Table 1
Analyses of association between AD biomarker with BMI measure at each age

	Global Aβ deposition				AD signature cortical thickness			
	B	SE	β	P	B	SE	β	P
Current BMI	-0.008	0.006	-0.091	0.184	0.008	0.004	0.139	**0.018**
Early adult BMI	-0.011	0.006	-0.118	**0.082**	0.007	0.004	0.108	**0.063**
Mid life BMI	-0.016	0.007	-0.152	**0.025**	0.003	0.004	0.039	0.504
Past BMI(20 to 50)	-0.015	0.007	-0.141	**0.037**	0.006	0.004	0.083	0.158

Abbreviations: BMI=body mass index. All analyses were Adjusted by age, gender, APOE4 carrier status, Vascular risk factors.

60-90, who participated in the Korean Brain Aging Study for Early Diagnosis and Prediction of Alzheimer's Disease (KBASE), were included in this study. All the subjects underwent comprehensive clinical and neuropsychological assessment, 11C-labelled Pittsburgh Compound B (PiB) positron emission tomography (PET), and Brain Magnetic resonance imaging(MRI). Mean cortical thickness values were obtained from AD-signature regions including the entorhinal, inferior temporal, middle temporal, and fusiform gyrus. BMI values for past lifetime periods((i.e., young adulthood: 20-30s and midlife: 40-50s) were calculated from self-recalled body weight and height, and current BMI was calculated from measured body weight and height. Multiple regression analyses were performed controlling age, gender, APOE e4 carrier status, and vascular risk scores. **Results:** For the overall subjects, past BMI, BMI at young adulthood in particular, was negatively associated with global cerebral Aβ deposition, while current BMI was not. In contrast, current BMI showed significant positive association with AD-signature region cortical thickness, while past BMI did not. When subgroup analyses were performed for each gender, very similar relationships between lifetime BMIs and Aβ deposition and cortical thickness were still found for males, whereas no significant association was observed between the variables for females. **Conclusions:** Our results suggest that relatively low past BMI, especially in male, may contribute to increase of cerebral Aβ burden and the risk of AD in late-life, while lower current BMI appears related with emerging neurodegeneration. The findings should be cautiously interpreted considering most of the subjects were in normal range for past and current BMI, and only small proportion of them were in overweight or obese state.

Table 2
Analyses of association between **PiB retention** and BMI at each age and sex group in participant

	Women		Men	
	β	P value	β	P value
Early adult BMI	-0.002	0.786	-0.038	**0.003**
Midlife BMI	0.003	0.673	-0.028	**0.009**
Past BMI(20 to 50)	0.001	0.944	-0.036	**0.003**
Current BMI	0.003	0.690	-0.021	**0.042**

BMI=body mass index. All analysis were Adjusted for age, APOE4 carrier status, vascular risk factors.

Table 3
Analyses of association between **AD sig cortical thickness** and BMI at each age and sex group in participant

	Women		Men	
	β	P value	B	P value
Early adult BMI	0.002	0.734	0.005	0.532
Midlife BMI	0.003	0.600	0.014	**0.022**
Past BMI(20 to 50)	0.003	0.621	0.012	**0.098**
Current BMI	0.006	0.211	0.013	**0.023**

BMI=body mass index. All analysis were Adjusted for age, APOE4 carrier status, vascular risk factors.

IC-P-016 INVESTIGATING THE CLINICAL IMPACT OF [^{18}F]FLUTEMETAMOL PET IN A TERTIARY MEMORY CLINIC SETTING IN PATIENTS WITH UNCERTAIN DIAGNOSIS

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Background: Since the first application of carbon-11 Pittsburgh Compound-B ([^{11}C]PIB) PET more than a decade ago, amyloid PET has been instrumental in advancing the research agenda for Alzheimer's disease (AD). By detecting a core feature of AD pathology, amyloid PET holds potential in clinical settings, particularly given the high rate of misdiagnosis. Clinical studies using recently approved amyloid PET tracers, however, have far been few, with these mainly in highly selected research cohorts. The aim of the present study was thus to investigate the added clinical value of [^{18}F]flutemetamol PET in memory clinic patients whose diagnosis remained uncertain following routine clinical work up. **Methods:** 135 patients were included from the Department of Geriatric Medicine, Karolinska University Hospital, Huddinge, Sweden, following referral from primary care physicians. Following standard diagnostic workup, including medical and neurological examination, clinical chemistry (including CSF Aβ_{1-42}), rating batteries for depression and neuropsychiatric symptoms, neuropsychological assessment, and structural imaging, the clinical picture remained unclear. [^{18}F]flutemetamol PET was thus performed, using a Biograph mCT PET/CT (Siemens/CTI, Knoxville, TN), with the acquisition protocol consisting of a static 20-min scan, 90-min post-injection of 185 MBq. In addition to visual assessment by an experienced nuclear medicine physician, [^{18}F]flutemetamol uptake was quantified on a region of interest basis using a fully automated software (Hermes Hybrid BRASS). Diagnoses before and after [^{18}F]flutemetamol investigations were reached using a multidisciplinary consensus based approach. **Results:** Based on preliminary results from 61 subjects (38 MCI, 13 AD, 6 dementia NOS, 2 SCI, one FTD, and one DLB), [^{18}F]flutemetamol investigations led to a change in diagnosis in 68% of patients. Agreement between visual and quantitative assessment of [^{18}F]flutemetamol images was high (89%).

Concordance between CSF $A\beta_{1-42}$ (<550 pg/mL) and [^{18}F]flutemetamol was 57% and 53%, using visual and quantitative approaches, respectively. Among discordant cases, most showed isolated [^{18}F] flutemetamol positivity (75% using visual, 77% using quantification). **Conclusions:** While further analyses are ongoing for the remaining 74 patients, preliminary findings highlight the added value of [^{18}F]flutemetamol over standard diagnostic work-up. Discordance between CSF $A\beta_{1-42}$ and [^{18}F]flutemetamol PET highlights the issue of biomarker interchangeability in clinical settings.

IC-P-017 VOXEL-WISE DETERMINATION OF SENSITIVITY, SPECIFICITY, AND THRESHOLDS FOR AMYLOID POSITIVITY USING [^{18}F]FLORBETAPIR PET

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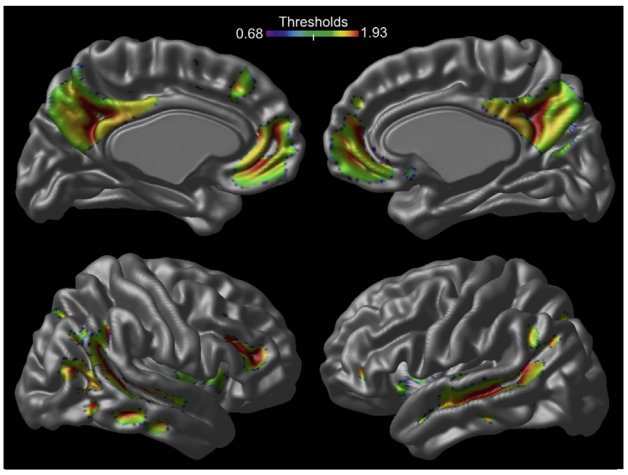
Background: Brain amyloid-β deposition is the core pathological feature of Alzheimer's disease (AD) and can be detected *in vivo* using positron emission tomography (PET). However, the importance of the regional patterns of amyloid-β abnormality has been highly questioned due to its widespread deposition over the cortex. Here, using a novel analytical framework free of conceptual assumptions, we assess the regional patterns of amyloid-β deposition that are associated with AD dementia. **Methods:** We assessed 211 control, 311 mild cognitive impairment, and 79 AD individuals who underwent [^{18}F]florbetapir PET at baseline as well as clinical assessments at baseline and at 2 years. Receiver operating characteristic curves, contrasting controls with AD individuals, assessed the least distance from point to the curve at every brain voxel, which provided the amyloid-β values with the best trade-off between sensitivity and specificity for AD. Finally, we generated a voxel-wise parametric map only with brain regions showing both sensitivity and specificity higher than 0.85. **Results:** Remarkably, the regions with the highest sensitivity and specificity for AD dementia were confined to the brain's default mode network in the precuneus, posterior cingulate, medial prefrontal, and lateral temporal cortices (Fig.1). In contrast, other brain regions with high amyloid-β burden such as the anterior cingulate had low sensitivity and specificity values. **Conclusions:** These results highlight that although amyloid-β deposition occurs widespread over the cortex, the deposition more strongly associated with dementia are confined to the brain's regions default mode network. Interestingly, our results showed



dissociation between the regional levels of amyloid-β burden and the sensitivity and specificity of this burden for a diagnosis of AD. This suggests that the selective regional vulnerability to the toxic effects of Aβ aggregates, at least, plays a role in the progression of AD.

IC-P-018 NEUROIMAGING-DEFINED AMYLOID AND CEREBROVASCULAR PATHOLOGY ARE ASSOCIATED WITH A NEUROMETABOLIC SIGNATURE OF ALZHEIMER'S DISEASE

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Background: To investigate whether white matter hyperintensities (WMH), an MRI-correlate of small-vessel cerebrovascular disease, are associated with a neurometabolic signature of Alzheimer's disease (AD), defined as the metabolic correlates of preclinical ß-amyloid (Aß) pathology and the apolipoprotein-E ε4 allele (APOE-ε4), the major genetic risk factor for sporadic AD. **Methods:** Cognitively normal participants (n=30, age=70±5.6 years, MMSE=29.2±1) received 11C-PiB-PET to quantify Aß, 7 Tesla fluid-attenuated inversion recovery MRI to quantitate WMH, and 7 Tesla high-resolution MR spectroscopic imaging to estimate N-acetylaspartate (NAA), myo-inositol (mI), total-choline (tCho), and creatine (Cr) in posterior cingulate and precuneus (PCP) gray and white matter. We examined relationships of Aß, WMH, and APOE-ε4, and their interactions, with brain metabolites. **Results:** Higher levels of Aß (r= -0.64, p<0.001) and higher WMH volume (r= -0.45, p=0.02) were associated with lower NAA/mI in gray matter. Participants with both high Aß and high WMH had lower NAA/mI compared to those with none or with high level of either Aß or WMH (significant Aß x WMH