No. 1360

SUGGESTIONS IN USING HO-166-CHITOSAN FOR HEPATIC CANCER TREATMENT. E. H. Kim*, C. W. Choi, S. M. Lim, Korea Cancer Center Hospital, Seoul, South Korea. (101250)

Objectives: Direct injection or intra-arterial injection of Ho-166-chitosan into the tumoral liver tissue has been tried to treat the hepatic cancer in Korea. In this study, preliminary dose estimation is performed to suggest the amount of Ho-166 activity to be injected to induce lethal dose to the tumoral liver tissue and to provide the guideline in selecting either direct injection or intra-arterial injection. **Methods:** Dose estimation is performed for a spherical tumor model. For direct injection, Ho-166 is assumed to be located at the tumor center. For intra-arterial injection, uniform distribution of Ho-166 inside the tumoral tissue is assumed. Dose point kernel for Ho-166 is produced by Monte Carlo simulation using the EGS4 code. Dose at a varying distance from the tumor center is calculated analytically using the dose point kernel data. **Results:** In direct injection of Ho-166chitosan into the tumor center, 1 *mCi* of Ho-166 injection leads to 122 Gy of dose at the boundary of a 1 cm-diameter tumor. 2 *Ci* of Ho-166 injection into the center of a 2 cm-diameter tumor results in 155 Gy at the tumor boundary. In intra-arterial injection, 5 *mCi*, 20 *mCi*, and 50 *mCi* of Ho-166 injections are required to induce dose around 100 Gy at the tumor boundary for a 3 cm-, 5 cm-, and 7 cm-diameter tumor, respectively. **Conclusion:** In dosimetric point of view, direct injection of Ho-166 chitosan is effective for treating a hepatic tumor of less than 2 cm in diameter. Intra-arterial injection is the method of choice for treating greater tumors. On the other hand, Ho-166chitosan injection into the tumoral liver tissue can be effectual when the tumor boundary is at least 4 mm apart from the critical part of the liver in a sense that dose to the critical part can be less than 1 % of dose at the tumor boundary.

No. 1361

EFFECT OF 5-ETHYNYLURACIL (EU) ON RADIATION DOSIMETRY OF 5-[^{18}F] FLUOROURACIL (FU). J. R. Bading*, N. G. Kundu, J. D. Fissekis, M. M. Alauddin, E. Kirkman, P. S. Conti, University of Southern California, Los Angeles, CA; Indian Association for Cultivation of Science, Jadavpur, India. (500351)

Objectives: We are developing methodology for measuring tumor uptake and anabolism of the chemotherapeutic drug FU using PET. To overcome problems caused by rapid breakdown of [^{18}F]FU, we pretreat with EU, a potent inhibitor of FU catabolism. The purpose of this study was to estimate radiation doses from [^{18}F]FU modulated by EU ("FU+EU") in comparison to unmodulated [^{18}F]FU ("FU-only"). **Methods:** Two male cynomolgus monkeys were anesthetized, given EU (1 mg/kg) or placebo IP and injected IV 1h later with 170-220 MBq of [^{18}F]FU (sp. act. > 19 GBq/mmol). Each animal was studied +/- EU. Five sequential whole-body PET scans were obtained 0-2h after [^{18}F]FU injection using a Siemens/CTI 953A tomograph. The resulting tissue time-activity data were used with a standard calculational model (MIRD) to estimate human radiation doses, taking account of continued ^{18}F clearance into the bladder after 2 h. Arterial blood samples were analyzed for ^{18}F-labeled metabolites by HPLC. **Results:** With the dosing schedule used, EU only partially suppressed FU catabolism. (At 2h, 50% of plasma ^{18}F was on catabolites for FU+EU vs. 100% for FU-only.) The biodistribution of ^{18}F changed noticeably with EU (less initial uptake in liver, less rapid urinary clearance), but the dosimetry estimates were little affected. Whole-body effective dose equivalents (EDE) and the highest organ dose equivalents are tabulated below. The calculations assume 80% voiding of the bladder every 2h beginning 2h post injection. **Conclusions:** Although differences might be greater with complete suppression of FU catabolism, EU clearly has only modest effects on the radiation dose from [^{18}F]FU. With or without EU, radiation doses from [^{18}F]FU appear to be within acceptable limits.

	Bladder	Kidneys	Liver	EDE
FU-only	0.26•0.05*	0.06•0.01	0.07•0.01	0.026•0.001
FU + EU	0.21•0.03	0.10•0.05	0.08•0.01	0.024•0.001

*Values are mean +/- sem in units of mSv/MBq; n=2 for each data entry.

No. 1362

DOSIMETRY FOR TWO FLUORINATED ANALOGS OF MIBG: *PARA-* AND *META*-[F-18]FLUOROBENZYLGUANIDINES (PFBG AND MFBG). P. K. Garg*, J. P. Seibyl, Yale University PET Center, West Haven, CT; Yale University, New Haven, CT. (101298)

Radiolabeled MIBG accumulates in the adrenergic neurons analogus to NE and has been widely used for their application in oncology and cardiology. To study accurate and quantitative tracer distribution using PET, two F-18 analogs of MIBG have been synthesized. Herein, we report the radiation absorbed dose (RAD) for the two tracers to assess their applicability for human studies from a radiation safety perspective. To calculate radiation dosimetry (RD), biodistribution studies were performed in rats by injecting 10μCi of either PFBG or MFBG. At 30, 60, and 120 min, animals (n=3-5) were killed, tissues of interest removed, washed, weighed and counted. Residence time and cumulative RD estimates for each organ were calculated using MIRD convention assuming ICRP 30 GI kinetics. RAD in $x10^{-2}$mGy/MBq for select organs is shown in Table 1. These results show a similar or slightly lower RAD for PFBG compared to MFBG in most organs. Primary contributors of radiation dose burden (RDB) to most organs is 'remainder of body' except for the heart, liver, small intestine, and urinary bladder where the primary contributor was the respective organ. A rapid urinary excretion resulted in identifying it as critical organ with an estimated radiation dose of $8.4x10^{-2}$mGy/MBq and $1.47x10^{-2}$ mGy/MBq for PFBG and MFBG respectively. Although, small deifferences in RDB exist, a 500 fold advantage over the literature values for MIBG existed for the F-18 compounds and exhibit their clinical utility.

Table 1. RAD for PFBG and MFBG

	adr	Brain	Kdn	Lvr	Lung	Spl	Hrt	Bone	W.Body
PFBG	2.25	0.41	1.64	1.75	1.34	1.89	2.64	2.04	1.89
MFBG	2.96	1.12	2.24	2.32	0.85	1.92	2.17	1.45	1.42

No. 1363

HUMAN DOSIMETRY OF TC-99M-VASOACTIVE INTESTINAL PEPTIDE (VIP). C. S. Marcus*, M. L. Thakur, S. Saeed, C. Minami, L. Diggles, H. L. Pham, R. Ahdoot, E. A. Kalinowski, Harbor-University of California at Los Angeles Medical Center, Torrance, CA; Thomas Jefferson University Hospital, Philadelphia, PA. (100052)

OBJECTIVE: The object of this study was to characterize the radiopharmacokinetic parameters and calculate the internal dosimetry for a parent vasoactive intestinal peptide (VIP) tracer prepared in kit form for Tc-99m labeling. This tracer was chosen because of the high concentration of receptors to this peptide which are found in a wide variety of cancers. **METHOD:** Human dosimetry using approximately 5 micrograms of VIP labeled with 10 mCi Tc-99m was estimated using MIRDOSE 3.0 for three normal volunteers for whom standard radiopharmacokinetic parameters were acquired over a 24 hour period. **RESULTS:** The effective dose equivalent of 10 mCi (370 MBq) Tc-99m-VIP was 0.374 rem (3.74 mSv). The primary target organ was the urinary bladder wall at 2.49 rad (24.9 mSv), and the secondary target organ was the upper large intestinal wall at 0.707 rad (7.07 mSv). After 24 hours, renal clearance accounted for 67% of the Tc-99m, with a halftime of 1.2 h, and liver clearance accounted for 20% of the tracer. **CONCLUSION:** Sequential imaging in normal volunteers showed organs of excretion and blood pool at early times. No concentration of the tracer was seen otherwise in any tissue. The excretion of Tc-99m-VIP was rapid and the dosimetry was estimated using MIRD methodology.

No. 1364

MONTE CARLO CALCULATION OF DOSE CONVERSION FACTORS FOR A NEW GENERATION OF DOSIMETRY PHANTOMS. M. G. Stabin*, H. Yoriyaz, A. B. Brill, B. M. Dawant, Universidade Federal de Pernambuco, Recife, Brazil; Instituto de Pesquisas Energeticas e Nucleares, IPEN-CNEN/SP, Sao Paulo, Brazil; Vanderbilt University, Nashville, TN. (100852)

Objectives: The ultimate goal of this research is the development of a new 'family' of phantoms for internal and external dosimetry. The main focus is to provide dose distributions for use in radionuclide therapy. A

fortuitous side benefit, however, is that dose conversion factors (DCFs) may be calculated for phantoms based on voxelized images of real individuals, instead of on stylized representations of average individuals. Previous work has shown the MCNP computer code to be useful for calculating dose distributions in voxel-based phantoms. In this report we present our first dose conversion factors (dose to a target organ per disintegration in a source organ) calculated for this new generation of phantoms. **Methods:** A FORTRAN-based computer code was used to convert voxel images into MCNP input file format, using MCNP's repeated structures algorithm. Input files were generated for the use of many internal organs in the voxel phantom of an adult male supplied by the group at Yale. In addition, voxel phantoms for various other individuals, including an adult female, have been obtained. Specific absorbed fractions (SAFs) were calculated for monoenergetic photons of various energies and compared with existing SAFs (MIRD and Cristy/Eckerman). **Results:** Reasonable results could be obtained within approximately 450-2700 minutes (with a Pentium II computer) for a single source organ. The SAFs often compared well with known published results; there were many significant differences, but these can be attributed to differences in source/target organ geometry (including many overlapping organs in the Yale phantom) and target organ mass. **Conclusions:** Current technologies now permit the development of DCFs for a new generation of more realistic phantoms for internal and external dosimetry.

Radiopharmaceutical Chemistry Track: New Chemistry - Oncology Posters

South Exhibit Hall J

No. 1365

BIOLOGICAL CHARACTERIZATION OF THREE DIASTEREOMERS OF [F-18]4-FLUORO-1-(2′-NITRO-1′-IMIDAZOLYL)-2,3-DIHYDROXYBUTANE AS PET AGENTS FOR TUMOR HYPOXIA EVALUATION. H. E. Wang*, R. S. Liu, F. D. Chen, C. W. Chang, H. M. Lin, C. H. Lin, H. J. Chen, National Yang-Ming University, Taipei, Taiwan ROC; National PET and Cyclotron Center, Taipei, Taiwan ROC; Institute of Nuclear Energy Research, Taoyang, Taiwan ROC. (100737)

Objectives: To prepare and characterize the biological behavior of three ^{18}F-labeled diastereomers of the title compounds (**1a**, D-form, (2R,3R); **1b**, L-form, (2S,3S); **1c**, meso form, (2S,3R) or (2R,3S)) for tumor hypoxia evaluation with PET. Methods: Diastereomers **1a**, **1b**, and **1c** were prepared via a four-step syntheses starting from D-threitol, L-threitol and meso-erythritol, individually. Octanol/water partition coefficient of these compounds was measured. The biodistribution and PET imaging of **1a**, **1b**, **1c** and [^{18}F]FMISO were conducted following a bolus injection of 0.4-0.6mCi (0.2mL) into the tail vein of KHT sarcoma-bearing C3H mice. Micro-autoradiography was performed with 5-7μm frozen slices of tumor tissue at 0.17, 0.5, 1 and 2h after injection of **1a**. Results: Octanol/water partition coefficient of these compounds was found 0.16(**1a**, **1b**) and 0.18(**1c**). Compared with that of FMISO, 0.43, the partition coefficients of these three diastreomers are significantly reduced due to the additional -CHOH- moiety in the side chain on the imidazole ring. The tumor-to-blood ratio, determined at 0.5, 1 and 2h post injection, was 1.06, 1.50 and 1.75 for **1a**; 1.03, 1.11 and 2.06 for **1b**; 0.80, 1.39 and 1.00 for **1c**; 1.24, 1.49 and 2.37 for FMISO. PET imaging of tumor-bearing mice with these compounds showed that the tumor could be clearly visualized at 1h after injection of **1a** and **1b**, but not for **1c**. The autoradiographs also indicated that **1a** was accumulated mainly in hypoxic, less in oxic or necrotic region in the tumor, at 1h post injection. Conclusions: Three ^{18}F-labeled diastereomers **1a**, **1b** and **1c** were synthesized and biologically characterized. Compared with [^{18}F]FMISO, ^{18}F-labeled **1a** is an effective PET agent for tumor detection and also for tumor hypoxia evaluation.

No. 1366

NONINVASIVE ASSESSMENT OF TUMOR HYPOXIA WITH ^{99M}TC-LABELED METRONIDAZOLE. D. J. Yang*, S. Ilgan, T. Higuchi, F. Zareneyrizi, N. Nair, C. S. Oh, E. E. Kim, D. A. Podoloff, The University of Texas M D Anderson Cancer Center, Houston, TX. (500113)

Objectives: The assessment of tumor hypoxia by imaging modality prior to radiation therapy would provide a rational means of selecting patients for treatment with radiosensitizers or bioreductive drugs. Misonidazole and derivatives have been known to be accumulated in hypoxic tissues. This study aimed to develop a ^{99m}Tc-labeled metronidazole (MN) using ethylenedicysteine (EC) as a chelator and evaluate its potential use to assess tumor hypoxia. **Methods:** EC was conjugated to amino analogue of MN using N-hydroxysuccinimide and 1-ethyl-3-dimethylaminopropyl carbodiimide as coupling agents, yielded 55%. Tissue distribution of ^{99m}Tc-EC-MN was evaluated in breast tumor-bearing rats at 0.5, 2, and 4 h. Planar imaging and whole-body autoradiograms were performed. The data was compared to that using ^{99m}Tc-EC (control), ^{18}F-fluoromisonidazole (FMISO) and ^{131}I-iodomisonidazole (IMISO). **Results:** *In vivo* biodistribution of ^{99m}Tc-EC-MN in breast tumor-bearing rats showed increased tumor-to-blood and tumor-to-muscle ratios as a function of time. Conversely, tumor-to-blood values showed time-dependent decrease with ^{99m}Tc-EC in the same time period. Planar images and autoradiograms confirmed that the tumors could be visualized clearly with ^{99m}Tc-EC-MN from 0.5 to 4 hours. There was no significant difference of tumor-to-blood count ratios between ^{99m}Tc-EC-MN and ^{131}I-IMISO at 2 and 4 hrs postinjection. From 0.5 to 4 hrs, both ^{99m}Tc-EC-MN and ^{131}I-IMISO have higher tumor-to-muscle ratios compared to ^{18}F-FMISO. **Conclusion:** The results indicate it is feasible to use ^{99m}Tc-EC-MN to assess tumor hypoxia.

No. 1367

SYNTHESIS OF ^{99M}TC-ETHYLENEDICYSTEINE-COLCHICINE FOR EVALUATION OF ANTIANGIOGENIC EFFECT. F. Zareneyrizi*, D. J. Yang, T. Higuchi, S. Ilgan, D. F. Yu, M. Mathai, E. E. Kim, D. A. Podoloff, The University of Texas M D Anderson Cancer Center, Houston, TX. (500114)

Objective: Angiogenesis is in part responsible for tumor growth and the development of metastasis. Radiolabeled angiogenesis inhibitors would be useful to assess tumor microvasculature density. Colchicine, a potent antiangiogenic agent, is known to inhibit microtubule polymerization and cell arrest at metaphase. This study aimed to develop a ^{99m}Tc-labeled colchicine (EC-COL) using ethylenedicysteine (EC) as a chelator to assess tumor microvascular density. **Methods:** EC was conjugated to trimethylcolchicinic acid (Raffauf et al., J Am Chem Soc. 1953, 75: 5292) using N-hydroxysuccinimide and 1-ethyl-3-dimethylaminopropyl carbodiimide as coupling agents, yielded 50-60%. Tissue distribution of ^{99m}Tc-EC-COL was evaluated in breast tumor-bearing rats at 0.5, 2, and 4 h. Planar imaging and whole-body autoradiograms were performed. The data was compared to that using ^{99m}Tc-EC (control). **Results:** *In vivo* biodistribution of ^{99m}Tc-EC-COL in breast tumor-bearing rats showed increased tumor-to-blood (0.52±0.12 to 0.72±0.07) and tumor-to-muscle (3.47±0.40 to 7.97±0.93) ratios as a function of time. Conversely, tumor-to-blood values showed time-dependent decrease with ^{99m}Tc-EC in the same time period. Planar images and autoradiograms confirmed that the tumors could be visualized clearly with ^{99m}Tc-EC-COL from 0.5 to 4 hours. **Conclusion:** ^{99m}Tc-EC-COL may be useful to assess antiangiogenic and therapeutic effect during chemotherapy.

No. 1368

2-DEOXY-2-[F-18]FLUORO-1,3,5-TRI-O-BENZOYL-α-D-ARABINOFURANOSE: A VERSATILE INTERMEDIATE FOR SYNTHESES OF F-18 ARABINONUCLEOSIDES. M. M. Alauddin*, P. S. Conti, T. Mathew, H. Abrahamian, J. D. Fissekis, G. K. Surya Prakash, K. A. Watanabe, University of Southern California, Los Angeles, CA; Memorial Sloan-Kettering Cancer Center, New York, NY. (500280)

Objectives: Fluorine-18 labeled 2′-fluoro-1-β-D-arabinonucleosides may be important tracers of DNA metabolism in cancer patients. The presence of the fluorine atom at the 2′position of these ligands prevents catabolism *in vivo*. 2′-Fluoro-5-[C-11]methyl-1-β-D-arabinofuranosyluracil ([C-11]FMAU) is one potential marker for cell proliferation by positron emission tomography. The short half-life of C-11 and air sensitive organometallic synthesis limits the production of the C-11 compound and its applications. Labeling with fluorine-18 may be more advantageous. The direct, stereospecific (*arabino*) introduction of fluorine at the 2′-position of the furanosyl moiety of FMAU has not been possible. Alternatively, incorporation of fluorine at the C-2 (*arabino*) position of the sugar followed by coupling with the pyrimidine is being explored. Fluorinations using KHF_2 and (Et)N 3HF are not suitable for incorporation of radiofluorine. Here we report a suitable method for stereospecific incorporation of radiofluorine into the protected sugar. **Methods:** 2-O-(Imidazolylsulfonyl)-1,3,5-tri-O-benzoyl-α-D-ribofuranose was converted to 2-O-(fluorosulfonyl)-1,3,5-tri-O-benzoyl-α-D-ribofuranose, which was