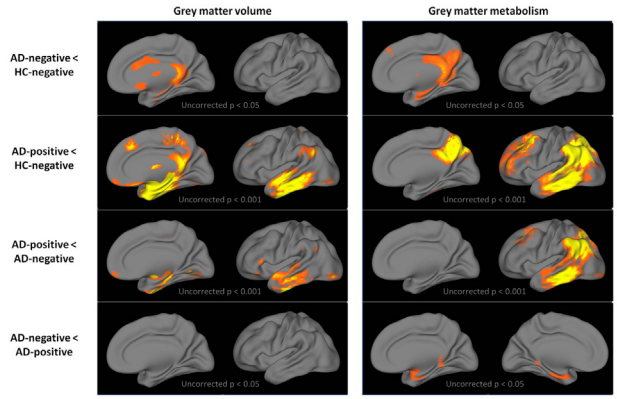
Table
Demographic characteristics of the samples

	AD-negative	AD-positive	HC-negative
N (males)	9 (5)	26 (12)	30 (14)
Age (mean±SD)	70.6±14.7	72.5±10.9	71.1±11.6
Education (mean±SD)	12.1±5.8	12.5±2.8	14.1±3.7
MMSE (mean±SD)	24.6±3	22.8±4.4	28.8±1
ApoE4 (n / n available)	14%	81%	14%



IC-P-010 CLINICALLY DIAGNOSED PROBABLE AD CASES WITH A NEGATIVE AMYLOID PET SCAN: CLINICAL FINDINGS

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Background: 10%-20% of patients clinically diagnosed with Alzheimer's disease (AD) in expert centers do not show high tracer retention on amyloid PET. The present study investigates the clinical and demographic features and longitudinal trajectory of this intriguing subgroup. **Methods:** 41 amyloid PET-negative patients carrying a pre-PET diagnosis of AD from 4 centers (Amsterdam, Melbourne, San Francisco, and Caen) were included in this study. Amyloid status was determined by visual reading and confirmed by quantitative analyses. Detailed clinical histories of all patients was collected, including the clinical diagnosis before and after results of the PET scan were known by the clinician, and at long term follow-up, when available. Patients were then classified according to their clinical phenotype as either typical (memory predominant), atypical (predominant language, visual or frontal symptoms), or aclassical (nonspecific presentation), both before and after the PET scan. **Results:** There were 17 typical, 15 atypical, and 8 aclassical AD-negative cases plus one unclassified. Subgroups didn't differ in age, education or MMSE except that typical cases had higher MMSE than atypical ones (p=0.03, see Table). After the PET scan, clinicians altered the diagnosis in 22 of the 34 cases in which they received results. Diagnosis changed to frontotemporal dementia (FTD, n=8), corticobasal syndrome (CBS, n=4), dementia with Lewy bodies (DLB, n=3), epilepsy-depression (n=1), primary progressive aphasia (n=1), non-fluent aphasia (n=1) and unknown diseases (n=4, see detailed table). Clinicians did not change their clinical diagnosis in 60% of typical patients, but nearly always changed the diagnosis in atypical and aclassical cases (83%, p=0.03). Typical cases were most often reclassified as FTD, atypical as FTD or CBS, and aclassical as DLB or unknown. **Conclusions:** Negative amyloid PET scans impacted clinical diagnosis, particularly in patients with non-amnestic clinical presentations. Amyloid PET negative AD likely represents a mixed population of initially misdiagnosed neurodegenerative or non-degenerative conditions, AD-mimics (e.g. hippocampal sclerosis or argyrophilic grain disease), and false negative scans.

Table
Demographic and clinical characteristics of the amyloid-negative AD patients by clinical phenotype subgroups

	All	Typical	Atypical	Aclassical
n	41	17	15	8
Age (mean±SD)	67.2±9.2	68.7±11.5	65.5±7.1	68.1±8.1
Education (mean±SD)	12.3±4.7	12.7±5.6	16.5±4.8	13.7±5.7
MMSE (mean±SD)	22.6±4.8	24.3±2.7	20.9±5.3	23.5±4.9
ApoE4 (n / n available)	5/27	3/14	1/6	1/6
Diagnosis change (n / n available)	22/34	6/15	10/12	5/6
Diagnosis when changed		FTD (n=4) DLB (n=1) Epilepsy-depression (n=1)	FTD (n=4) CBS (n=4) Primary progressive aphasia, no specific subtype (n=1) Non-fluent aphasia (n=1)	DLB (n=2) Unknown (n=3)

IC-P-011 COMPARING LIBERAL AND CONSERVATIVE THRESHOLDS FOR AMYLOID PET POSITIVITY IN AUTOPSY-PROVEN CASES

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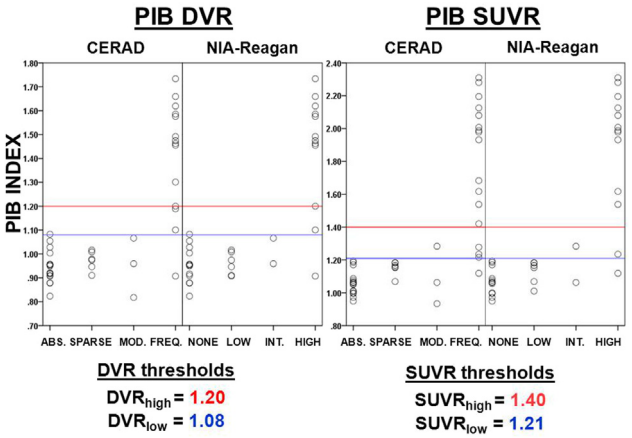
Background: Variable quantitative thresholds have been proposed to define amyloid positivity on PET, but few studies have compared these thresholds to post-mortem amyloid burden as the "standard of truth." **Methods:** We included 43 individuals who underwent PIB-PET during life and brain autopsy (mean age at PET=66.8±8.0, T autopsy -T PET =3.0±1.8 years). Patients were evaluated clinically at UCSF (N=36) and UC Davis (N=7), and all underwent PET at Lawrence Berkeley Laboratory. Clinical diagnoses included Alzheimer's disease (AD, N=10), frontotemporal dementia (N=24), other dementia (N=2), mild cognitive impairment (N=5) and cognitively normal (N=2). Global amyloid was measured with a PIB Index (gray cerebellum reference) via 0-90 minute Distribution Volume Ratios (DVR, N=39) and/or 50-70 min Standardized Uptake Value Ratios (SUVR, N=41). Amyloid at autopsy was classified using CERAD (N=43) and NIA-Reagan criteria (N=33, 10 cases unclassifiable). We compared conservative PIB thresholds in the literature (SUVR high =1.40, DVR high =1.20) and more liberal proposed thresholds (SUVR low =1.21, DVR low =1.08, see Villeneuve et al., submitted) to CERAD frequent neuritic plaques (NP) and NIA-Reagan high-likelihood AD. Receiver operator characteristic (ROC) analyses were performed to empirically derive optimal thresholds. **Results:** The liberal DVR low and SUVR low thresholds captured all but one patient with CERAD frequent NP, and each threshold misclassified one patient with lower amyloid burden (sensitivity 93-94%, specificity 96%, see Figure - blue line). Conservative thresholds were considerably less sensitive (DVR high 71%, SUVR high 77%) but 100% specific (Figure - red line). Liberal thresholds performed similarly well in capturing NIA-Reagan high-likelihood AD (sensitivity 92%, specificity 95% for both DVR low and SUVR low), whereas conservative thresholds were again less sensitive (DVR high 75%, SUVR high 85%) but 100% specific. ROC analyses yielded areas under the curve ranging from 0.929-0.971 (all p<0.001). The optimal thresholds derived from ROC were nearly identical to our a priori liberal thresholds (DVR=1.09 and SUVR=1.20-1.21). **Conclusions:** Liberal thresholds for PIB-positivity were highly sensitive and specific for high-burden amyloid pathology. Conversely, more widely used conservative thresholds appeared to be overly stringent in defining amyloid positivity. More work is needed to verify these findings in subjects with intermediate pathology and independent cohorts.



IC-P-012 AUTOMATED REPORTING OF AMYLOID PET QUANTIFICATION ON BRAIN SURFACE THROUGH A WEB INTERFACE

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Background: Molecular brain imaging using Positron Emission Tomography (PET) is a robust diagnostic tool for which several tracers labelled with either 11C or 18F are available. For visual inspection of the images, cortical surface based visualisation presents the advantage of providing a compact and more convenient display than volumetric scans. We have developed an automated reporting tool to display the semiquantitative PET signal for several common tracers without the need of a MRI and using several standard normalisation methods (i.e. using the Pons, the whole Cerebellum WCB and the cerebellum cortex CB-CTX). This tool is available on-line to registered users and the processing is performed remotely (http://milxcloud.csiro.au/capaibl). The method was validated by comparing the surface signal computed with and without MRI. **Methods:** Three hundred and thirty nine participants from the AIBL cohort underwent MRI and PET scans with different tracers: 18F-Flutemetamol (n=101), 11C-PIB (n=91), 18F-Florbetapir (n=77), 18F-FDG (n=38), 18F-Florbetaben (n=14) and 18F-NAV4694 (n=18). Each individual PET image was spatially normalised to the MNI space and SUVR corrected with a common mask. Radiotracer retention was then estimated vertex-wise within several GM prior atlases. Atlas selection and Bayesian fusion were then used to estimate retention on the cortical surface. For comparison with MR-based approach, radiotracer retention was also estimated for each vertex with the individual GM segmentation and projected onto the individual cortical surface. The difference in radiotracer estimation between the MRI-dependent and CAPAIBL (Computational Analysis of PET from AIBL) approaches was measured by absolute difference of SUVR values at each vertex. The SUVR differences were averaged over vertices and over the total subjects. **Results:** Visual inspection revealed high concordance between PET only and MRI based surface projection; the surface projection was defined on 8 standard views for consistent reporting (Fig 1). Across the 6 tracers tested, the average absolute error over the brain surface with and without MRI was 0.12, whereas the average variance was 0.018. **Conclusions:** The proposed MRI-less surface projection method demonstrated better estimation of 11C-PIB retention than recently published methods displaying similar accuracy for various 18F labelled radiotracers. CAPAIBL provides an efficient reporting tool for PET imaging easily accessed remotely through a web interface.

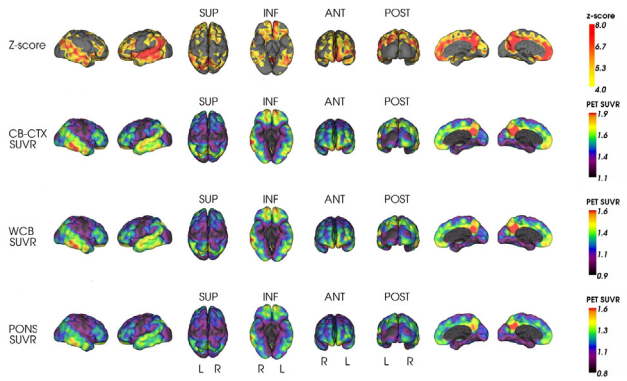

Fig 1. Example of CAPAIBL inspection on a positive 18F-Florbetapir. The report displays the radiotracer retention z-score when compare to a normal negative population followed by normalisation with cortical cerebellum, whole cerebellum and Pons.