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CLINICAL VALIDATION OF A DEEP LEARNING FRAMEWORK FOR DETECTING AMYLOID PATHOLOGY VIA STRUCTURAL MRI

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INTRODUCTION

Amyloid pathology is a defining hallmark of Alzheimer's disease (AD). Yet conventional amyloid detection methods remain expensive, invasive, and limited in accessibility—restricting early detection and large-scale screening. The current study validates an algorithm that synthesizes *amyloid-pathology* images using routine MRI scans. This approach offers a scalable, cost-effective, and non-invasive method to detect amyloid pathology that could facilitate early Alzheimer's screening and clinical phenotyping.

METHODS

A deep convolutional neural network was trained to synthesize amyloid pathology images from T1-weighted MRI scans. The model was evaluated on 192 participants across the AD spectrum. We compared SUVRs (standardized uptake value ratios) calculated using the whole cerebellum as the reference region from AV-45 PET images and the amyloid pathology images. Amyloid positivity was defined using both, gold standard PET SUVR > 1.11 (Landau et al., 2021) and CSF tTau/A β 42 > 0.28 (Amft et al., 2022) as ground truths, independently. A comparison of SUVRs from the PET and amyloid pathology images was performed using correlation, equivalence testing, and classification metrics.

CLINICAL RELEVANCE AND APPLICATION

- Enables non-invasive, cost-effective and accessible amyloid pathology detection from routine MRI.
- Leverages standard clinical neuroimaging to support scalable, cost-effective screening, especially in low-resource settings.
- Facilitates early intervention through screening, therapy eligibility assessment and disease phenotyping.
- Supports clinical decision making by enabling longitudinal monitoring and informing Alzheimer's disease management strategies.

RESULTS

The amyloid pathology image-derived SUVRs showed significant correlation with gold standard PET SUVRs ($r = 0.66$, $p < 0.0001$) and a mean absolute percentage difference of 10.16%. Equivalence testing confirmed statistical equivalence (95% CI: 0.0057 to 0.0477, $p < 0.001$). Using amyloid PET SUVR as ground truth, the model achieved an accuracy of 82%, sensitivity of 73%, specificity of 88%, and AUROC of 85%. While using CSF derived ground truth, the model achieved 81% accuracy, 82% sensitivity, 80% specificity and 81% AUROC. Subgroup analysis revealed the greatest absolute SUVR difference in MCI, followed by AD, and the least in cognitively normal (CN) participants.

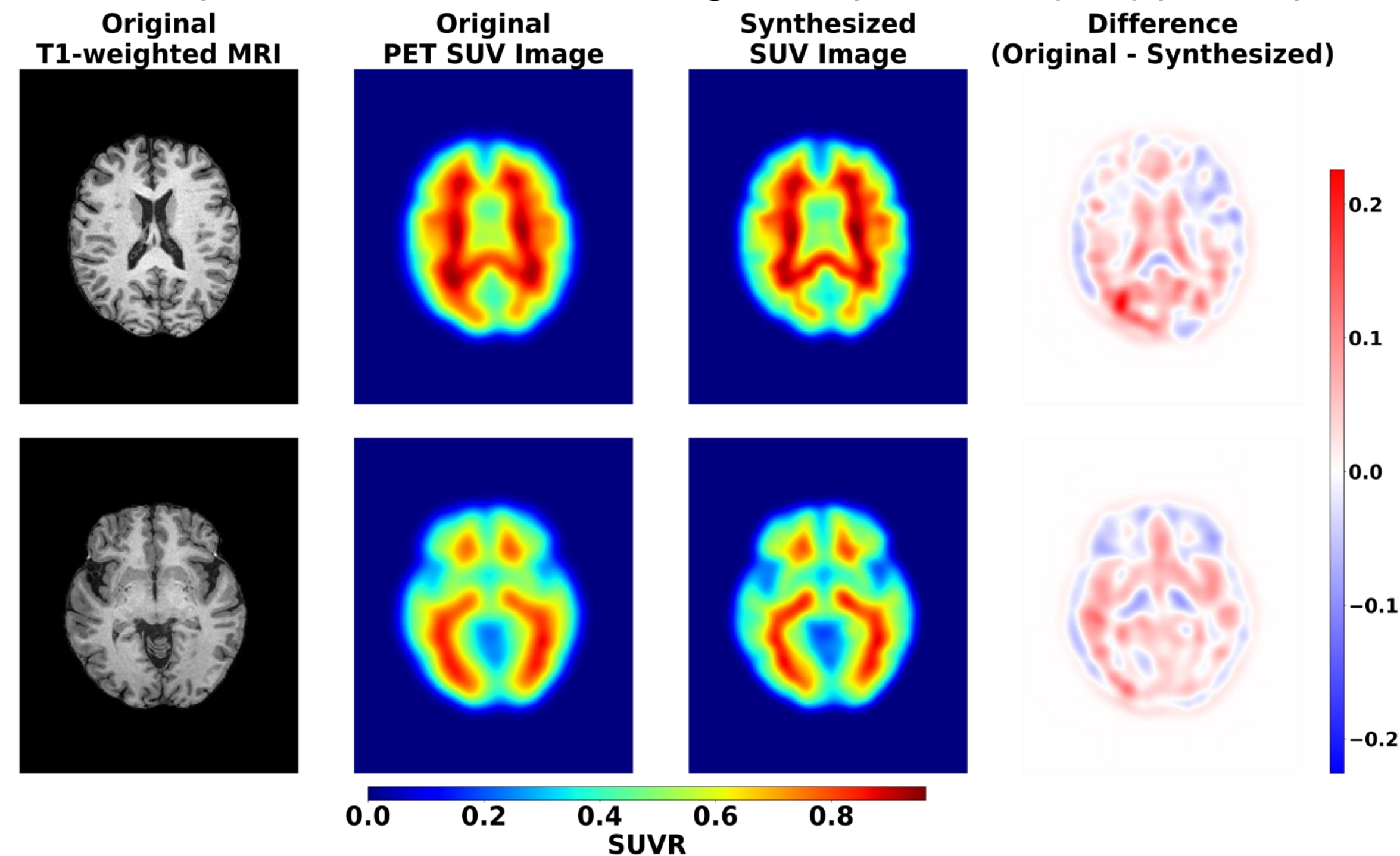


Figure 1: Figure representing the T1-weighted MRI, SUV images (original and synthesized) and the difference between the two images

Table 2: Groupwise Δ SUVR %

Group	N	Composite	Frontal	Cingulate	Parietal	Temporal
AD	26	9.79	11.20	10.66	8.70	10.15
MCI	134	10.40	11.00	10.86	10.99	9.77
CN	32	9.43	10.27	10.41	9.84	8.11

REFERENCES

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- Amft, M., Ortner, M., Eichenlaub, U. et al. (2022) The cerebrospinal fluid biomarker ratio A β 42/40 identifies amyloid positron emission tomography positivity better than A β 42 alone in a heterogeneous memory clinic cohort. *Alz Res Therapy* 14, 60.

Classification Performance Metrics

Performance Metrics	Ground Truth *	
	Original PET SUVR	CSF Biomarker
Accuracy	81.77%	80.83%
Sensitivity	73.08%	82.14%
Specificity	87.72%	79.69%
AUROC	84.66%	80.92%

CONCLUSION

This proof-of-concept study demonstrates the feasibility of extracting amyloid pathology signal from routine brain MRI. SUVRs extracted from both images demonstrate significant alignment with both PET- and CSF-derived ground truths, showing potential as a reliable screening tool. These findings suggest that it is possible to derive clinically meaningful inferences about Alzheimer's pathology without the need for invasive or expensive procedures, paving the way for scalable and accessible early detection solutions.