Final Project Report

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Project Information

Contact List

Project Advisor: Dr. Hesam Jahaninan - hesamj@uw.edu

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Google Drive Organizational Summary

Documents
- Fall Presentation
- Final Presentation
- Final Project Report
- Needs Assessment
- Progress Reports
- Scheduling/Planning
- Surveys
- Testing and Verification

HIC
- 1 Page Business Summary
- 5-7 Page Business Summary
- Pitch
- Prototype Idea Drafting

Meetings
- Meetings with Dr. Jahanian
- Meetings with Dr. Jahanian's Lab
- Meetings with Peter

Project Work
- 1. Image Classification
- 2. NIFTI Conversion
- 3. MNI Space Conversion
- 4. GAN Training
- Misc Organization, Query Extraction, etc

References
- Project Background

Essential Papers

- ➔ Ouyang, J., Chen, K. T., Armindo, R. D., Davidzon, G. A., Hawk, K. E., Moradi, F., Rosenberg, J., Lan, E., Zhang, H., & Zaharchuk, G. (2023). Predicting FDG‐PET images from Multi‐Contrast MRI using deep learning in patients with brain neoplasms. *Journal of Magnetic Resonance Imaging*. https://doi.org/10.1002/jmri.28837
    - ◆ Similar project to ours, worked on by a collaborator of Dr. Jahanian's. Acts as proof of concept, training on all MRI images and producing PET images.
- ➔ Chen, K. T., Gong, E., De Carvalho Macruz, F. B., Xu, J., Boumis, A., Khalighi, M., Poston, K. L., Sha, S. J., Greicius, M. D., Mormino, E. C., Pauly, J. M., Srinivas, S., & Zaharchuk, G. (2019). Ultra–Low-Dose18F-Florbetaben Amyloid PET Imaging Using Deep Learning with Multi-Contrast MRI Inputs. Radiology, 290(3), 649–656. https://doi.org/10.1148/radiol.2018180940
    - ◆ Similar project to ours, worked on by a collaborator of Dr. Jahanian's. Compares model trained with just low-dose PET, PET only, and PET and MR imaging.
- ➔ *Diagnosing Alzheimer's: How Alzheimer's is diagnosed*. (2022, May 7). Mayo Clinic. https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/in-depth/alzheimers/art-20048075
    - ◆ Article giving background on Alzheimers diagnosis - excellent background for the problem addressed and need for this project.
- ➔ Kancherlapalli, J. (2023, October 2). *The cost of PET scans | Inpatient VS outpatient settings*. Cardiac Imaging. https://www.mobilecardiacpet.com/blog/the-cost-of-pet-scans-for-treatment-planning-efficiency/
    - ◆ Article giving background on cost of PET scans - excellent background for the problem addressed and need for this project.
- ➔ Nordberg, A., Rinne, J. O., Kadir, A., & Långström, B. (2010). The use of PET in Alzheimer disease. *Nature Reviews Neurology*, *6*(2), 78–87. https://doi.org/10.1038/nrneurol.2009.217
    - ◆ Paper giving background on use of PET in Alzheimer's diagnosis - excellent background for the problem addressed and need for this project.

Problem Overview

Alzheimer's disease (AD) remains one of the most significant medical challenges of our time, affecting over 26 million people across the globe, and is forecasted to increase dramatically due to the aging population. The pathway to a confirmed diagnosis is slow, marked by months or even years of uncertainty. This delay is critical; early detection is a key determinant in managing the disease effectively, yet the path is hindered by the current diagnostic gold standard: fluorodeoxyglucose positron emission tomography (FDG-PET). While FDG-PET is standard for the assessment of neurodegeneration, it comes with substantial barriers. The financial burden is daunting with costs that can escalate up to $20,000, which is rarely fully covered by health insurance. Furthermore, there are several accessibility barriers to FDG-PET scans. The use of radiotracers carries the inherent risk of radiation exposure, limiting its suitability for all patients. In rural areas, the lack of this specialized diagnostic equipment forces patients to undertake significant travel to access necessary care. Additional challenges include long wait times, fasting beforehand, staying still during the scan, and anxiety/claustrophobia.

Need Statement

Clinicians and radiologists treating AD need an alternative imaging solution that utilizes non-invasive and widely available methods to accurately replicate PET scan details; addressing time, financial, and accessibility barriers, in order to enhance diagnostic capabilities and patient safety.

Stakeholder Interview and Analysis

The stakeholders in the development of this technology are clinicians, patients, hospitals, hospital staff, medical imaging companies, and medical insurance companies. In a survey we conducted, UW radiologists identified lack of insurance coverage and difficulty of scheduling a PET scan as more common barriers patients have. One radiologist indicated that the largest distance they had seen a patient travel for access to a PET scan was in the range of 500 - 1000 miles, as well as the highest cost they had seen a patient pay out of pocket was in the range of $10,000 - $20,000. These findings illustrate the urgent need to address the barriers to AD diagnosis through innovative technological solutions. As a future direction, AD patients' families and care providers should be interviewed about the diagnostic process to learn from their first-hand perspectives. This perspective may lead to additional insights on how a new technology could fit into the diagnostic process, as well as insights into patient and caretaker willingness to partake in new diagnostic technology.

Solution Design

Our design is a novel application of AI technology for AD diagnostics, informed by similar AI applications from the work of Dr. Hesam Jahanian's lab. Our solution employs a Generative

Adversarial Network (GAN), a sophisticated machine learning model typically utilized for generating realistic images. It consists of two primary components: a generator, which creates images, and a discriminator, which evaluates them. The generator uses a Deep Convolutional Network (DCNN), that will be specifically engineered for Alzheimer's pathology to create synthesized PET images from MRI data. Meanwhile, the discriminator evaluates these images against real PET scans, ensuring their accuracy and medical viability.

To create a sophisticated machine learning model, the first step is data preprocessing which is crucial for preparing the raw imaging data for GAN training. A Python script is used to traverse patient directories and metadata, logging the necessary details (e.g., patient information, corresponding scans, imaging modality and location, etc.) into an Excel file. This process ensures that all diagnostically relevant information is organized and accessible, as well as allows the exclusion of patients missing significant information. Another Python script ensures that all verified MRI and PET scan information is stored correctly in our server corresponding to each patient. Raw scan data from MRI and PET machines are stored as DICOM files, which are individual image slice files unideal for deep learning models, so they were converted to a zip NIfTI, a 3D representative file format to enhance data usability. These scans undergo skull stripping to remove non-brain tissues, followed by normalization to standardize the intensity values across different scans. All patient scans are co-registered to their individual corresponding T1 contrast MRI images, leveraging their detailed anatomical views. This step involves using the FMRIB Software Library developed by Oxford University, which allows for aligning the MRI and PET scans to a common reference space. The data then is standardized to the MNI (Montreal Neurological Institute, standard imaging reference image for deep learning) space using FSL tools. This involves both linear and non-linear registration steps to ensure anatomical alignment and uniform image resolution. This processed dataset is then ready to train the deep learning model.

Our proposed machine learning architecture leverages a GAN architecture tailored for synthesizing FDG-PET images from multi-contrast MRI scans. For our first iteration training model, we will use T1, ASL, and FLAIR as input modalities, and FDG as the target modality we aim to generate. The process begins with the Split Input Module, which integrates the multi-contrast MRI inputs using channel-wise attention mechanisms. This module links features from each MRI modality, providing a comprehensive representation of the brain's structural and functional information. The linked output is then fed into a Convolutional Neural Network (CNN) composed of several down-sample blocks. These blocks progressively reduce the spatial dimensions while increasing the feature depth, capturing complex patterns and relationships within the MRI data. The CNN's encoded representation is then tokenized and projected into a sequence suitable for the Transformer layers. Within the Transformer Layers, the embedded sequences undergo multiple stages of self-attention and feed-forward neural networks. This allows the model to capture long-range, big-picture dependencies and interactions within the

MRI data, enhancing its ability to synthesize accurate PET images. The transformer's output is reshaped and passed through several up-sample blocks to generate the synthesized PET image. The Attention Module ensures that the model focuses on the most relevant features, and enhances the quality and realism of the generated PET images. Finally, the Discriminator evaluates the synthesized PET images against real PET scans. It consists of multiple convolutional layers that assess the authenticity of the images, guiding the generator to produce medically viable outputs. This training process ensures that the synthesized PET images are indistinguishable from real scans.

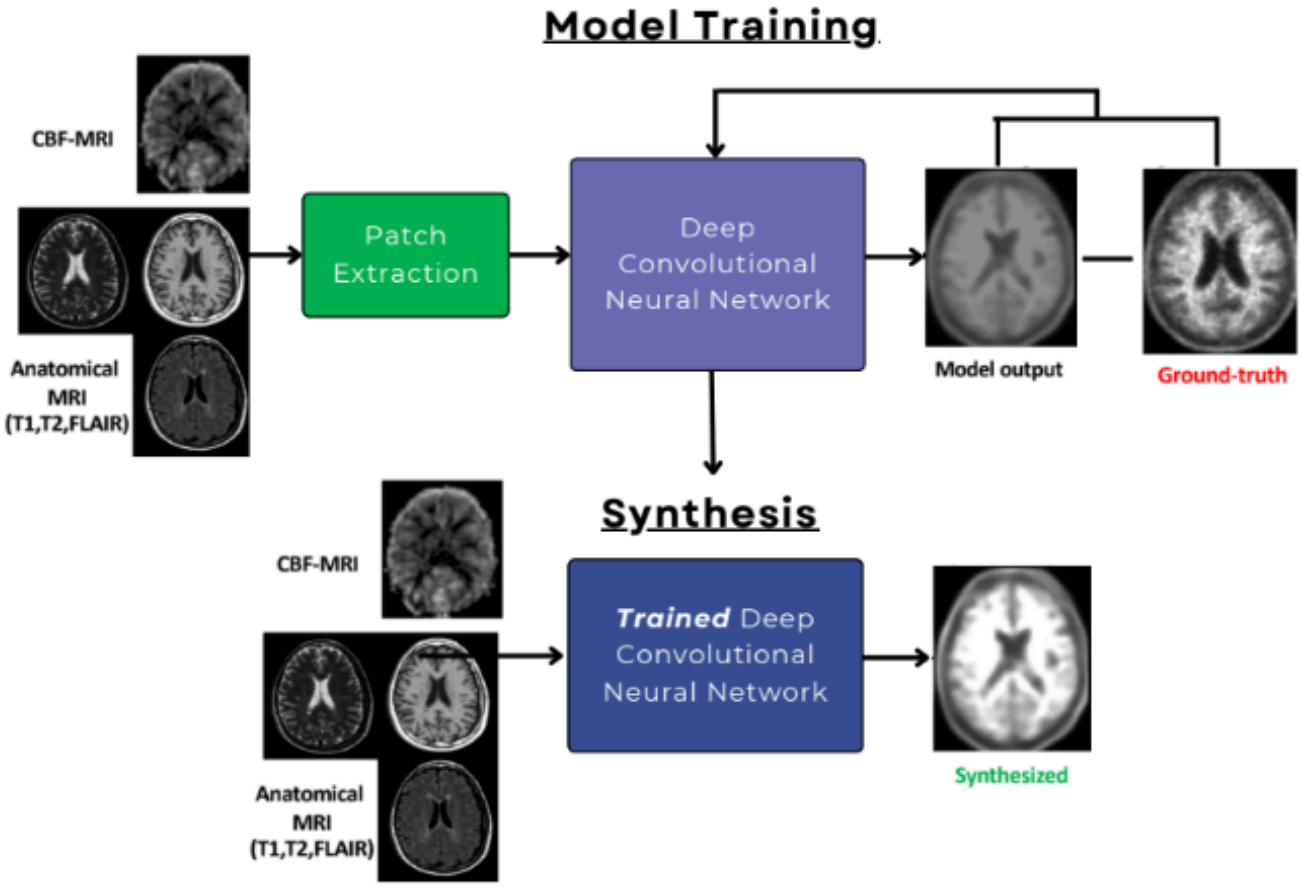

Figure 1. Simplified Representation of GAN architecture

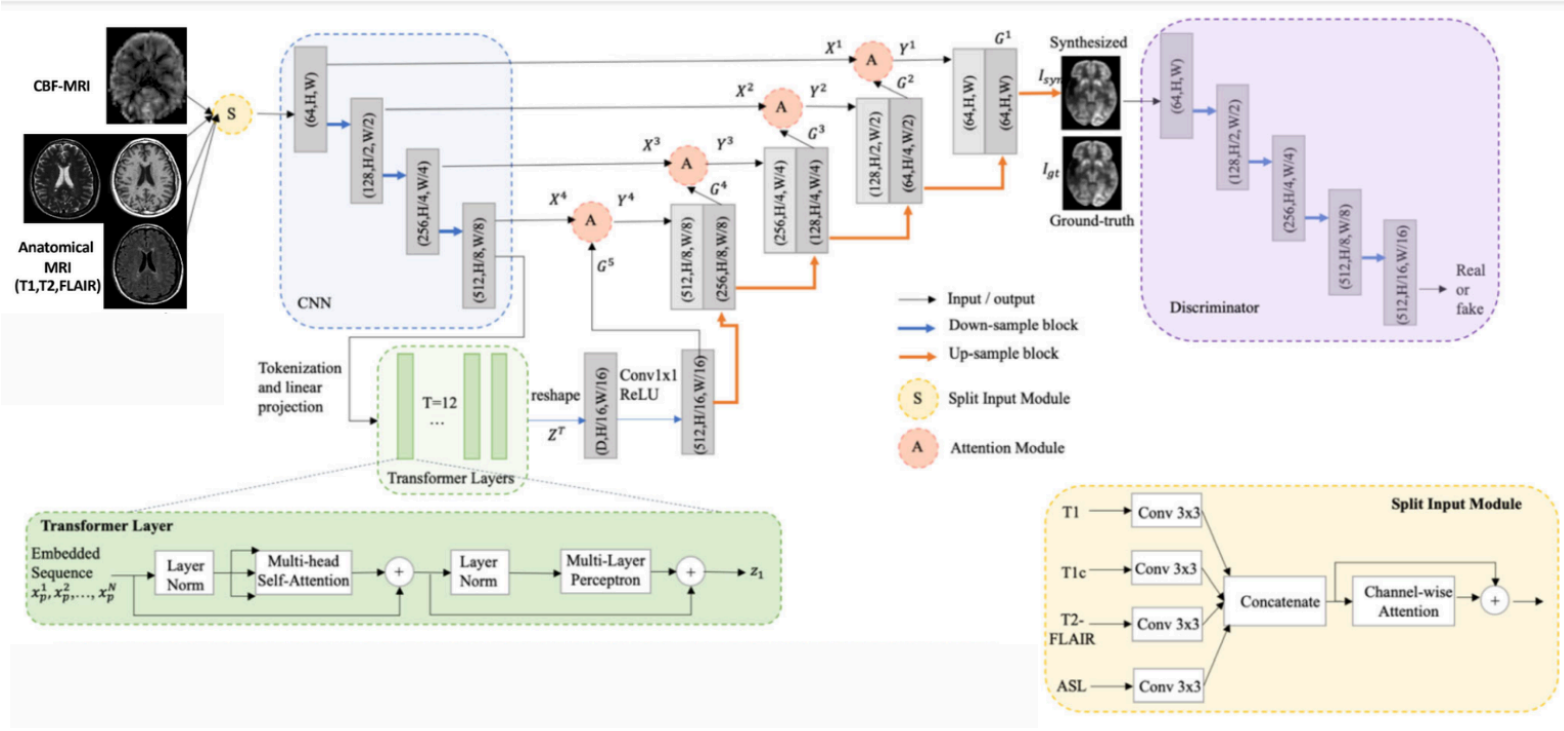

Figure 2. Technical Representation of GAN architecture

Building on our initial demonstrations which synthesized PET images from a limited dataset of 20 patients, we are now expanding our training with access to a collection of hundreds of patients from the Alzheimer's Disease Neuroimaging Initiative (ADNI) repository, UW Medicine's Memory and Brain Wellness Center (MBWC), and Alzheimer's Disease Research Center (ADRC). This diverse dataset promises to further refine and enhance the model's medical accuracy and ability to generalize to real, diverse world data.

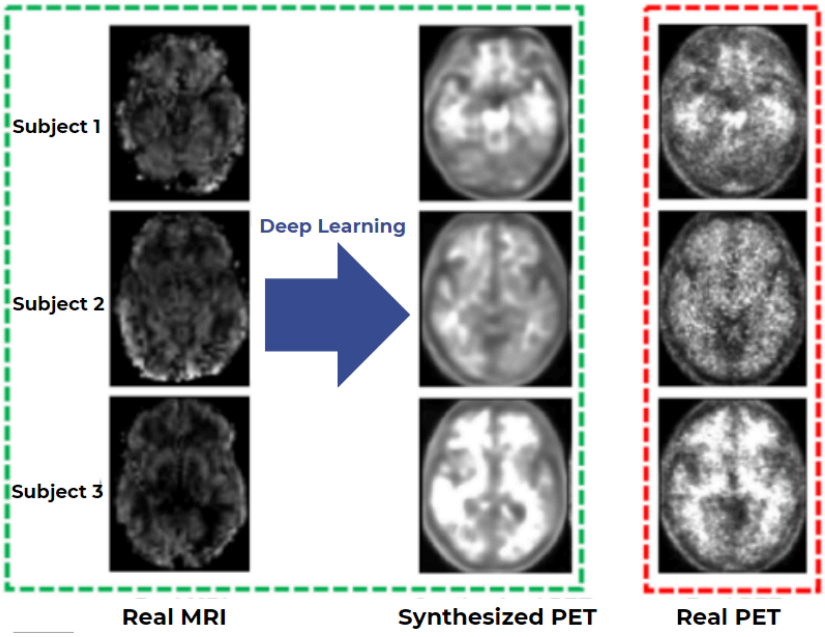

Figure 3. Initial demonstration trained on only 20 patients

Testing and Verification

Our testing and verification protocols are designed to ensure the reproducibility and reliability of our AI diagnostic tool. These protocols include both structural and functional testing of the processed data and the generated PET images. The testing process is divided into data processing verification and GAN model output evaluation.

The initial step involves verifying the integrity and accuracy of the data preprocessing pipeline. This includes ensuring that all MRI and PET scans have been correctly co-registered to the T1 contrast images, standardized to the MNI space, and converted to NIfTI format. The verification process involves utilizing the cost function as the primary measure of alignment accuracy between the T1 and MNI images. The cost function is taken from the T1 alignment as all other scans will have the same transfer function applied as T1, meaning all other modalities should have a negligibly similar cost function and alignment. The cost function represents the discrepancy between these images, where values closer to 0 indicate better alignment. Visual inspection of each patient file is also conducted to ensure anatomical correctness and absence of artifacts. Higher cost function values identify areas where further processing may be needed, guiding improvements in the pipeline.

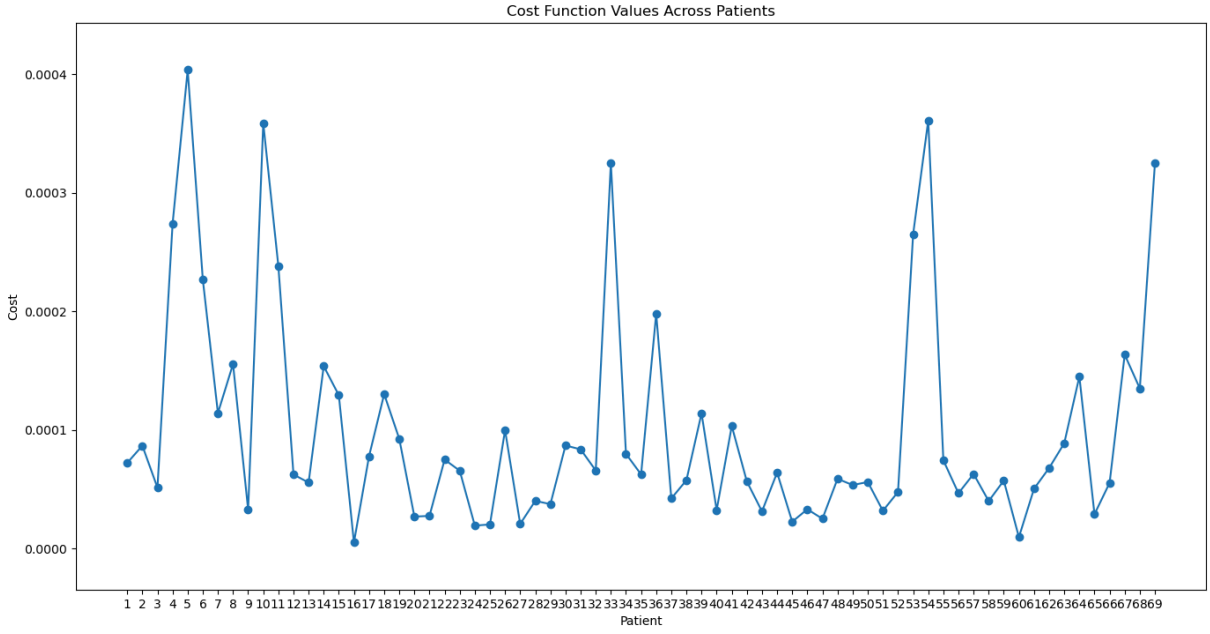

Figure 4. Cost Function Values Across Preprocessed Patients

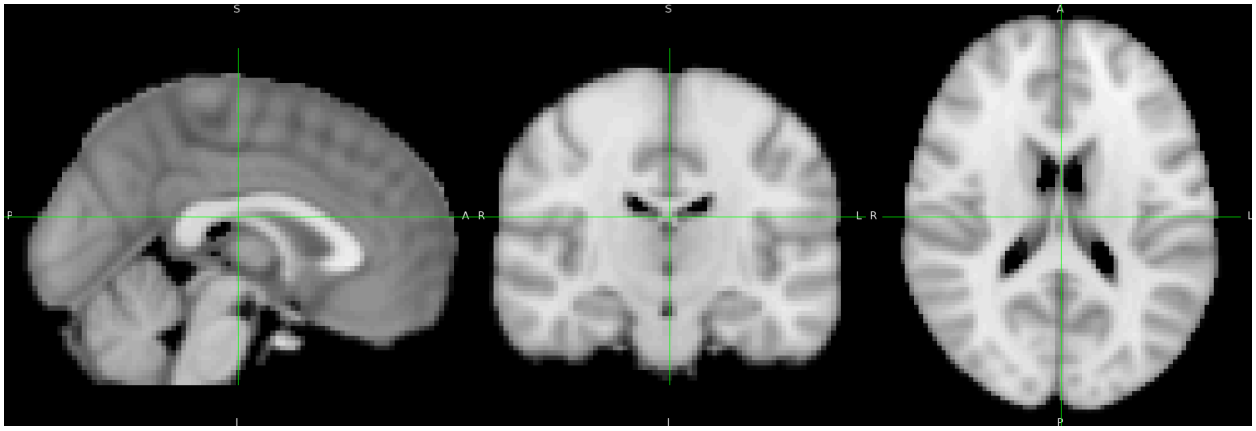

Figure 5. MNI template for reference. All modalities are standardized to this size and orientation.

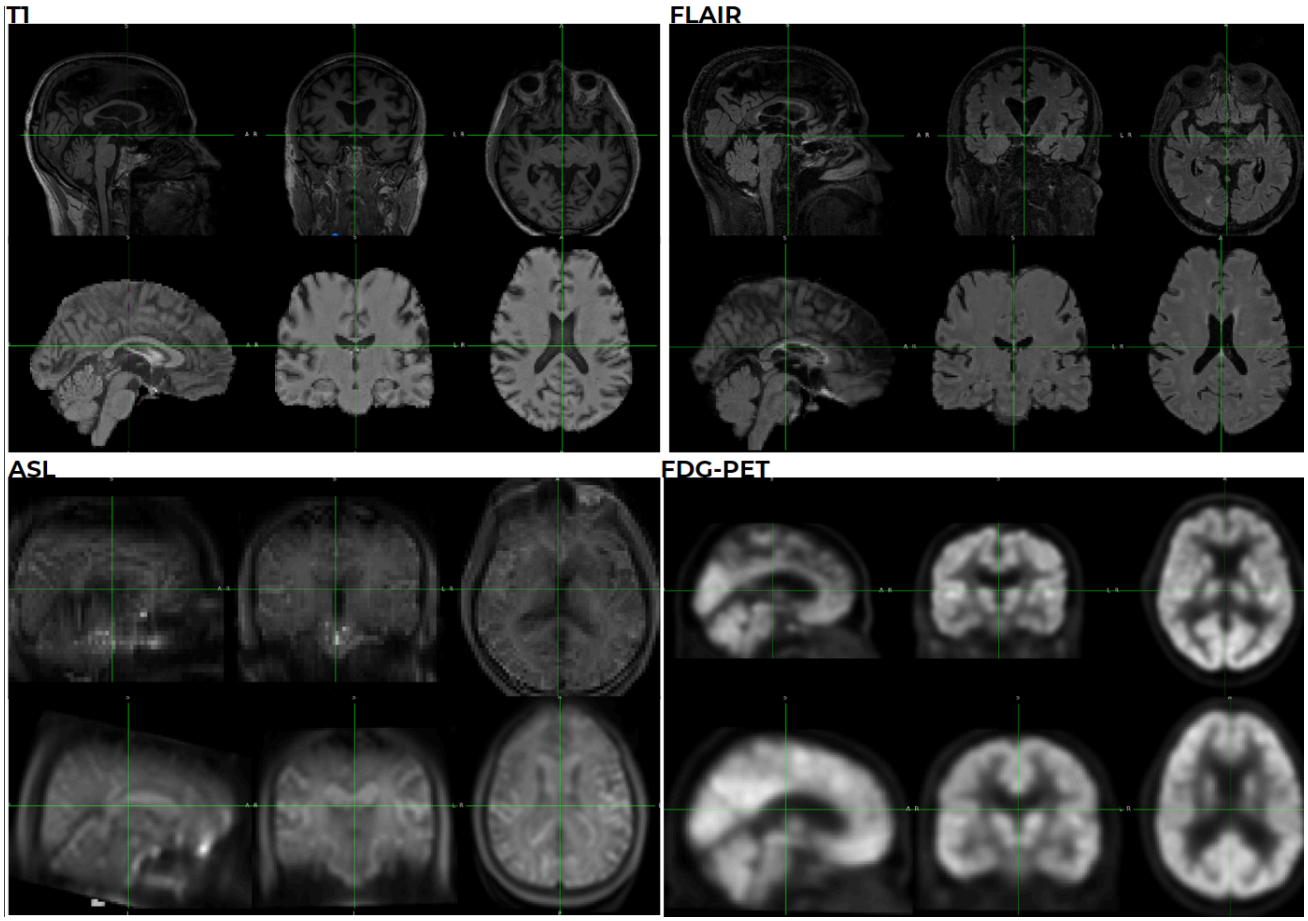

Figure 6. Example visual patient alignment to MNI template with all training scan modalities.

Once the data preprocessing is verified, the next step is testing the output of the trained GAN model. This includes structural and functional testing of the synthesized FDG-PET images. Structural testing involves conducting a thorough visual inspection of the synthesized PET images to check for anatomical correctness and the absence of artifacts. Experts should assess

whether the quality of the image produced would be conducive to diagnosis. Quantitative metrics, such as the Structural Similarity Index (SSIM), Peak Signal-to-Noise Ratio (PSNR), and Mean Squared Error (MSE), are used to evaluate the structural similarity between the synthesized PET images and the real PET images. These metrics will provide a quantitative measure of image quality and accuracy in addition to the visual, qualitative assessment.

Summary of Results and Analysis

Our preliminary testing results have demonstrated that the data preprocessing pipeline is robust and reliable, indicated by low-cost function values, all at 0.0004 or significantly below. The co-registration and standardization steps have produced high-quality NIfTI files that align accurately with the MNI template. The next steps will involve adding a final preprocessing stage to one of the MRI modalities (detailed in the next steps section) before training the GAN model. Once this step is completed, we will proceed with training the GAN to ensure it generates accurate and high-quality FDG-PET images with the metrics detailed previously.

Initial GAN training on a dataset of 20 patients yielded visually promising results. Visual inspections validated the anatomical accuracy and absence of artifacts in the generated images. These findings suggest that our model can effectively replicate PET scan details from MRI data, offering a potential non-invasive and accessible diagnostic tool for Alzheimer's disease. With the preprocessing of hundreds of additional patient files, the model's accuracy and robustness are expected to improve significantly. This expanded dataset will enhance the model's ability to generalize across diverse patient data, leading to more reliable and accurate synthesized PET images.

Next Steps, Future Directions

Our immediate next step involves further processing of the ASL images using the BASIL tool from the FMRIB Software Library, as they were less processed than initially anticipated. The ASL scans are in 4D, capturing a time series of blood flow measurements due to the nature of ASL (Arterial Spin Labeling) imaging, resulting in a sequence of images over time, reflecting different phases of blood flow. To generate a single representative ASL image, it is necessary to perform appropriate subtractions between control and labeled pairs in the time series to isolate the perfusion signal. Additionally, motion correction and signal averaging may be required to enhance the quality of the final ASL image. Despite these complexities, the current alignment without additional processing looks promising, so we anticipate the fully processed ASL images with integrate easily with our already established processing pipeline.

Following this additional preprocessing of ASL scans, we will train our GAN model using the combined data from T1, FLAIR, ASL, and FDG categories. We will focus on tuning the hyperparameters to achieve optimal results. This phase will involve extensive experimentation to

fine-tune the model for the best performance. In the longer term, we plan to explore the trade-offs between using a larger training dataset versus incorporating a wider variety of training scans. This will help us understand how to balance dataset size and scan diversity to enhance model accuracy and robustness. When a successful balance of data and appropriate hyperparameters are selected and our verification protocol validates the model, we would then aim to integrate our solution into the Alzheimer's disease diagnostic workflow within hospital systems. This will involve navigating regulatory and approval processes to ensure compliance with medical standards. Our goal is to commercialize the technology by developing user-friendly software for hospital computers. This software would be designed for easy use by clinicians and radiologists, ensuring it can be implemented worldwide.

Market Space

The PET scanner market, valued at $1.94 billion in 2023, is projected to grow to $2.57 billion by 2030, with a compound annual growth rate (CAGR) of 5.4%. Similarly, the Alzheimer's Diagnostics and Therapeutics Market is anticipated to expand from $7.65 billion in 2024 to $9.78 billion by 2029, experiencing a CAGR of 5.06%. These market trends indicate a substantial opportunity for innovative diagnostic solutions in the healthcare sector. Our analysis estimates a total addressable market (TAM) for AI-driven Alzheimer's diagnostics at $105 billion. Within this, the serviceable addressable market (SAM) is approximately $3.4 billion, and the targeted serviceable obtainable market (SOM) is projected to reach $551 million by 2030. These figures highlight a significant growth potential for our AI diagnostic solution, indicating a strong demand for advanced, non-invasive diagnostic tools.

Our commercialization strategy is to develop a robust and user-friendly software solution that integrates into hospital diagnostic workflows. Key steps in our commercialization plan include navigating the necessary regulatory pathways to ensure compliance with medical standards and obtaining the required clinical use approvals. We will create a software platform that is intuitive and accessible for clinicians and radiologists, designed for global use with a focus on minimizing accessibility barriers. Implementing a phased market entry strategy, we would aim to initially target hospitals and medical centers specializing in Alzheimer's diagnostics, leveraging partnerships with medical imaging companies and healthcare providers to facilitate distribution. Additionally, we would secure patents and trademarks for our AI and software to protect our intellectual property. Forming strategic alliances with industry leaders in medical imaging and AI technology would further enhance our product's capabilities and market reach.

Concerns and Pitfalls to Avoid

One significant concern was the poor communication with our advisor regarding the timeline, availability, and need for help and resources throughout the project. It is crucial to have clear and regular communication to align expectations and deadlines. Not asking for enough information

initially caused delays, as we also learned how busy our mentor was and that we needed to take full advantage of our time once a week with him. Our mentor may not have fully understood our background and expertise, so it was essential to ask plenty of questions, take thorough notes, and ask for any supplementary material we needed as soon as possible.

Another major issue was focusing too much on the AI aspect before significant data processing. Comprehensive, accurate, and reliable data processing, especially when using such a large training set is the most critical part of training an effective machine learning model and requires substantial time and effort. Issues with server permissions and downloading data also caused minor delays. To avoid this, it is helpful to set up a virtual environment locally to run scripts and bypass server-related permissions issues. Additionally, understanding the baseline of each scan modality, including how they are collected and their dimensions, can prevent issues like the one encountered with ASL image processing.

Conclusion

This project has made significant progress in developing an AI-driven diagnostic tool for Alzheimer's disease. Our data preprocessing pipeline successfully co-registered and standardized MRI and PET scans to the MNI space, producing high-quality NIfTI files. Preliminary visual inspections have shown promising results, with a revision to occur on ASL scans that should be easily integrated back into the data processing pipeline.

As we proceed, our immediate focus will be on further preprocessing the ASL images and training our GAN model with the expanded dataset. The projected growth in the PET scanner and Alzheimer's diagnostics markets presents a substantial opportunity for our solution. By developing a user-friendly software platform and navigating regulatory pathways, the ultimate goal is to integrate our diagnostic tool into hospital workflows globally. This project lays a strong foundation for enhancing early detection and patient outcomes in Alzheimer's disease.