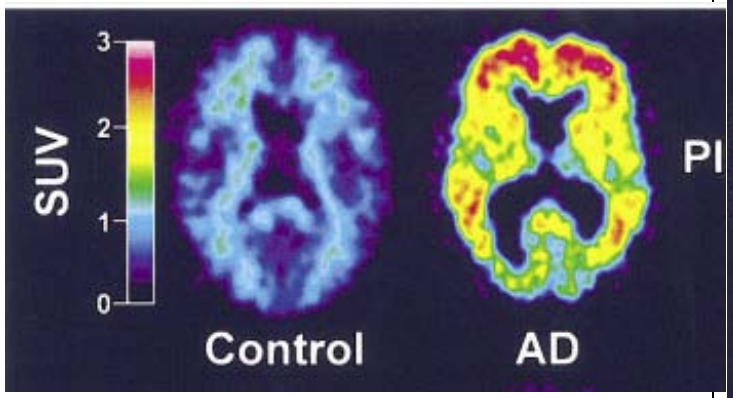
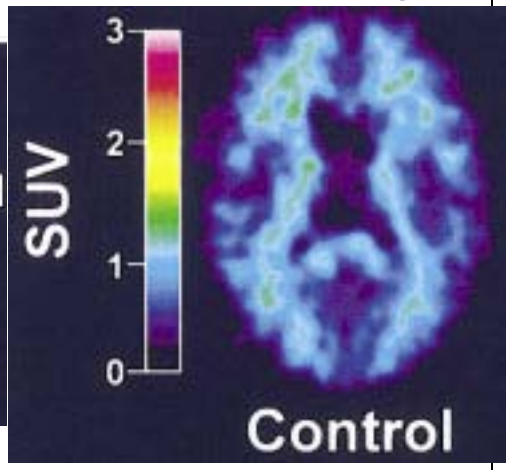
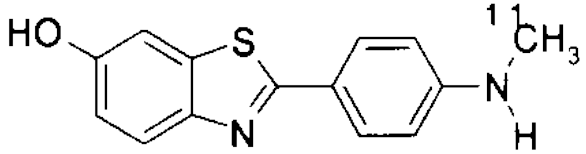
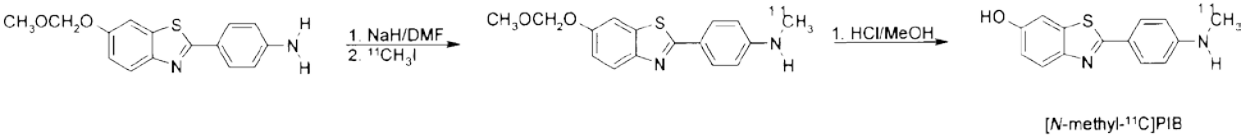
C-11 PIB

C-11 Pittsburgh Compound B

SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

Radiopharmaceutical Name	N-Methyl-[^{11}C]-2-(4'-methylaminophenyl)-6-hydroxybenzothiasole; [^{11}C]-Pittsburgh Compound B; [^{11}C]-PiB; [^{11}C]6-OH-BTA-1	
Radiopharmaceutical Image  **Image from: Klunk et al. Figure 4 Annal. Neurol. 2004; 55:306-319.**	**Normal Biodistribution Sample**  **Image from: Klunk et al. Figure 4 Annal. Neurol. 2004; 55:306-319.**	**Radiopharmaceutical Structure**  [*N*-methyl-^{11}C]PIB **Image from: Klunk et al. Annal. Neurol. 2004; 55:306-319**
Radionuclide	^{11}C Half-life 20.4 minutes Emission: positron Emax 0.961 MeV	
Molecular Formula and Weight	$C_{14}H_{12}N_2OS$ Molecular Weight 256.32 g.atom mole^{-1}	
General Tracer Class	Diagnostic PET radiopharmaceutical: β-amyloid plaque imaging	
Target	β-amyloid plaques in the brain	
Molecular Process Imaged	Amyloid neuritic plaques that are associated with Alzheimer's Disease (AD) and mild cognitive impairment (MCI)	

Mechanism for in vivo retention	Nonspecific binding to aggregated amyloid plaques
Metabolism	Humans: PiB metabolites are polar and metabolism was not different between normal subjects and Alzheimer's Disease patients. PiB in plasma was 65.5±8.7% in normal and 68.1±12.9% in AD patients 5 minutes; 0.7 ± 7.3% (Normal controls) and 33.5 ± 8.9% (AD) 12 minutes, and 7.2± 3.6% (normal controls) and 9.8 ± 3.0% (AD) 60 minutes after IV injection. Ref: Klunk WE, Engler H, Nordberg A, et al. Imaging Brain Amyloid in Alzheimer's Disease with Pittsburgh Compound-B. Ann Neurol 2004;55:306–319.
Radiosynthesis	Reaction of $^{11}CH_3I$ (carbon-11 methyliodide) with 2-(4'-aminophenyl)-6-methoxymethoxybenzothiazole  References: image from (Klunk et al. Annals of Neurol. 2004; 55:306-319. Also: Mathis CA, Wang Y, Holt DP, et al. Synthesis and evaluation of ^{11}C-labeled 6-substituted 2-aryl benzothiazoles as amyloid imaging agents. J Med Chem 2003;46:2740–2754. Mathis, CA, Mason NS, Loresti BJ, and Klunk, WE. Development of Positron Emission Tomography **β**-Amyloid Plaque Imaging Agents. Semin Nucl Med . 2012 November ; 42(6): 423–432.
Availability	The short half-life means that it has to be made in-house using a cyclotron, or within a range consistent with the 20 minute half-life
Status with USP / EuPh	Investigational. Similar compounds radiolabeled with ^{18}F, florbetapir F 18 (Amyvid), flutemetamol F 18 (Vizamyl) have been approved by the FDA
Recommended Activity and Allowable mass	First study in humans administered ~ 300 MBq (8.1 mCi) per subject. There is no recommended dose. Amyloid plaque binding is 1-2 nanomolar affinity (k_D) but no limit specified. Original paper in humans specific activity of [^{11}C]-PiB was 25 GBq/umol (range, 6-74) at end of synthesis. Klunk WE, Engler H, Nordberg A, et al. Imaging Brain Amyloid in Alzheimer's Disease with Pittsburgh Compound-

	B. Ann Neurol 2004;55:306–319.
Dosimetry	Effective dose (ED) 5.29 ± 0.66 µSv/MBq. Critical organ gallbladder wall: 44.80 6 29.30 **m**Gy/MBq. Next highest doses urinary bladder wall (26.30 ± 8.50 **m**Gy/MBq), liver (19.88 **±** .58 **m**Gy/MBq), and kidneys (12.92 ± 3.37 **m**Gy/MBq). Reference: O'Keefe GJ, Sunder TH, Ng S, Ackerman U, et al. Radiation Dosimetry of β-Amyloid Tracers ^{11}C-PiB and ^{18}F-BAY94-9172. J Nucl Med 2009; 50:309–315.
Pharmacology and Toxicology	No toxicity observed: microdose genotoxicity (chromosomal aberration, mouse lymphoma mutagenesis, bacterial reverse mutation assay, and mouse micronucleus assay), rats: single dose toxicity: non-human primate (Rhesus) cardiopulmonary physiology . ref: Bergstrom M, Grahnen A, Långstrom B. PET-microdosing, a new concept with application in early clinical drug development. Eur J Clin Pharmacol 2003;59:357–366. No pharmacologic response at the low levels administered.
Current Clinical Trials	Seven Reported clinical trials on www.clinical trials.gov. Three actively recruiting subjects an additional two studies enroll by invitation only as of Feb. 1, 2014. Studies enrolling subjects: Amyloid-related Imaging Abnormalities (Microbleeds) in Atypical AD NCT01723553, Mayo Clinic PiB PET Scanning in Speech and Language Based Dementias NCT01623284, Mayo Clinic Implications of Amyloid Pathology NCT00900770, National Institute on Aging (NIA)
Reference Site / Person	The University of Pittsburgh / William E Klunk, MD, PhD; Chester A Mathis, PhD
Imaging Protocol	No specified protocol. Carbon-11 labeled PiB is rapidly cleared from the plasma and the cerebral clearance between normal subjects and Alzheimer's disease patients begins to diverge approximately 15 minutes after injection but imaging later will have less nonspecific background. Imaging out to 90 minutes has been performed but typical imaging is 40 minutes to 70 minutes post-injection and an SUV is used for analysis.
Human Imaging Experience	**Hundreds of articles have been published.** **Original article:** Klunk WE, Engler H, Nordberg A, et al. Imaging Brain Amyloid in Alzheimer's Disease with Pittsburgh Compound-B. Ann Neurol 2004;55:306–319.

	Review article: Mathis, CA, Mason NS, Loresti BJ, and Klunk, WE. Development of Positron Emission Tomography **β**-Amyloid Plaque Imaging Agents. Semin Nucl Med . 2012 November ; 42(6): 423–432.

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