specific technique of detecting pre-morbid atherosclerotic vascular disease (ASVD). We synthesized and evaluated a series of PK11195 congeners containing both iodine and fluorine. We evaluated the effect of the position of iodine on the 1-phenyl ring and fluoropropyl and fluoroethyl substitution on the 3-carboxamide. The affinities of the analogs for the peripheral BZ receptor was determined using *in vitro* competitive binding assays with [H-3]PK11195. The results from the binding studies demonstrated that the 1-(2-iodophenyl) N-CH3 N-CH2CH2CH2F derivative was the most potent (Ki = 0.25 nM) analog of this series and is an excellent lead compound for additional studies for labeling with both fluorine-18 and iodine-123 to determine whether it possess the desired *in vivo* behavior in lesioned NZW rabbits by PET and SPECT imaging, respectively. The radioiodinated [1-(2-iodophenyl)-N-methyl-N-(fluoropropyl)-3-isoquinoline carboxamide] (1) was prepared via iododestannylation of a key trimethylstannyl amide substrate 2. Substrate 2 was prepared by treating 1 (Me3Sn)2 in toluene in the presence of Pd catalysts. [I-123]1 was prepared by treatment of 2 with no carrier added [I-123]NaI and H2O2/HCl . [I-123]1 was purified by HPLC on a 8 X 20mm C-18 reverse phase column by elution with MeOH/H2O/Et3N (75:25:0.2). Radioiofluorinated 1 was prepared by treating 3-tosyloxypropylmethylamine (3) with NCA K[F-18]/K222 for 5 min in CH3CN at 100°C to give [F-18] 3-fluoropropylmethylamine (4). Coupling of [F-18] 4 with [1-(2-iodophenyl)-3-isoquinoline carboxychloride] afforded [F-18]1 following HPLC purification. Pharmacokinectic analysis and PET and SPECT imaging in rabbits will be presented. Research supported by NIH.

No. 16

SYNTHESIS, IN VITRO AND IN VIVO STUDIES OF RADIOIODINATED ARYLETHYLENEDIAMINES (AED's): NEW SIGMA RECEPTOR PROBES. C.S. John, B.B. Lim, B.J. Vilner, B.C. Geyer, and W.D. Bowen. George Wash Univ. Washington, DC and LMC, NIDDK, NIH, Bethesda, MD.

Haloarylethylenediamines have been shown to possess high affinity for both sigma-1 and sigma-2 subtype receptors. This study was undertaken to study SAR, in-vitro binding, and in-vivo clearance of radioiodinated AED's. Several AED's were synthesized and characterized. Sigma-1 affinities (Ki) in guinea pig brain membranes using [H-3](+)pentazocine for AED's ranged from 1.47 - 5.29 nM, whereas sigma-2 affinities in rat liver using [H-3]DTG ranged from 14.6 - 30.0 nM. Three radioiodinated regio-isomers of N-[(I-125)iodophenyl)ethyl] - N-methyl-2-(1-homopiperidinyl) ethylamine (IEN7) were prepared from their tributyl stannyl precursors in high yields (78-93%) using choramine-T as an oxidising agent. Sites in guinea pig brain membranes labeled by 3-[I-125]EN7 showed high affinity for haloperidol, BD1008 and 3-IEN7 (Ki = 40.5±7.43, 15.8±0.13, 8.72±0.12 nM respectively). Similar high affinity profiles were also obtained for 2-[I-125]EN7 in guinea pig brain membranes confirming labeling of sigma sites. Sites labeled by 2-[I-125]EN7 or 3-[I-125]EN7 in guinea pig brain membranes in the presence of 400 nM haloperidol exhibited a dose dependent high affinity binding (IC50 = 5 - 50 nM) when AED's are used as competing ligands, suggesting labeling of a newly described haloperidol insensitive sigma subtype (Soc. Neurosci. Abstr. 21, 526, #219.5, 1995). A high affinity inhibition of binding (Ki = 18 - 52 nM) for the sites labeled by 2-[I-125]EN7 was obtained for competing AED in both melanoma and breast cancer cells. Competition binding studies of 2-[I-125]EN7 with AED's in melanoma cells showed multiple binding sites. Biodistribution studies of the three radioiodinated IEN7 isomers in rats showed a rapid hepatobiliary clearance. The hepatic clearance for ortho was faster than meta and para derivatives. The in-vivo blocking studies for 4-[I-125]EN7 with 2µmol BD1008 showed 40%, 55% and 54% decrease respectively in liver, brain, renal (organs expressing sigma receptors) activity at six hours postinjection. Similarly, blocking of sigma binding sites was also observed for 3-[I-125]EN7 with BD1008.

No. 17

SELECTIVE RELEASE OF IODOHIPPURIC ACID FROM A COVALENTLY CONJUGATED PROTEIN IN LYSOSOMES BY A PLASMA-STABLE METABOLIZABLE AMIDE LINKAGE. Y. Arano, K. Wakisaka, T. Uezono, H. Akizawa, M. Ono, Y. Iida, A. Yokoyama. Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan.

A linkage that is stable in plasma and can be metabolized in lysosomes to release the designed radiometabolite would ideally favor the target/nontarget ratio of administered radiolabeled (poly)peptides. We have developed a new reagent with a peptide linkage that facilitates the release of *meta*-iodohippuric acid, 3'-(tri-*n*-butylstannyl)hippuryl N-ε-maleoyl-L-lysine (HML) in nontarget tissues. HML possesses a maleimide group for polypeptide conjugation and a butylstannyl group for high yield and site-specific radioiodination. The hepatic parenchymal cells were used as the model nontarget tissue. I-131-HML was conjugated to a galactosyl-neoglycoalbumin (NGA) by a thiol group of NGA. For comparison, an I-125-labeled reagent with an ester bond (MIH) to liberate *meta*-iodohippuric acid (J. Med. Chem. 37, 2609-2618, 1994) was conjugated to NGA. When incubated in 50 % murine plasma for 24 h, I-125-MIH-NGA liberated 35 %, whereas less than 5 % of the total radioactivity was released from I-131-HML-NGA. In biodistribution studies, both radioiodinated NGAs exhibited more than 93 % of the injected radioactivity in liver at 5 min postinjection, followed by rapid elimination of radioactivity from liver to urine of mice with a similar rate. Urinoanalyses at 6 h postinjection of I-131-HML-NGA indicated a single peak that coincided with *meta*-iodohippuric acid fractions. Our findings indicated that the plasma-stable amide bond of HML released *meta*-iodohippuric acid from a covalently conjugated polypeptide after lysosomal proteolysis in hepatic parenchymal cells. Such characteristics would render HML as a potentially useful reagent for radioiodination of (poly)peptides for diagnostic and therapeutic purposes.

Instrumentation and Data Analysis: Young Investigators Competition

1:30–3:00 **Session 4 Rooms: C102, 104, 106**

Moderator: Tom K. Lewellen, PhD
Comoderator: John A. Correia, PhD
Judges: Members of the SNM Instrumentation Council

No. 18

HIGH ENERGY SLIT APERTURE AND PINHOLE SPECT, A PROPOSED METHOD FOR CORRECTING APERTURE PENETRATION TO ENHANCE RESOLUTION AND MINIMIZE PENETRATION BACKGROUND. M.C. Wrobel, N.H. Clinthorne, J.A. Fessler, Y. Zhang and W.L. Rogers. Division of Nuclear Medicine, The University of Michigan, Ann Arbor, Michigan, USA

Pinhole collimators and slit apertures can provide very high resolution images of small organs, as required for animal imaging. Work to date has been limited to low energy (140 keV) imaging because of penetration of the collimator by high energy photons, resulting in a decrease of both resolution and contrast. At 511 keV, approximately 50% of projection counts were attributable to penetration. This paper describes a devised method to correct high energy projection data acquired on a full-ring SPECT system for aperture penetration to restore resolution and reduce the uniform penetration background.

SPRINT-II is a full ring tomograph with in-plane resolution determined by a rotating six slit lead and depleted uranium aperture. The slit-detector geometry provides a factor of three object to image magnification factor, resulting in images with less than 2 mm resolution (FWHM) at 140 keV. For 511 keV imaging, the slit aperture was modified so that alternate slits were blocked by depleted uranium bars. Tomographic acquisition was changed from a normal 40 step, 60 degree rotation to an 80 step, 120 degree rotation which permitted acquisition of two complete projection sets: an open slit projection set measuring both true signal and aperture penetration, and a blocked slit projection set measuring a spatially variant fraction of the true signal and aperture penetration. The blocked slit projection set was spatially weighted to compensate for an overestimation of the penetration background in the central regions of the projection. Image reconstruction was then performed using filtered back-projection and SAGE iterative reconstruction, where the weighted blocked projection set served as a penetration background estimate.

F-18 line sources imaged without correction for penetration had a resolution of 8.8 mm FWHM and 18 mm FWTM due to large penetration tails. The same lines reconstructed with penetration subtraction resulted in 5.0 mm FWHM and 8.6 FWTM resolution. An F-18 filled micro-Jaszczak phantom consisting of holes ranging from 1.5 to 4.0 mm in diameter was also imaged. In uncorrected images, the 4 mm line set was barely discernible and a uniform background level was present. Images produced with correction resulted in clear observation of the 3 mm holes and negligible background.

Clear improvement in SPECT imaging can be obtained through the proposed penetration correction method, with a matched sacrifice in time resolution. Further improvements are predicted using iterative reconstruction methods which accurately model the imperfect attenuation of the depleted uranium block. The method devised should be generally applicable to both planar and SPECT imaging on single or multiple head gamma cameras.

No. 19

ANALYSIS OF THE INVERTIBILITY AND NOISE PROPERTIES OF MULTIPLE ENERGY WINDOW PROJECTION DATA IN SPECT D.J. Kadrmas, E.C. Frey and B.M.W. Tsui. The University of North Carolina at Chapel Hill, Chapel Hill, NC 27599