

SUPPLEMENTARY TABLES

Supplementary Table 1A. Performance metrics of derived AD-RAI, HV and HF in differentiating converters and stable subjects from ADNI-2 database among all subjects (n=158).

Measures	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value	Negative predictive value	Accuracy
AD-RAI (≥ 0.5)	0.64 (0.50-0.76)	0.79 (0.69-0.86)	63.79%	79.00%	73.42%
HV (≤ 6.44mL)	0.67 (0.53-0.79)	0.62 (0.52-0.71)	50.65%	76.54%	63.92%
HF (≤ 0.42%)	0.64 (0.50-0.76)	0.56 (0.46-0.66)	45.68%	72.73%	58.86%

AD-RAI=Alzheimer's disease resemblance atrophy index; HV=hippocampal volume; HF=hippocampal fraction; ADNI=Alzheimer's Disease Neuroimaging Initiatives; CI=confidence interval.

Supplementary Table 1B. Performance metrics of derived AD-RAI, HV and HF in differentiating converters and stable subjects from ADNI-2 database among MCI subjects (n=85).

Measures	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value	Negative predictive value	Accuracy
AD-RAI (≥ 0.5)	0.80 (0.63-0.91)	0.60 (0.45-0.73)	58.33%	81.08%	68.24%
HV (≤ 6.07mL)	0.66 (0.48-0.80)	0.62 (0.47-0.75)	54.76%	72.09%	63.53%
HF (≤ 0.41%)	0.63 (0.45-0.78)	0.54 (0.39-0.68)	48.89%	67.50%	57.65%

AD-RAI=Alzheimer's disease resemblance atrophy index; HV=hippocampal volume; HF=hippocampal fraction; ADNI=Alzheimer's Disease Neuroimaging Initiatives; MCI=mild cognitive impairment; CI=confidence interval.

Supplementary Table 1C. Performance metrics of derived AD-RAI, HV and HF in differentiating converters and stable subjects from ADNI-2 database among NC subjects (n=73).

Measures	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value	Negative predictive value	Accuracy
AD-RAI (≥ 0.5)	0.39 (0.20-0.61)	0.98 (0.88-1.00)	90.00%	77.78%	79.45%
HV (≤ 6.64mL)	0.70 (0.47-0.86)	0.62 (0.47-0.75)	45.71%	81.58%	64.38%
HF (≤ 0.44%)	0.65 (0.43-0.83)	0.58 (0.43-0.72)	41.67%	78.38%	60.27%

AD-RAI=Alzheimer's disease resemblance atrophy index; HV=hippocampal volume; HF=hippocampal fraction; ADNI=Alzheimer's Disease Neuroimaging Initiatives; NC=normal control; CI=confidence interval.

Supplementary Table 2. Performance metrics of AD-RAI, HV, HF and MTA among dementia subjects in CU-SEEDS cohort (n=10).

Measures	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value	Negative predictive value	Accuracy
AD-RAI (≥ 0.5)	0.90 (0.54-0.99)	NA	100.00%	0	90.00%
HV ($\leq 5.71\text{mL}^*$)	0.80 (0.44-0.96)	NA	100.00%	0	80.00%
HF ($\leq 0.38\%^*$)	0.50 (0.20-0.80)	NA	100.00%	0	50.00%
MTA (Adjusted by age ^{**})	0.80 (0.44-0.96)	NA	100.00%	0	80.00%

AD-RAI=Alzheimer's disease resemblance atrophy index; HV=hippocampal volume; HF=hippocampal fraction; MTA=medial temporal lobe atrophy; CU-SEEDS= The Chinese University of Hong Kong - Screening for Early Alzheimer's Disease; CI=confidence interval. *The cutoff of HV ($\leq 5.71\text{mL}$) and HF ($\leq 0.38\%$) used here were also derived from previous study [1]. **The cut-off scores of MTA: under 75 years ≥ 1.5 and ≥ 75 years ≥ 2 [2].

Supplementary Table 3A. Performance metrics of AD-RAI and MTA among MCI and CU subjects harboring A+ (n=128).

Measures	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value	Negative predictive value	Accuracy
AD-RAI (≥ 0.5)	0.65 (0.49-0.77)	0.94 (0.85-0.98)	86.11%	81.52%	82.81%
HV ($\leq 6.44\text{mL}$)	0.65 (0.49-0.77)	0.78 (0.67-0.86)	63.27%	78.48%	72.66%
HF ($\leq 0.42\%$)	0.46 (0.32-0.61)	0.94 (0.85-0.98)	81.48%	74.26%	75.78%
MTA (≥ 1)	0.48 (0.34-0.63)	0.90 (0.81-0.95)	74.19%	74.23%	74.22%

AD-RAI=Alzheimer's disease resemblance atrophy index; HV=hippocampal volume; HF=hippocampal fraction; MTA=medial temporal lobe atrophy; CI=confidence interval.

Supplementary Table 3B. Performance metrics of AD-RAI, HF, HV and MTA among MCI subjects harboring A+ (n=50).

Measures	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value	Negative predictive value	Accuracy
AD-RAI (≥ 0.5)	0.86 (0.66-0.95)	0.86 (0.64-0.96)	88.89%	82.61%	86.00%
HV ($\leq 6.07\text{mL}$)	0.68 (0.48-0.83)	0.95 (0.75-1.00)	95.00%	70.00%	80.00%
HF ($\leq 0.41\%$)	0.54 (0.34-0.72)	0.95 (0.75-1.00)	93.75%	61.76%	72.00%
MTA (≥ 1)	0.64 (0.44-0.81)	0.86 (0.64-0.96)	85.71%	65.52%	74.00%

AD-RAI=Alzheimer's disease resemblance atrophy index; HV=hippocampal volume; HF=hippocampal fraction; MTA=medial temporal lobe atrophy; MCI=mild cognitive impairment; CI=confidence interval.

Supplementary Table 3C. Performance metrics of AD-RAI, HF, HV and MTA among CU subjects harboring A+ (n=78).

Measures	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value	Negative predictive value	Accuracy
AD-RAI (≥ 0.5)	0.35 (0.16-0.59)	0.97 (0.87-0.99)	77.78%	81.16%	80.77%
HV ($\leq 6.64\text{mL}$)	0.70 (0.46-0.87)	0.91 (0.80-0.97)	73.68%	89.83%	85.90%
HF ($\leq 0.44\%$)	0.35 (0.16-0.59)	0.97 (0.87-0.99)	77.78%	81.16%	80.77%
MTA (≥ 1)	0.25 (0.10-0.49)	0.91 (0.80-0.97)	50.00%	77.94%	74.36%

AD-RAI=Alzheimer's disease resemblance atrophy index; HV=hippocampal volume; HF=hippocampal fraction; MTA=medial temporal lobe atrophy; CU=cognitively unimpaired; CI=confidence interval.

SUPPLEMENTARY REFERENCES

1. Abrigo J, Shi L, Luo Y, Chen Q, Chu WCW, Mok VCT; Alzheimer's Disease Neuroimaging Initiative. Standardization of hippocampus volumetry using automated brain structure volumetry tool for an initial Alzheimer's disease imaging biomarker. *Acta Radiol.* 2019; 60:769–76.
<https://doi.org/10.1177/0284185118795327>
PMID:[30185071](https://pubmed.ncbi.nlm.nih.gov/30185071/)
2. Pereira JB, Cavallin L, Spulber G, Aguilar C, Mecocci P, Vellas B, Tsolaki M, Kłoszewska I, Soininen H, Spenger C, Aarsland D, Lovestone S, Simmons A, Wahlund LO, Westman E; AddNeuroMed consortium and for the Alzheimer's Disease Neuroimaging Initiative. Influence of age, disease onset and ApoE4 on visual medial temporal lobe atrophy cut-offs. *J Intern Med.* 2014; 275:317–30.
<https://doi.org/10.1111/joim.12148>
PMID:[24118559](https://pubmed.ncbi.nlm.nih.gov/24118559/)