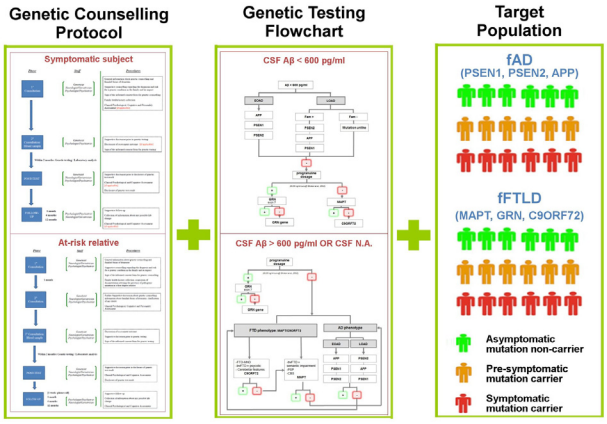
Table

Marker	Targeted population	Collected variables	Reference protocol
Clinical and Neuropsychological	fAD and fFTLD	Neurological, physical, psychological, cognitive	GenFI for fFTLD DIAN for fAD
MR Imaging	fAD and fFTLD	3T MRI (3D-T1, T2/FLAIR, DTI, rs-fMRI, ASL)	GenFI for fFTLD DIAN for fAD
PET Imaging	fAD and fFTLD fAD	18F-FDG PET Amyloid PET	DIAN Ligand-specific
Biological Samples	fAD and fFTLD	DNA; RNA; Serum; Plasma; Lymphoid cells; CSF; Urine; Fibroblasts	Customised (synthesis of GenFI and DIAN)
Neurophysiological	fAD and fFTLD	Resting-EEG (open- and closed-eyes)	IMI-Pharmacog



IC-P-070 VALIDATION OF HIPPOCAMPAL TEXTURE FOR EARLY ALZHEIMER'S DISEASE DETECTION: GENERALIZATION TO INDEPENDENT COHORTS AND EXTRAPOLATION TO VERY EARLY SIGNS OF DEMENTIA

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Background: We previously saw that hippocampal magnetic resonance imaging (MRI) texture provided volume-independent information in Alzheimer's disease (AD) diagnosis (AAIC 2012, P1-157) and was capable of predicting conversion from mild cognitive impairment (MCI) to AD (AAIC 2013, P3-085). Both results were obtained using Alzheimer's Disease Neuroimaging Initiative (ADNI) data. The purpose of this study was further validation of texture for early AD detection by investigating generalization to The Australian Imaging Biomarkers and Lifestyle (AIBL) cohort and extrapolation to very early signs of dementia in a healthy, middle-aged population. **Methods:** Three different T1-weighted structural MRI datasets were considered (Table 1). ADNI: baseline MRIs from normal controls (CTRLs) and AD patients in the "complete annual year 2 visits" 1.5T standardized ADNI dataset. AIBL: baseline MRIs from the imaging arm. Metropolit: follow-up MRIs from 192 subjects from The Metropolit 1953 Danish Male Birth Cohort, of which 97 had established loss of cognitive performance from approximately age 20 to 56. The hippocampi were segmented in all MRIs using cross-sectional FreeSurfer (v5.1.0), providing the region of interest. Hippocampal fraction (HF) defined as hippocampal volume divided by FreeSurfer's estimate of intracranial volume was computed as well. The texture-based marker was trained on the ADNI dataset and was subsequently applied to score the AIBL and the Metropolit dataset. Texture was adjusted for HF by linear regression. **Results:** Generalization to AIBL (area under receiver operating characteristic curve; texture / HF-adjusted texture): CTRL vs. AD 0.907 ($p<0.001$) / 0.790 ($p<0.001$), MCI-converters vs. MCI-non converters 0.831 ($p=0.003$) / 0.816 ($p<0.001$). Extrapolation to Metropolit (Pearson correlation with cognitive score; texture / HF / HF-adjusted texture): Mini-Mental State Examination (MMSE) -0.213 ($p=0.003$) / 0.181 ($p=0.012$) / -0.180 ($p=0.013$), AddenbrookeÊ¼s Cognitive Examination (ACE) -0.250 ($p<0.001$) / 0.018 ($p=0.808$) / -0.251 ($p<0.001$). **Conclusions:** Previously reported ADNI results were reproduced in AIBL, enhancing our confidence in hippocampal texture as an imaging biomarker for early AD detection. Texture correlated with both MMSE and ACE in Metropolit, demonstrating extrapolation to a cohort with different characteristics. HF only correlated with MMSE, further advocating texture in structural MRI-based early AD detection, since ACE is an extension of MMSE designed for early dementia detection.

Table 1
Characteristics of the three datasets. Baseline age, MMSE score and MRI scan are reported for ADNI and AIBL whereas follow-up data, incl. ACE score, are reported for Metropolit

	n	Age, years (mean±std)	MMSE (mean±std)	ACE[a] (mean±std)	MRI field strength (1.5T/3T)
ADNI					
CTRL	169	76.0±5.1	29.2±1.0		169/0
AD	101	75.3±7.4	23.2±1.9		101/0
AIBL					
CTRL	88	75.2±7.2	28.9±1.3		1/87
AD	28	73.6±8.1	21.2±5.6		0/28
MCI-C	8	80.7±7.6	25.6±2.0		0/8
MCI-NC	21	76.2±6.7	27.7±1.8		0/21
Metropolit					
CTRL	95	58.4±0.6	29.5±0.8	96.0±3.2	0/95
Cognitive loss	97	58.6±0.7	29.1±1.0	92.1±5.0	0/97

[a] One observation from the Metropolit cognitive loss group is missing.

IC-P-071 PERSONALIZED BIOMARKERS OF NEURODEGENERATIVE DISEASES USING IMAGING PATTERN ANALYSIS AND MACHINE LEARNING METHODS: THE POWER OF COMBINING MULTIPLE TYPES OF INFORMATION

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Background: Although a variety of biomarkers has been used in studies of neurodegenerative disorders, including a variety of imaging biomarkers, it has been challenging to derive indices that are highly sensitive and specific on an individual basis. Moreover, it has been challenging to capture the