Machine Learning Driven Discovery of Alzheimer's Disease Biomarkers

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Introduction

- **Alzheimer's disease (AD)** is a progressive neurodegenerative disorder and a **leading cause of dementia, affecting over 6.9 million Americans aged 65 and older. (7)**
- **Early and accurate diagnosis remains a major clinical challenge.** Current biomarkers, such as hippocampal volumetry, amyloid PET, and CSF tau levels, face limitations due to invasiveness, cost, or limited accessibility.

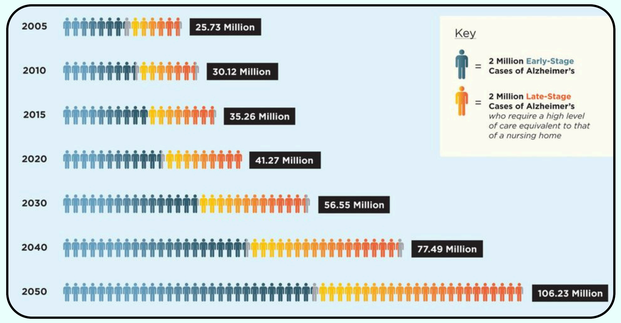

Figure 1: Depicts the worldwide projections of Alzheimer's disease for the years 2005 to 2050 in millions. (2)

Hypothesis

We hypothesize that **radiomic texture features** derived from **T1-weighted MRI scans** capture early neurodegenerative changes and, when combined with **volumetric and demographic features**, **enhance the accuracy of Alzheimer's disease classification** compared to volumetric or texture features alone.

Methods

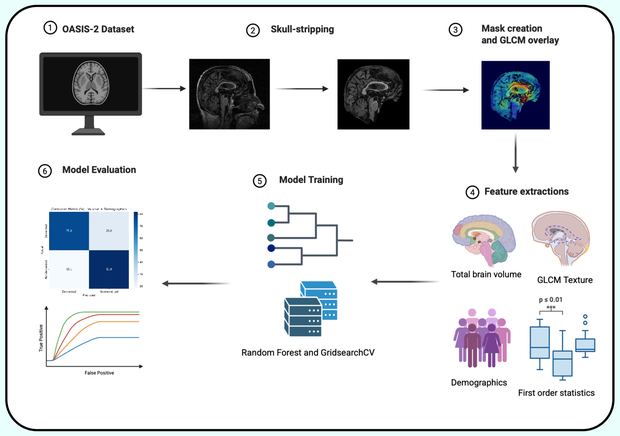

Figure 2: Workflow for the methodology utilized in the study

•**Dataset** - Open Access Series of Imaging Studies 2 (OASIS-2) longitudinal dataset

•**Sample** - 120 participants (48 demented, 72 nondemented) (converted subjects excluded)

Results

Feature Group	Accuracy	AUC
Volume + Demographics	0.7917	0.8430
GLCM + Volume + Demographics	0.7333	0.7935
Volume	0.7250	0.7773
GLCM + Volume	0.6583	0.7183
GLCM + Demographics	0.6250	0.6808
Demographics	0.6167	0.6644
GLCM	0.5750	0.5784

Table 1: Table depicting accuracy and AUC for all the feature groups analysed in this study.

• **7 feature combinations**: "GLCM features only", "volume only", "demographics only", "GLCM + volume", "GLCM + demographics", "volume + demographics" and "GLCM + volume + demographics".

• **Volume and demographic features** achieved the highest performance **(accuracy: 79.2%, AUC: 0.8430)**

• **GLCM-only model** showed the **weakest** classification ability (accuracy: 57.5%, AUC: 0.5784)

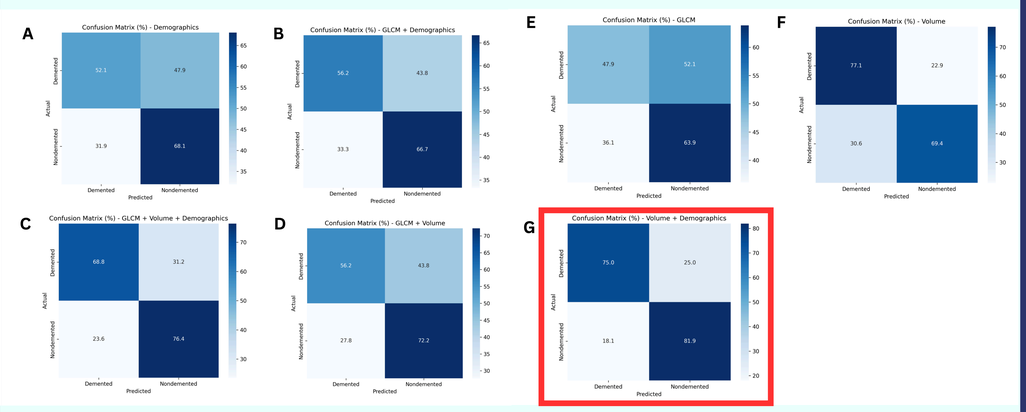

Figure 4: Confusion matrices for each of the seven classification models based on different feature group combinations. The heatmap representing the confusion matrices shows the percentage of predictions (as depicted by the scale) by actual diagnosis group (demented vs. nondemented), with axes labeled as Predicted and Actual.

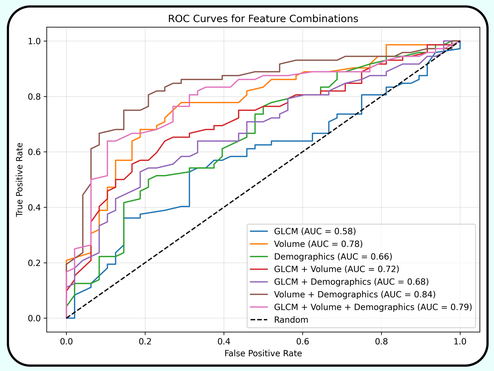

Figure 5: Figure displays ROC curves across all feature combinations. The x-axis represents the false positive rates, and the y-axis represents the true positive rates.

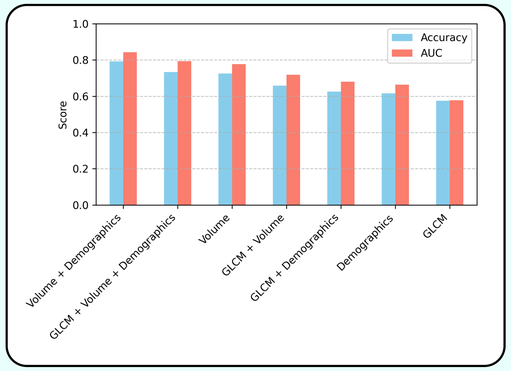

Figure 3: Bar plot representing accuracy and AUC across feature combinations. The x-axis represents each of the feature combinations and the y-axis represents the AUC and accuracy scores as a percentage.

Discussion

- This biological degeneration and social determinants contribute meaningfully to Alzheimer's disease (AD) risk and expression. (5) (1)
- Sample may be underpowered for capturing subtle radiomic variations, especially given the high dimensionality of texture features.(6)
- Study **aligns with literature emphasizing the potential of radiomics as a non-invasive and scalable tool** for neurodegenerative disease monitoring. (4) (3)
- Results emphasize that **dementia risk is multifaceted**, highlighting the **importance of combining biological and social factors** when developing diagnostic tools.

Limitations and future directions

- Isolated Discriminative Power - The actual independent performance was limited. **2D GLCM-derived features did not have** enough discriminative **power** to separate from demented and non-demented adults.
- Modest Combined Synergy - I**ntegrating volumetric and demographic data** had **most improvements** in classification performance, but incremental gains were relatively insignificant.
- Constraints by Model Capability - Held back by **2D slice-based design**, **small sample size**, and **lack of integrating temporal data**
- **Analyze 3D texture with full brain volumes**
- **Perform longitudinal modeling**
- **Increase the sample size**
- **Consider hybrid models by combining deep learning and interpretable radiomics**

References

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