

Radiosynthesis of ^{18}F -AZD4694

The ^{18}F -AZD4694 was synthesized using the following procedure. No-carrier-added (nca) aqueous ^{18}F -fluoride prepared by the $^{18}\text{O}(\text{p},\text{n})^{18}\text{F}$ nuclear reaction on an enriched [^{18}O] water (98%) target was passed through a preconditioned (10 mL 0.05 M K_2CO_3 , 10 mL deionized water) Sep Pak Light QMA cartridge (Waters). The ^{18}F -fluoride is then eluted off the QMA cartridge and into the reactor with a solution of 1.5 mL acetonitrile containing 11 ± 1 mg Kryptofix 2.2.2. and 15–20 μmol potassium carbonate. The solution is then evaporated to dryness repeatedly with additional acetonitrile at a temperature of 95 $^\circ\text{C}$, a stream of inert gas and reduced pressure. After 15 min, a solution of 3 mg of precursor (AZD4694) in 1 mL DMSO is added to the reactor, and is heated to 105 $^\circ\text{C}$ for 7 min. During this step, the product ^{18}F -NAV4694 in its protected form is generated (Supplemental Fig. 1).

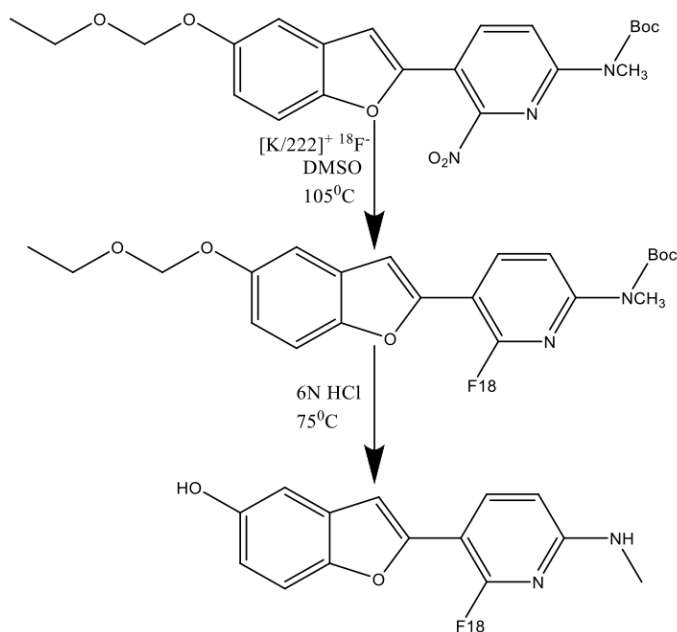
The reactor is then cooled to 75 $^\circ\text{C}$, and 0.5 mL 6N HCl is added, and heated to 75 $^\circ\text{C}$ for 5 min for deprotection. Then 0.5 mL 5N sodium hydroxide solution and 0.5 mL HPLC solvent (20 mM ammonium formate/methanol; 40/60) is added. The resulting mixture is transferred into an injector loop of the HPLC system and is purified on a Phenomenex Luna 10 μ C-18 column, with a flow of 3 mL/min. The desired product elutes at a retention time of 24–28 min. Impurities as well as radioactive impurities and unreacted fluoride elute at earlier retention times, and are thus transferred into the waste container. The product peak is collected into a vial containing 15 mL of water and 25 μL ascorbic acid. The solution is passed through a C18 cartridge. The cartridge is washed with an additional 10 mL of water. The product is eluted from the cartridge into a sterile vial with 0.5 mL of ethanol followed by 9.5 mL of sterile phosphate buffer and 25 μL of ascorbic acid.

Supplemental Table 1: Optimal cut-offs for 18F-AZD4694 PET positivity

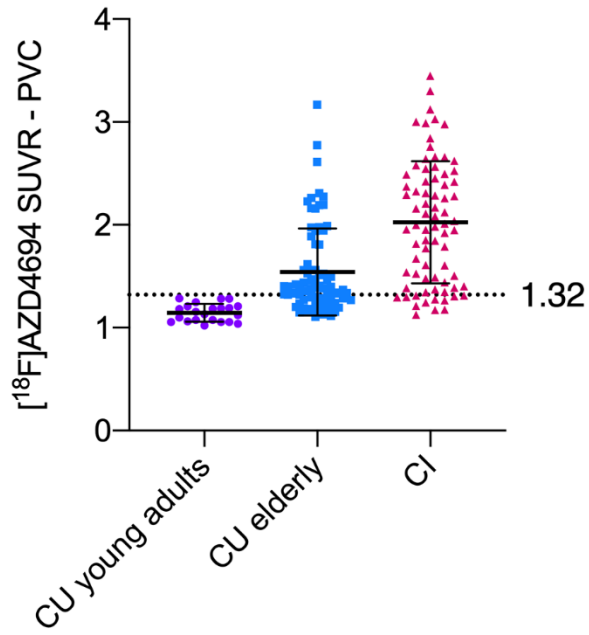
	2 SD above mean of young controls	CSF A β ₄₂ /A β ₄₀ positivity	ROC curve contrasting AD dementia and CU elderly	ROC curve contrasting visual ratings	Gaussian Mixture Modeling
18F-AZD4694 SUVR threshold	1.33	1.51	1.56	1.55	1.55
% of CU elderly A β positive according to threshold	52%	29%	25%	26%	26%

This table summarizes the SUVR cut-point derived from each of the five methods assessed in this study, along with the corresponding percentage of the CU elderly population that would be labeled as positive according to each method. A β : amyloid- β ; AD: Alzheimer's disease; CSF: Cerebrospinal Fluid; CU: Cognitively unimpaired; ROC: Receive Operating Characteristic; SD: Standard deviation; SUVR: Standardized Uptake Value Ratio.

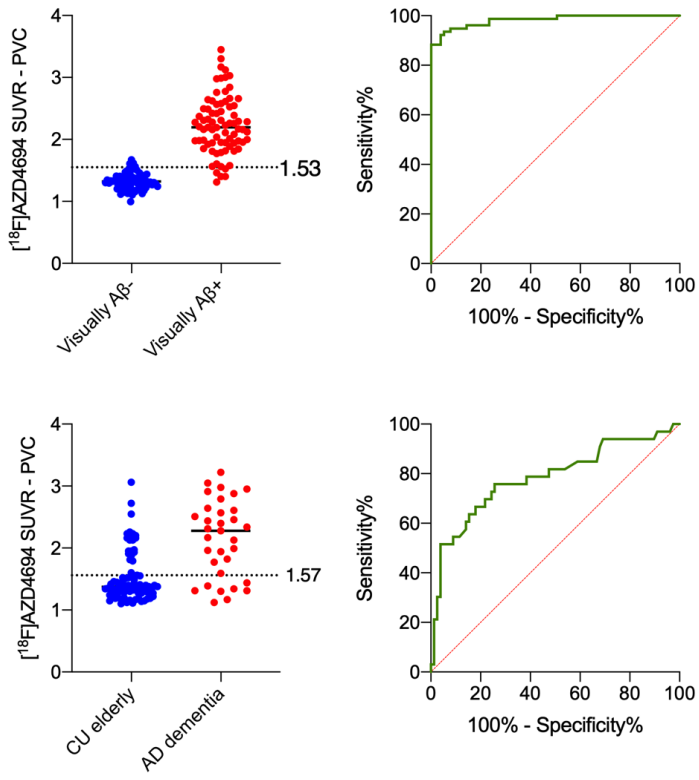
Supplemental Fig. 1



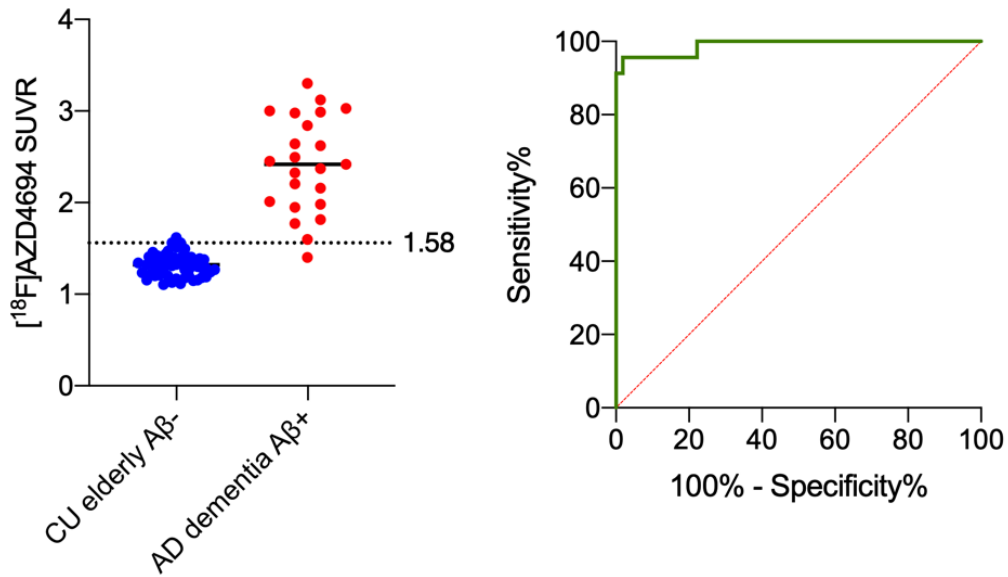
Supplemental Fig. 2



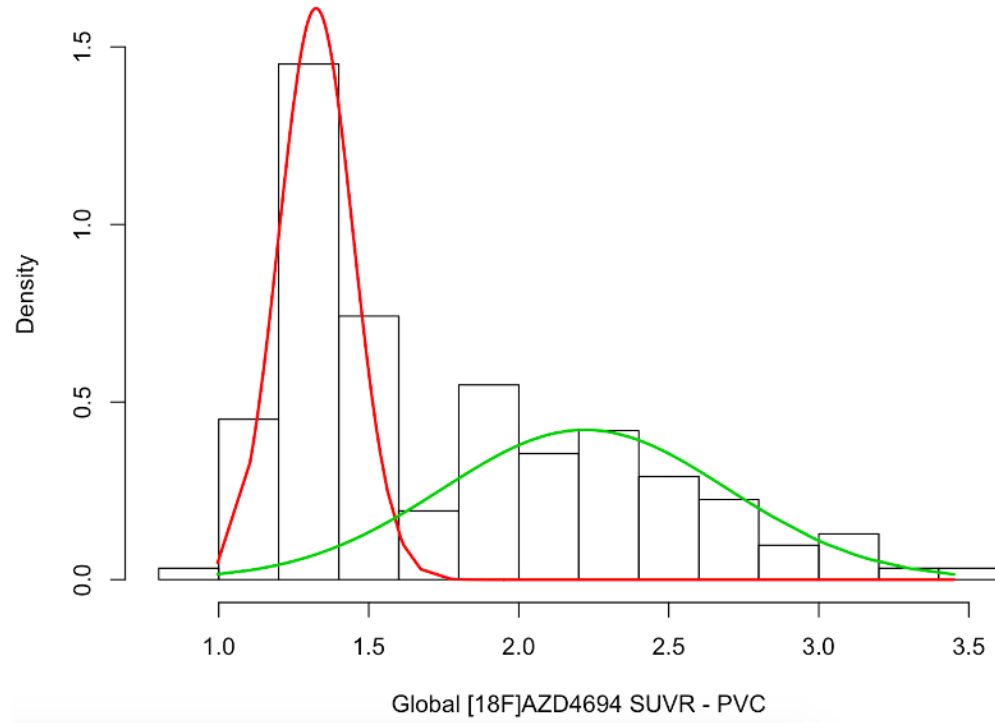
Supplemental Fig. 3



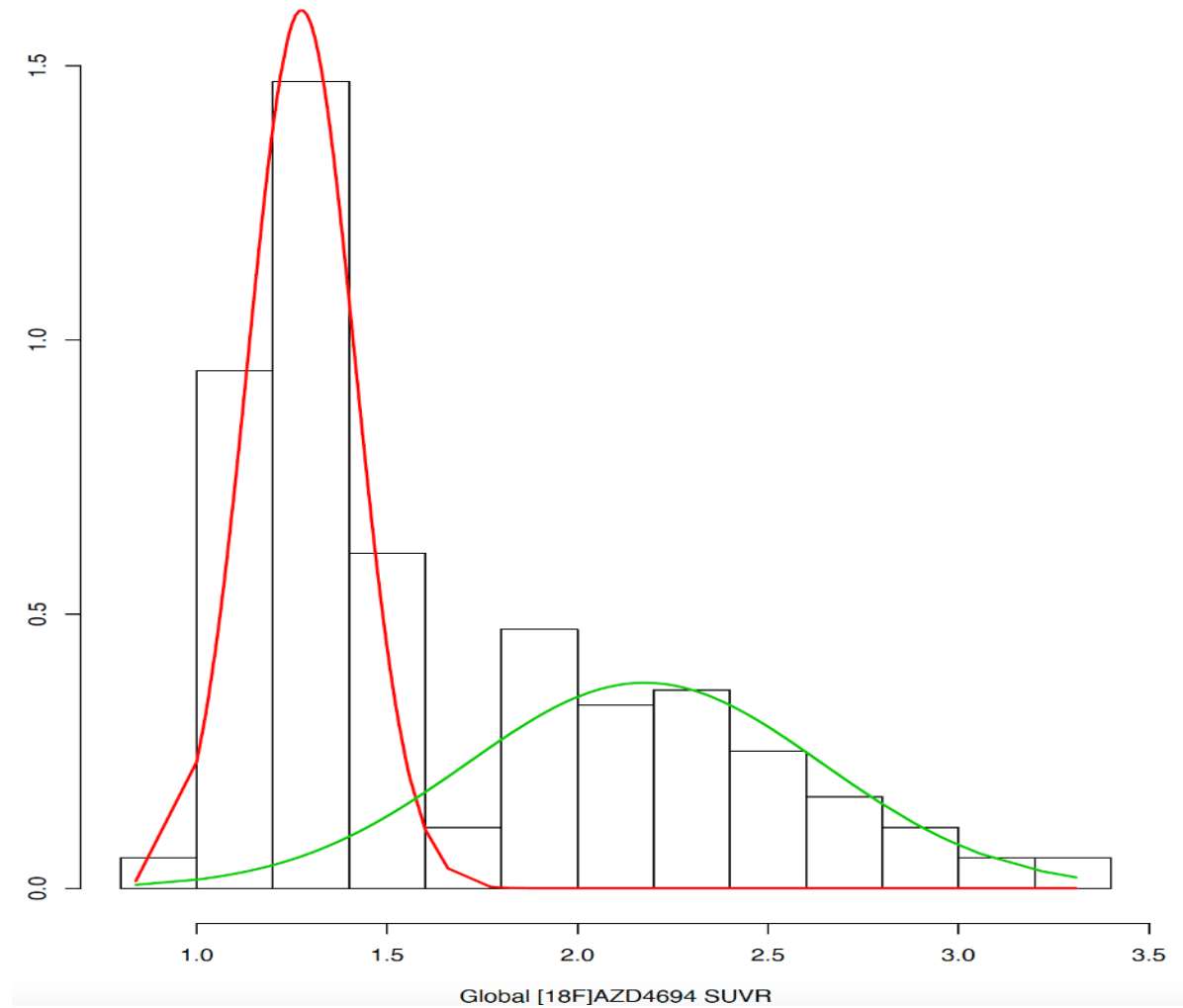
Supplemental Fig. 4



Supplemental Fig. 5



Supplemental Fig. 6



Supplemental Fig. 7

