MATERIALS AND METHODS

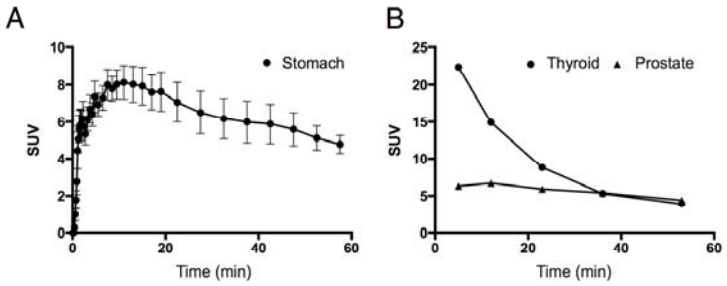
Chemicals

Acetonitrile, dimethyl sulfoxide (DMSO), and iodine were from Bie & Berntsen. Donepezil hydrochloride and 5-O-desmethyl donepezil were purchased from Toronto Research Chemicals. Sterile water, ethanol, and 70 mmol/L NaH_2PO_4 were supplied by the Pharmacy at Aarhus University Hospital.

Radiochemistry

^{11}C-Carbon dioxide was prepared by ^{14}N(p,α)C proton bombardment with either a GE Healthcare PETtrace 200 cyclotron or IBA 18/18 Cyclone and was converted to ^{11}C-methyl iodide using the GE MeI Box (reduction of CO_2 to CH_4, followed by gas-phase reaction with iodine). ^{11}C-Methyl iodide (6–9 GBq after 30-min bombardment at 40 μA) was trapped in DMSO (300 μL) containing NaOH (1 μL, 2 mol/L) and 5-O-desmethyl donepezil (0.5 mg) in a 1-mL vial.

This mixture was heated at 80°C for 5 min. Purification of ^{11}C-donepezil was performed by high-performance liquid chromatography (HPLC) (PerkinElmer model 200). The mobile phase, consisting of 70% aqueous 70 mmol/L NaH_2PO_4 and 30% acetonitrile, was delivered at a rate of 8 mL/min to a Sphereclone ODS(2) C-18 (Phenomenex, 250 × 10 mm) semi-preparative column. The reaction was quenched by adding 500 μL of HPLC eluent to the vial, and the mixture was transferred to the injection loop. Product elution was monitored with online γ-detection of an in-house design and ultraviolet (UV)–visible detection (model 759A, λ = 280 nm; Applied Biosystems). The fraction containing ^{11}C-donepezil (retention time, 5-6 min) was collected and diluted with 50 mL sterile water. The product was retained on a C8 Sep-pak, washed with 10 mL sterile water and reformulated with sterile ethanol (1 mL) followed by isotonic saline (9 mL). Finally, the product was transferred through a sterile filter (0.22 μm) to the final product vial.



SUPPLEMENTAL FIGURE 1. The stomach showed an initial steep accumulation profile followed by a highly variable washout among subjects (**A**). Prostate and thyroid data were available from only one subject (the whole-body dosimetry scan), and displayed slow and fast wash-out kinetics, respectively (**B**).