correlation between global FMM retention and brain atrophy in any groups. There were positive correlations between THK retention in the frontal, parietal, occipital cortices or precuneus and FMM retention in the frontal, parietal cortices or precuneus. EOAD had weak positive correlation between THK and FMM retention only in the occipital cortex. **Conclusions:** LOAD showed gradual increase in both tau and amyloid and those two pathologies have association to each other. Whereas, in EOAD, tau and amyloid may develop more abruptly and independently. Brain atrophy was associated with tau burden in EOAD, however, was not correlated with amyloid burden in EOAD or LOAD. These findings suggest LOAD and EOAD may have different courses of pathomechanism.

## IC-01-04 A ROBUST, SIMPLIFIED BRAAK-TYPE CLASSIFICATION SCHEME FOR FLORTAUCIPIR F-18 TAU PET IMAGES

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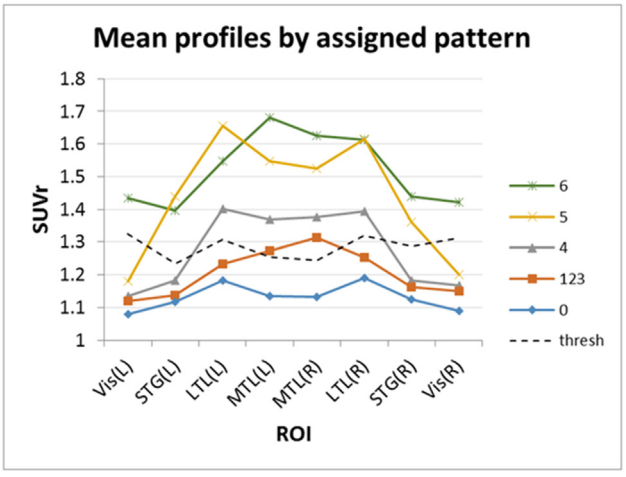
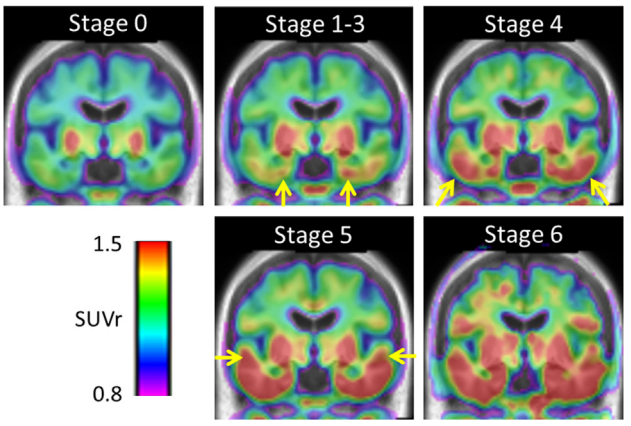
**Background:** Using ROIs based on the Braak staging scheme, patterns of [18F]-flortaucipir binding consistent with expectations from tau neuropathology can be observed in vivo [Schwarz et al., Brain 2016]. However, small regions of interest (ROIs) are potentially sensitive to variations in image preprocessing, atrophy and experimental noise. Medial temporal lobe (MTL) regions distinguishing stages 1-3 are prone to contamination from adjacent extraparenchymal signals and binding to the choroid plexus. Our aim was to identify a simplified and practical flortaucipir PET staging scheme for AD, robust to the above nuisance factors. **Methods:** Four ROIs were defined from standard Harvard-Oxford or Juelich (FSL) atlas structures: (1) an MTL ROI comprising the anterior hippocampus, the parahippocampal/entorhinal and fusiform gyri; (2) a lateral temporal lobe (LTL) ROI comprising the anterior inferior and middle temporal gyri; (3) anterior superior temporal gyrus; and (4) primary visual cortex. We compared larger and smaller variants on these ROIs, and evaluated the effect of grey-matter masking. Individual subject ROI profiles were binarized at 3SD above the mean signal in each ROI from 14 young controls and matched to predefined Braak-like patterns. Staging (0, 1-3, 4, 5 or 6) was performed on each hemisphere independently and the most advanced stage taken. Stages 1-3 were not differentiated. Performance was




evaluated in terms of maximizing test-retest consistency (N=21) and minimizing the number of unassigned profiles (N=21+236). The algorithm was then prospectively applied to flortaucipir scans from ADNI-2 (N=101). **Results:** The larger ROIs and simplified staging scheme yielded higher test-retest consistency and reduced number of unassigned profiles than the published approach. The variant ROIs and grey matter masking did not improve performance. Applied to the ADNI data set, 91% of subjects were classified into a typical predefined estimated Braak stage pattern (Figure). Higher stage tau patterns were associated with more advanced disease severity and amyloid positivity. **Conclusions:** This simplified flortaucipir staging scheme provides a practical and robust means of classifying tau patterns in vivo in terms of involvement of the sentinel brain regions proposed by Braak. It is easily implemented using widely available atlases, and may complement other tau PET summary measures.

## IC-01-05 FIRST-IN-HUMAN PET STUDIES WITH THE NEXT GENERATION TAU AGENT 18-F PI-2620 IN ALZHEIMER'S DISEASE, PROGRESSIVE SUPRANUCLEAR PALSY, AND CONTROLS

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**Background:** Intracellular tau deposition is a key pathologic feature of Alzheimer's disease (AD) and other neurodegenerative disorders. Recently, positron emission tomography tau probes have been developed for in vivo detection of brain tau load, although quantification is challenging due to high off-target binding and slow kinetics. Further, different tau radiotracers have different affinities for tau species. PI-2620 is a novel tracer with an IC50 of 1.8 nM for tau in AD brain homogenate competition-assays and binds specifically to tau deposits in AD brain sections (Braak I-VI), Pick's, and progressive supranuclear palsy (PSP) pathologies. This first-in-human study assesses 18-F-labelled PI-2620 in AD, PSP, and healthy volunteers. **Methods:** In an ongoing clinical imaging study, participants diagnosed with mild Alzheimer's (AD), non-AD tauopathies (e.g. PSP), and healthy volunteers (HV) undergo dynamic PET imaging for over 3 h following 370 MBq bolus

injection of 18F-PI-2620. Venous blood is obtained to characterize the kinetics of parent compound and metabolites. **Results:** Initial imaging data shows robust brain uptake and fast wash-out in non-target regions with peak SUV = 4-4.5. There was no increased uptake seen in choroid plexus, striatum, amygdala, or other regions noted in first generation tau agents. In AD, focal asymmetric uptake was evident in temporal and parietal lobes, precuneus, and cingulate. SUVr time curves demonstrate a plateau at 90-100 min post injection with resultant SUVrs of 2.5-2.8.in abnormal regions, whilst HV demonstrated shorter time to secular equilibrium (60-70 min) and lower SUVrs (1.0-1.2) in comparable brain regions. Finally, PSP subjects demonstrated focal and symmetric increased uptake in the globus (SUVr=1.99-2.11) and midbrain (SUVr=2.41-2.58). Blood data confirmed fast kinetics with 20% of parent compound present at 60 min and the presence of polar metabolites. **Conclusions:** Initial PI-2620 PET first-in-human studies demonstrate excellent brain penetrance, favorable kinetics, and high target specificity with low nonspecific binding and high signal in regions of expected tau pathology.

## SATURDAY, JULY 15, 2017
## ALZHEIMER'S IMAGING CONSORTIUM
## IC-02
## PRECLINICAL AD

### IC-02-01 THE RELATIONSHIP OF ELEVATED MEDIAL TEMPORAL LOBE AND DIFFUSE BRAIN TAU-PET SIGNAL IN CLINICALLY NORMAL PARTICIPANTS

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**Background:** Medial temporal lobe (MTL) uptake on tau-PET is seen in AD dementia but also in the aging population. Some AD dementia patients have much less MTL tau-PET signal compared to other isocortical signal. The relationship of these findings to the development of AD dementia needs to be better understood. **Methods:** Tau-PET with AV-1451 was performed on 439 cognitively normal (CN) participants ages 50-94. For each cortical region we defined abnormal tau-PET as cortical to cerebellar crus grey matter ratio (SUVr) greater than the 95th percentile among 71 CN participants ages 30-49. We included entorhinal cortex, parahippocampal gyrus, and hippocampus as MTL regions. All other cortical regions were considered extra-MTL regions. Off-target regions, such as pallidum, were excluded. The number of CNs with and without abnormal MTL regions and those with or without extra-MTL abnormalities were determined. We characterized the age, PiB and *APOE* status of the groups. **Results:** Of CN participants, 37% (163/439) had MTL abnormalities. Of those with MTL findings, 95% (155/163) had extra-MTL abnormality with most having more than one (Figure 1). Of the 276 without an MTL abnormality, 29% (81/276) had extra-MTL abnormalities (Figure 2). Participants having MTL abnormalities tended to be older ($p<0.001$) and have elevated amyloid ($p<0.001$). Among those having MTL abnormalities, no age or PIB differences were seen between those with or without extra-temporal abnormalities. There were no significant differences in the percentage of *APOE* e4 carriers. **Conclusions:** MTL tau-PET signal is often associated with abnormal extra-MTL tau-PET signal in CN participants and likely represents neurofibrillary tangle development in participants likely to develop AD dementia. Tau-PET signal exclusively outside of the MTL is seen in 29% of CN participants and could be the initial finding in a unique subset of participants in the AD dementia pathway. These findings need to be evaluated with longitudinal data.

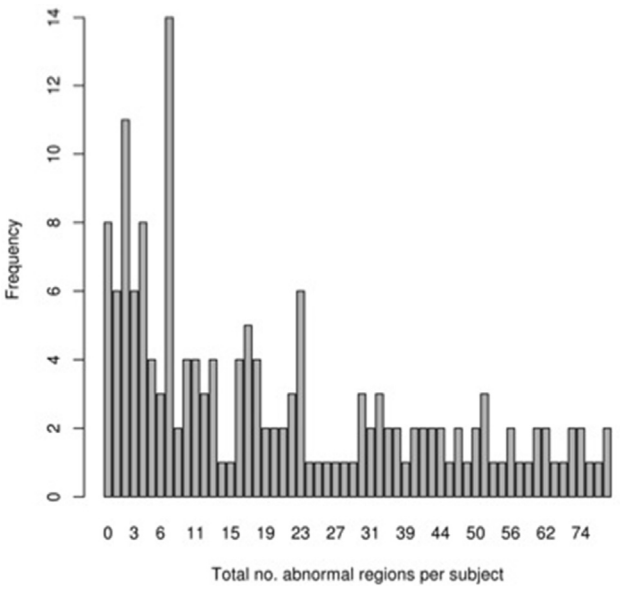


Figure 1. Numeric distribution of regional abnormalities outside medial temporal lobe (MTL) among those having any MTL abnormality.

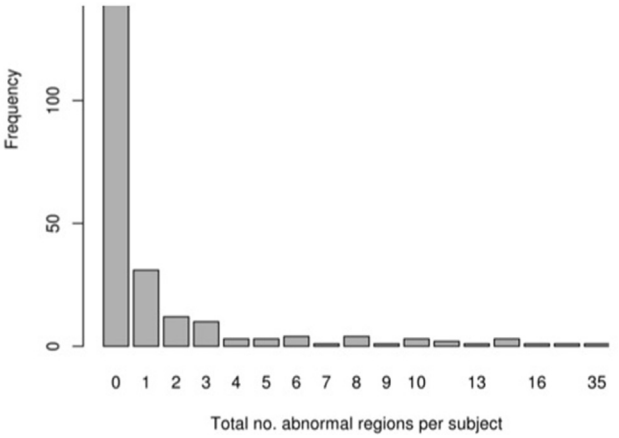


Figure 2. Numeric distribution of regional abnormalities outside medial temporal lobe (MTL) among those having any MTL abnormality.

### IC-02-02 RELATIONSHIP BETWEEN TAU POSITRON EMISSION TOMOGRAPHY WITH [18F]-AV-1451 AND LONGITUDINAL CORTICAL ATROPHY IN ALZHEIMER DISEASE

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**Background:** Neurofibrillary tau pathology is a marker of neurodegeneration and can be evaluated using the PET tracer [18F]-AV-1451 (flortaucipir, T807). Many studies have added tau imaging to ongoing longitudinal cohorts. We wanted to evaluate whether longitudinal MRI scans could predict tau PET positivity in preclinical and symptomatic Alzheimer disease (AD). **Methods:** 87