Amyloid-β plaques have been visualized in the brain of Alzheimer’s disease (AD) patients with positron emission tomography (PET) tracers like $^{11}$C-PIB. Yet, the short half-life of carbon-11 (20min) limits its use to clinical facilities close to a cyclotron. To support multicenter clinical trials for novel AD therapies, we are developing a fluorine-18 ($t_{1/2}: 110$min) amyloid-β PET tracer.

In vitro binding and autoradiographic studies were performed on cortical tissue from AD and aged-matched controls with $[^3H]$MK-3328. Three healthy subjects (56-59 years) participated in $[^18]F$MK-3328 dosimetry studies, 3 additional healthy subjects (58-76 years) underwent brain PET imaging. $[^18]F$MK-3328 DVR and SUVR were calculated using cerebellum as reference region.

$[^3H]$MK-3328 binds to amyloid-β plaques with a Kd of 17±4 nM (n=5) and a Bmax of 1600±419 nM (n=5). Despite unexpected contribution of MAO-B binding to background signal, autoradiographic experiments with $[^3H]$MK-3328 revealed a punctated expression pattern associated with amyloid-β plaques in AD cortex. Human studies of radiation exposure showed a favorable safety profile (Effective Dose = 18.2 ± 2.0 mSv/MBq). $[^18]F$MK-3328 DVR could be satisfactorily estimated using 90 or 60 min scan length and both cortical DVR and SUVR in healthy elderly were similar to reported PIB values.

Despite unanticipated MAO-B binding, these results indicate that MK-3328 has a favorable pharmacological profile and initial clinical observations support the potential of MK-3328 as a novel fluorine-18 PET tracer for the detection of brain amyloid-β. Ongoing clinical studies will further establish the value of $[^18]F$MK-3328 for the detection of amyloid-β plaques in AD patients.