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NEW IMAGING METHODS

Problems using structural MRIs from the oldest-old, and some solutions: Lessons learned from The 90+ Study and ADNI

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Abstract

Background: The oldest-old (≥85 years) have the highest rates of dementia. However, because of pronounced brain atrophy, standard neuroimaging programs face unique challenges in this cohort. Here, using data from both *The 90+ Study* and Alzheimer's Disease Neuroimaging Initiative (ADNI), we report the prevalence of errors when processing brain MRIs from oldest-old participants using standard approaches and present some strategies for ameliorating these issues.

Method: First, we analyzed image quality issues and segmentation errors (FreeSurfer) for the last available scans by age-groups (oldest-old, ≥85 years, vs younger-old, 55 to 85 years) in ADNI. Second, we evaluated the utility of an age-specific template (the 90+ T1w Template) for realigning MRIs from the oldest-old compared to a standard template (Montreal Neurological Institute T1w template, MNI) using linear and nonlinear registration (FSL) and evaluating alignment quality using visual and deformation (Jacobian) measures for oldest-old participants (≥90 years) in both *The 90+ Study* and ADNI. Lastly, we evaluated whether stringent preprocessing (bias field removal, denoising, brain extraction, intensity normalization using Computational Anatomy Toolbox (CAT12)) helped reduce FreeSurfer segmentation errors in frontal, parietal, and temporal regions in MRIs from the oldest-old. Comparisons were performed using Chi-square tests.

Result: In ADNI data (*Table-1*), MRIs from oldest-old participants (~10% of cohort) were around twice as likely to have image quality issues (20% vs 13%, P<0.001) and brain segmentation errors (45% vs 29%, P<0.001) compared to younger-old participants. *Figure-1* shows a histogram of image quality issues and segmentation errors, which become more common with greater age. Compared to the MNI template, MRIs from participants aged 90 and older from both *The 90+ Study* (N=163, *Table-2*) and ADNI (N=75) had fewer registration errors (~5% vs ~23%, P<0.001 for all) and less severe deformation when using the 90+ T1w Template (*Figure-2*). Our proposed preprocessing pipeline (see *Figure-3* for example) roughly halved segmentation errors in the oldest-old (P<0.001 for all regions, *Figure-4*).

Conclusion: Our results show that adapting pipelines specifically for processing brain MRIs of oldest-old participants minimizes errors, enabling more effective use of neuroimaging to study neural correlates of neurodegeneration and dementia in this important portion of our aging population.

Table 1. ADNI participant characteristics for image quality and FreeSurfer quality data.

Measures	Image Quality (N=1765)	FreeSurfer Quality (N=2334)
Age (SD) [Range]	74.0 (7.67) [55.1, 95.7]	75.9 (7.8) [54.6, 97.4]
Oldest Old (%)	161 (9.1%)	307 (13.2%)
Women (%)	877 (49.7%)	1113 (47.7%)
Education (SD)	16.3 (2.60)	16.1 (2.75)
Normal Cognition (%)	711 (40.3%)	798 (34.2%)
MCI (%)	640 (36.3%)	748 (32.0%)
Dementia (%)	414 (23.5%)	788 (33.8%)

Table 2. Participant characteristics for *The 90+ Study* (N=163).

Age (SD) [Range]	94.1 (3.1) [90.2 - 102.7]
Women (%)	111 (68.1%)
College Education (%)	81 (49.7%)
Normal Cognition (%)	110 (67.5%)
Cognitive impairment no dementia (CIND) (%)	43 (26.4%)
Dementia (%)	10 (6.1%)

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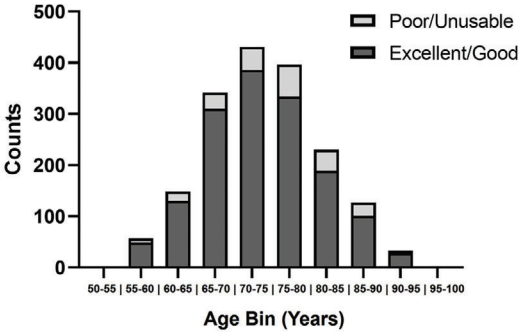
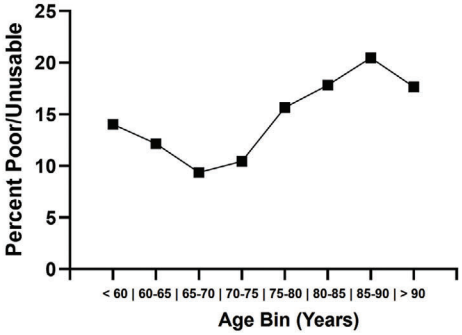
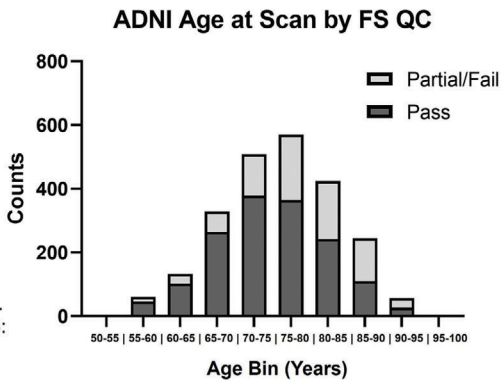
Figure-1. Image quality and segmentation issues in ADNI Participants.

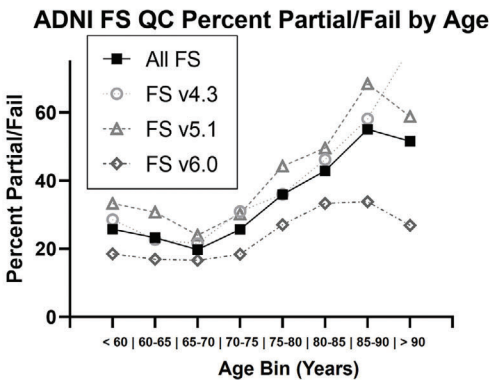
Image Quality (N=1,765)





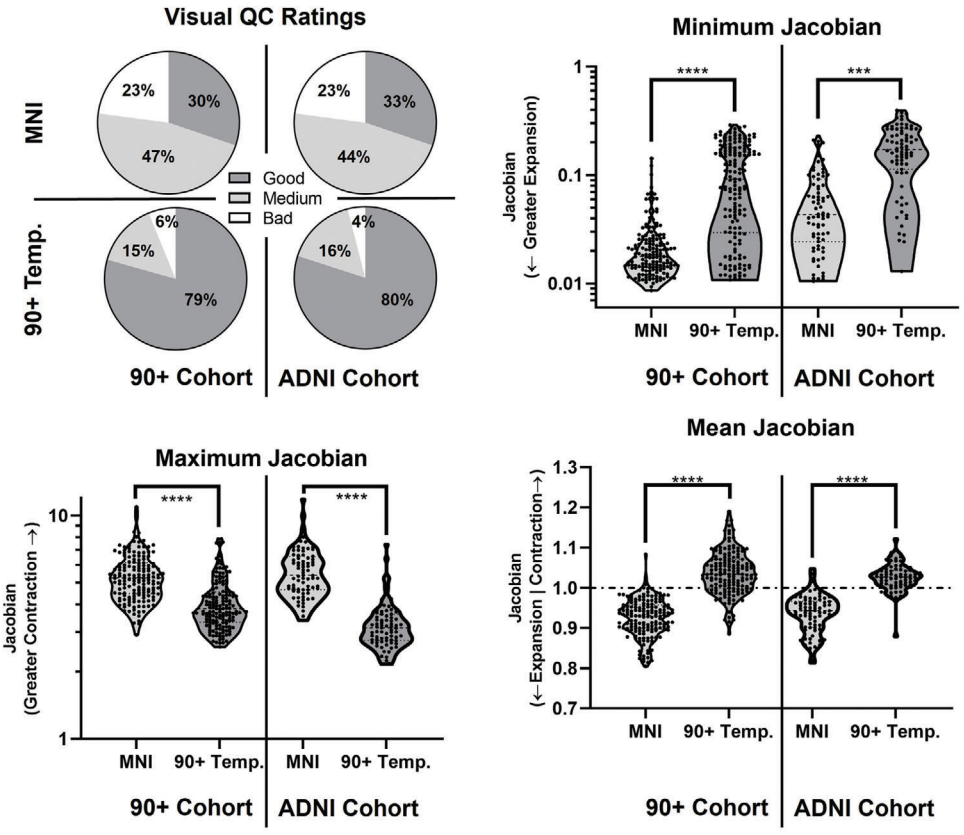
FreeSurfer Segmentation Quality (N=2,334)





Abbreviations: ADNI: Alzheimer's Disease Neuroimaging Initiative. QC: Quality control. FS: FreeSurfer.

Figure-2. Quality control measures of registrations to MNI and 90+ templates for participants from The 90+ Study (N=163) and partipicants ≥90 years from ADNI (N=75).



Abbreviations: MNI: Montreal Neurological Institute T1w Template. ADNI: Alzheimer's Disease Neuroimaging Initiative. 90+ Temp.: 90+ T1w Template.

Figure-3. Illustration of preprocessing using Computational Anatomy Toolbox (CAT12) to improve reliability of FreeSurfer (FS) segmentations in the oldest-old.

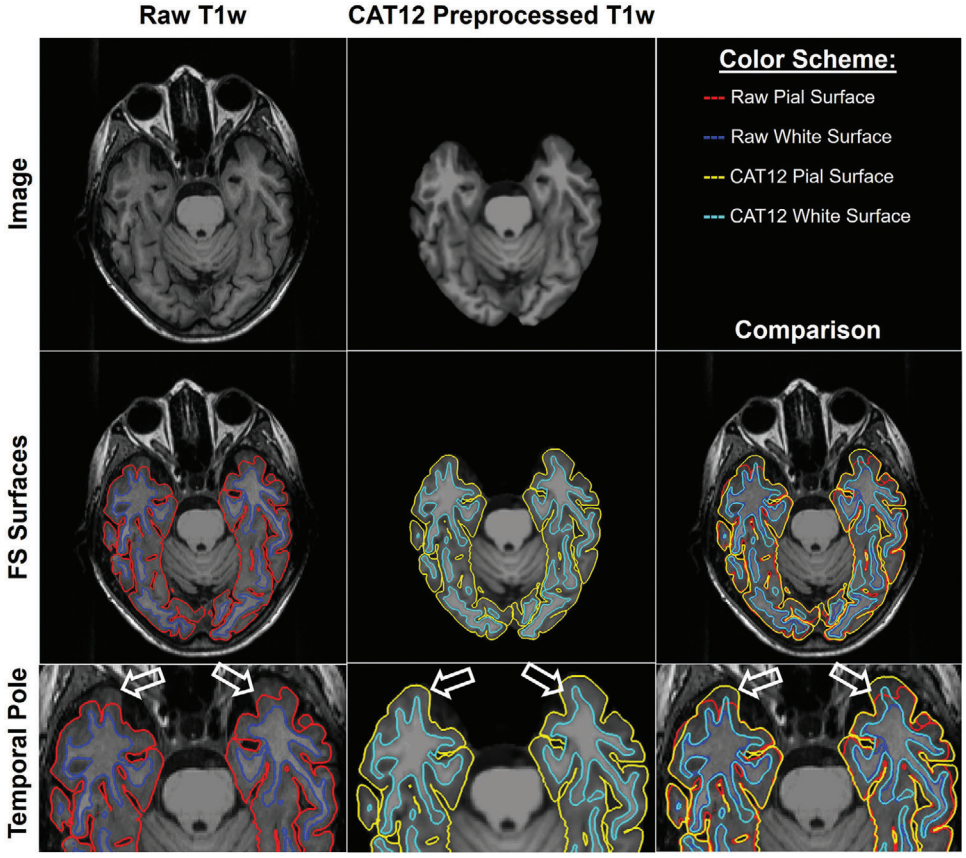


Figure-4. Segmentation quality control for raw FreeSurfer and Computational Anatomy Toolbox (CAT12) preprocessed scans in ADNI and The 90+ Study participants.