SUVs between the non-AGR and AGR methods.

2.5 Matlab

2.5.1 Data

I utilized MATLAB R2023a to analyze the extent to which the AGR method improved SUVs between the gray matter (GM) and white matter (WM) of a region of interest. To analyze the data, I created ratios between gray matter and white matter SUVs and corrected it by a reference region, which in this case, was the cerebellum WM region (Figure 3). This helped me determine the level of improvement in the Florbetapir-F18 uptake and therefore the diagnostic quality of the PET image as a result of the implementation of the Anatomically Guided Reconstruction method.

2.5.2 Violin Plots and Scatter Plots

I made violin plots between both the AGR and non-AGR methods to examine the extent to which the SUVs matched up between both methods. In doing so, these visual plots easily view the differences in SUV values between the SUV in the original and AGR PET images. The violin plots were created by utilizing code that created a ratio value between the GM and WM uptake of a particular ROI and setting a ratio with that value against the cerebellum WM SUV, which is the particular reference region that has been utilized for this study, as mentioned previously (Figure 3). Violin plots and scatter plots were created to test how closely the SUV of the two methods align through the ability of visualizing the % difference in SUV are between the two forms of PET images.

2.5.3 Line Plots

In order to identify how the AGR method influenced SUV_rs in individual cases, I created line plots between both the AGR and non-AGR methods using MATLAB R2023a. I was then able to see the original SUV_r and the AGR SUV_r for each individual patient and was able to see whether the SUV_r increased, decreased, or stayed the same. Additionally, I was able to group patients based on their SUV_r into several categories: severe, characterized by gray matter uptake being greater than the white matter uptake; moderate, characterized by gray matter being equivalent to white matter uptake; mild, characterized by gray matter being the equivalent of approximately twice the level of white matter; and negative, which is characterized by a low gray matter uptake. This allowed me to categorize individuals more effectively on the basis of SUV_rs, which are a major indicator of AD pathology, and thereby identify trends within various groups of individuals with similar levels of pathology¹⁹.

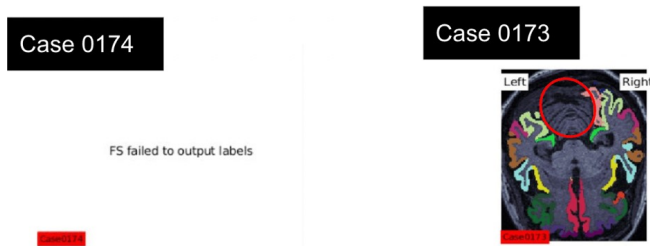


Fig. 4 Examples of FreeSurfer cases with segmentation errors. Case 74, which is listed as Case 0174 in the bottom left of the figure, had no segmentation output due to a FreeSurfer error, whereas Case 73, which is listed as Case 0173 in the bottom left of the figure, has missing gray matter segmentations on the left hemisphere of the brain, as highlighted by the red circle, which hence makes the segmentation asymmetrical.

Table 1. Regions of interest (ROI) and their respective Gray Matter/Cerebellum White Matter standard uptake value ratios (SU-V_rs).

Brain ROI	GM/Cerebellum GM SUV (avg.)	GM/Cerebellum GM/SUV AGR (avg.)	Correlation Coefficient	P
Whole Temporal Lobe:	1.097335526	1.094397368	0.9985	0.94272
Whole Superior Frontal:	1.097335526	1.094397368	0.9996	0.91928
Whole Precuneus:	1.185546053	1.185213158	0.9995	0.98383
Whole Hippocampus	1.236186842	1.234469737	0.9956	0.98383
Whole Lateral Occipital Lobe:	0.9491039474	0.9489605263	1.0000	0.98677

2.6 Statistical Analysis

The effects of age and gender have been investigated as covariates. Descriptive statistics were used for demographic characteristics, including mean standard deviation of continuous

variables and proportion of categorical variables. p-values ≤ 0.05 were considered significant. A Kolmogorov-Smirnov test was used to determine whether the data distribution was normal for an N sample size greater than 50. Since the data for all of the ROI investigated were not normally distributed, a Mann-Whitney U test was conducted to determine the statistical significance of the difference between the AGR and non-AGR values.

3 Results

3.1 Brain ROI Segmentations

Prior to examining the extent to which the AGR method improves the diagnostic quality of a PET image, gray matter segmentations of the PET scans were analyzed to determine the quality of the images. The PET images were segmented with the use of the FreeSurfer software by color, and good segmentation is indicated by largely symmetrical colors, the gray matter being mostly segmented, and no skull or cerebellum regions being wrongly segmented. Upon reviewing the PET images and evaluating their diagnostic quality based on the aforementioned information, the majority of the PET images had sufficient segmentation quality for further analysis to test the effect of the AGR method on diagnostic accuracy. However, there were several cases where the segmentations of the PET images had notable inaccuracies, along with Case 174, which had no FreeSurfer segmentation output at all (Figure 4). One example of a case with poor segmentation was Case 173. The PET segmentation for this case had an asymmetrically segmented cortical surface and had a missing segmented cortex in the left hemisphere of the brain (Figure 4). Despite these segmentation issues, further analysis with comparing the non-AGR SUV ratios with the AGR SUV ratios was conducted with all 76 cases in the study.

3.2 GM/Cerebellum GM Correlation

Ratios created between the gray matter standard uptake value of the brain region of interest, corrected by the cerebellum gray matter standard uptake value, were created for both the non-AGR and AGR PET scans. In the brain regions with high prevalence of AD pathology, such as the left frontal lobe, the correlation coefficient between the uncorrected GM/Cerebellum GM SUV_r and the AGR GM/Cerebellum SUV_r was 0.9985 (p=0.92806) (Table 1). Additionally, for the whole temporal lobe, the correlation coefficient between the uncorrected GM/Cerebellum GM SUV_r and the AGR GM/Cerebellum SUV_r was 0.94272. Similar results were found across all of the ROI investigated (Table 1). These results suggest that the AGR method did not have a significant effect on the SUV_r of the PET scan when the gray matter uptake of the images was corrected by the

gray matter of the cerebellum across all of the ROI investigated (Whole Temporal Lobe: $p=0.94272$; Whole Superior Frontal: $p=0.91928$; Whole Precuneus: $p=0.98383$; Whole Hippocampus: $p=0.98383$; Whole Lateral Occipital Lobe: $p=0.98677$).

4 Discussion

The primary objective of this study was to determine whether the AGR method had a significant impact on the diagnostic quality of Amyloid PET images for AD. To do this, I utilized MATLAB 2023a to conduct various statistical analyses and create graphs that visualized the differences between the AGR and non-AGR ratios for each ROI that was selected for investigation. In this study, the AGR method did not have a significant effect on the PET images in all of the brain ROI investigated (Whole Temporal Lobe: $p=0.94272$; Whole Superior Frontal: $p=0.91928$; Whole Precuneus: $p=0.98383$; Whole Hippocampus: $p=0.98383$; Whole Lateral Occipital Lobe: $p=0.98677$).

4.1 AGR Method on PET Image Quality

The AGR method had a very minimal effect on the SUV_r of each of the ROIs investigated (Table 1), which suggests that the AGR method did not significantly affect the diagnostic quality of the PET image in each of the ROI tested (Whole Temporal Lobe: $p=0.94272$; Whole Superior Frontal: $p=0.91928$; Whole Precuneus: $p=0.98383$; Whole Hippocampus: $p=0.98383$; Whole Lateral Occipital Lobe: $p=0.98677$). This finding is inconsistent with findings from previous studies that have investigated the effect of the AGR method on PET image quality in various settings, however this is the first study to test the AGR method on Amyloid PET images for the purpose of diagnosing Alzheimers Disease^{8,9}.

In a study conducted by Kang & Lee, 2021, an anatomically guided PET reconstruction method was implemented to fix the problem of over smoothing that is often faced with Bowsher PET scans during second order smoothing, which is a process that is utilized to improve PET image quality by reducing high frequency noise that often interferes with the quality of the PET image²⁸. The study found that by incorporating second-order smoothing within the Bowsher framework, the reconstruction achieves a balance between reducing noise and maintaining important anatomical features, leading to higher-quality images for analysis.

In another study by Xie and Qi, 2020, a PET anatomical reconstruction method, named the maximum likelihood (ML) expectation-maximization (EM) algorithm, was implemented on several PET scans²⁹. In the study, the ML EM algorithm is described as a new co-learning 3D convolutional neural network (CNN) designed to extract modality-specific features from pairs of PET/CT images and integrate complementary features to produce high-quality PET images²⁹. This study also observed

results that suggest that the PET reconstruction method that was utilized in the study improved the image quality and produced a better lesion contrast vs. background standard deviation trade-off curve than existing methods.

4.2 SUV_rs on PET Diagnostic Quality of Alzheimers Disease

The assessment of amyloid buildup in the cerebral cortex, which is strongly associated with the onset of Alzheimers Disease, can be quantified by the use of standard uptake value ratios. In this study, I investigated whether the AGR method would increase the SUV_r signal in various brain regions of interest that are prone to amyloid beta deposition in AD pathology. In this study, the AGR method did not have a significant effect on SUV_rs measuring the gray matter uptake in the brain ROIs tested (Whole Temporal Lobe: $p=0.94272$; Whole Superior Frontal: $p=0.91928$; Whole Precuneus: $p=0.98383$; Whole Hippocampus: $p=0.98383$; Whole Lateral Occipital Lobe: $p=0.98677$). These results suggest that the AGR method did not improve the signal of gray matter uptake associated with amyloid beta protein accumulation in the PET scans. Higher tracer uptake areas in a PET scan of the brain suggest the presence of pathological brain tissue associated with Alzheimers Disease, resulting in higher SUV_rs that demonstrate an increased likelihood of the tissue being pathological AD tissue^{19,20}.

Therefore, the AGR method did not improve the diagnostic quality of the PET image as there was minimal improvement in the detection of the gray matter uptake, as indicated by the lack of change in the SUV_r in the brain ROI, after employing the AGR method.

4.3 Limitations

There are several limitations to this study due to a lack of ROI information. The FreeSurfer WM segmentations were limited in various brain regions that were investigated in the study, including the lateral occipital cortex. Furthermore, the hippocampus was wrongly selected as a brain ROI for the study as a region where amyloid beta plaque deposition is prevalent, but in reality, the hippocampus had very little to no gray matter uptake due to the fact that this brain region is actually one of the least prone regions to amyloid beta plaque deposition.

Additionally, patients in this study were not grouped based on diagnosis, and during the Free-Surfer quality control pipeline, case 0174 failed to produce any segmented images, and case 0173 lacked proper GM segmentation in the left hemisphere. There were other images in the pipeline that had minor issues with the proper gray matter segmentations as well. Finally, the sample size in this study was limited, which may have affected the generalizability of the findings. A larger sample size would have produced more robust data and reliable results.

5 Conclusion & Future Studies

My study successfully investigated whether the AGR method had a significant impact on the diagnostic quality of Amyloid PET images for AD. I analyzed the effect of the AGR method on the SUVrs in various brain regions of interest that are prone to early amyloid beta plaque deposition in Alzheimers pathology. Utilizing a dataset of 76 PET scans from anonymized patients with the onset of AD, I was able to create SUVrs for each ROI that I investigated that quantified the gray matter uptake in the region of interest, which indicates that pathological AD tissue is present¹⁹. While it was initially hypothesized that the AGR method would significantly improve the diagnostic quality of the PET image for early onset AD by improving the gray matter SUVrs in the ROIs investigated, the AGR method had no significant effect on the SUVrs in each of the ROIs tested (Whole Temporal Lobe: $p=0.94272$; Whole Superior Frontal: $p=0.91928$; Whole Precuneus: $p=0.98383$; Whole Hippocampus: $p=0.98383$; Whole Lateral Occipital Lobe: $p=0.98677$). Thus, the AGR method did not have the expected effect of improving the diagnostic quality of PET images for AD.

This study emphasizes the need for robust quantitative frameworks, and contributes to the ongoing effort to develop more effective, scalable, and sustainable imaging techniques. This research can be further expanded by applying additional analysis methods that can be utilized to better discern the improvement in the diagnostic quality of the PET image for early onset Alzheimers Disease. If given more time, I would continue this research by involving data from a larger subset of patients for investigation to improve the sample size of the present study. Additionally, I would create a step function alongside the computed GM/Cerebellum GM ratios to evaluate the delineation between the GM and WM regions of the brain, which would be another measure to assess the improvement in the diagnostic quality of the PET image. To further research the extent to which the AGR method influences the diagnostic quality of the PET image, a new study can be proposed in the future to analyze the measure in improvement of another aspect of diagnostic quality of a PET image, such as the effect of the AGR method on the signal-noise ratio of the PET image. Such studies can allow radiologists to better understand the holistic effect that the AGR method has on the diagnostic quality of the PET images in AD patients.

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appropriate laboratory equipment and data utilized for analysis.

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