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1647

[18F]FPRGD2 PET/CT imaging of integrin αvβ3 in renal carcinomas: Correlation with histopathology. N. Withofs*[1], N. Signolle[2], E. Mutijima Nzaramba[3], D. Thonon[4], M. Léonard[4], J. Aerts[4], D. Waltregny[5], D. Cataldo[2], S. S. Gambhir[6], R. Hustinx[1]; 1. Nuclear Medicine Division, CHU Liege, Liege, Belgium; 2. LBTD, GIGA-Research, University of Liege, Liege, Belgium; 3. Department of Pathology, CHU Liege, Liege, Belgium; 4. Cyclotron Research Center, University of Liege, Liege, Belgium; 5. Department of Urology, CHU Liege, Liege, Belgium; 6. Department of Radiology, MIPS, Stanford University, Stanford, California. (1313187)

Objectives: (18)F-FB-mini-PEG-E[c(RGDyK)](2), [18F]FPRGD2, is a novel radiopharmaceutical targeting the integrin αvβ3. The aims are to correlate [18F]FPRGD2 uptake with integrin αvβ3 expression and to verify whether the uptake is correlated with any marker of tumor angiogenesis or proliferation. **Methods:** To date, we prospectively included 6 patients (3M/3F; mean age 71±14) with a renal mass. We performed [18F]FPRGD2 PET/CT prior to surgical resection (median 1d). The PET/CT images were acquired 60 minutes after IV injection of 300 MBq of [18F]FPRGD2. After surgery, 4 samples were collected at 4 poles of each renal mass. Two observers independently estimated the tumor uptake of [18F]FPRGD2 (SUVmax & mean) in a 1 ml volume of interest set in the corresponding areas. We then compared the [18F]FPRGD2 uptake to quantitative immunohistochemistry (integrin αvβ3, CD31 & 105, Ki67, PCNA), PCR (PlGF; VEGFR-1&2) and ELISA measurements (VEGF121, 165 & 189). **Results:** All renal masses were renal carcinomas (3 clear cells, 2 papillary & 1 chromophobe RC). The [18F]FPRGD2 uptake (mean SUVmax ± SD) within the 6 RC was 4.6 ± 1.3. Tumor uptake of [18F]FPRGD2 was significantly correlated with integrin αvβ3 expression in RC samples (Spearman R=0.66 with SUVmax and R=0.69 with SUVmean). The [18F]FPRGD2 uptake was inversely correlated with the surface area of staining of the proliferation markers Ki67 and PCNA within the RC (R> -0.64). There was no significant correlation between the uptake and any of the other parameters. **Conclusions:** We demonstrate, for the first time in patients, a positive correlation between the uptake of [18F]FPRGD2 and the level of expression of integrin αvβ3 in renal carcinoma. We did not find any correlation with other angiogenic markers.

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1648

Preliminary evaluation of a new angiogenesis radiotracer. E. A. Oliveira*, B. L. Faintuch, J. C. Oliveira Jr., J. Mengatti; Radiopharmacy, Institute of Energetic and Nuclear Research, Sao Paulo, SP, Brazil. (1314819)

Objectives: Angiogenesis plays an important role in tumor initiation, growth and metastasis. Radiotracer targets in tumor vasculature offer a noninvasive method for early detection of malignancy growth and efficient monitoring of response to therapies. The GX1 (CGNSNPKSC) peptide motif, selected from a display peptide library, specifically binds to tumor neovasculature. This study endeavored to develop of a new radiotracer for angiogenesis detection in tumors by evaluation of radiolabeling and biodistribution of conjugated HYNIC-PEG4-GX1. **Methods:** The conjugated peptide was radiolabeled with 99mTc (74-1850 MBq), using the tricine and EDDA exchange protocol (Faintuch et al, 2005). Radiochemical evaluation was performed by ITLC and was confirmed by HPLC analysis. Partition coefficient of the radiotracer was also evaluated. Biodistribution studies were conducted by injection of 99mTc-HYNIC-PEG4-GX1 (0.1mL/18.5 MBq) in Balb/c mice with measurements at 5, 30, 60, 120, 240, 360 and 1440 min post-injection (p.i.). R... Radiochemical purity of the radiotracer was 99.35 +/- 0.13 %. Parti... coefficient pointed towards a hydrophilic profile (log P = -3.61). A... 60% of the product cleared from the blood in 30 min and 95% in 240 ... p.i. The excretion of the radiotracer was exclusively renal, with ki... uptake of 9.66 +/- 1.55% 1h p.i. Uptake by other organs and tissues ... under 1%ID/g. **Conclusions:** The radiotracer was obtained with high radiochemical purity. Biodistribution highlighted renal excretion with ... blood clearance pattern quite favorable for imaging diagnosis. An ongoing protocol for angiogenesis detection in a glioma model is confirming the hypothesis of the investigation. **Research Support:** The authors are grateful for a postgraduate Grant by Fundacao de Amparo a Pesquisa do Estado de Sao Paulo (Fapesp 2011/12405-0).

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1649

Evaluation of phage display discovered peptides as ligands for PSMA. F. Xie*[1], D. Shen[2], W. Edwards[1]; 1. Radiology, University of Pittsburgh, Pittsburgh, Pennsylvania; 2. Radiology, Washington University in St. Louis, St. Louis, Missouri. (1315329)

Objectives: Prostate specific membrane antigen (PSMA) is over-expressed in human prostate cancer cells and is an excellent target for imaging and therapy of prostate cancer. The purpose of this study is to develop peptide ligands for PSMA with high specificity and high affinity for nuclear and/or optical imaging of prostate cancer. **Methods:** A naive phage displayed peptide library (15-mer) was screened against the ectodomain of PSMA. Sequences of phage isolated after 3 rounds of screening were used to synthesize the peptide ligands for PSMA. LnCap (PSMA+) cells and PC3 (PSMA-) cells were used to evaluate the specificity of these peptide ligands. The peptide/PSMA affinity was evaluated by AlphaScreen technology, a homogenous assay. **Results:** A total of 12 clones were isolated from the phage displayed peptide library after screenings. Three consensus sequences, -SHSFSVGS-, -GDHSPFT- and -EVPRLSLLAVFL- were discovered among these PSMA-binding peptides. One of the discovered peptides, GRFLTGGTGRLLRIS, was synthesized and had a sub-μM affinity (IC50 = 592 nM) to PSMA. **Conclusions:** Promising peptide ligands specific for PSMA were discovered by phage display. The preliminary evaluation showed a sub-μM affinity between the tested peptide ligand and PSMA. The results of binding affinities of the discovered peptides, along with their serum stabilities and enzyme inhibitory capacities (against N-acetyl-aspartyl-glutamate, a natural substrate of PSMA) will be reported.

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1650

Stabilized-tetrazine *trans*-cyclooctene ligation for rapid construction of ^{18}F labeled probes. Z. Li*[1], R. Selvaraj[2], S. Liu[1], M. Hassink[2], D. Li[1], J. M. Fox[2], P. S. Conti[1]; 1. University of Southern California, Los Angeles, California; 2. University of Delaware, Newark, Delaware. (1315601)

Objectives: The fast rates of tetrazine *trans*-cyclooctene ligation enable fast reactivity at low micromolar concentrations within minutes and without an excess of either reactant. Recently, we have successfully established an efficient ^{18}F-labeling method based on this reaction. However, the resulting conjugate only demonstrated moderate stability *in vivo*. In this study, we introduced the second generation ^{18}F-labeling system based on stabilized-tetrazine (*s*-tetrazine), which has less electron withdrawing phenyl groups instead of pyridines. **Methods:** ^{18}F-labeled *trans*-cyclooctene (^{18}F-TCO) was obtained through one step ^{18}F-fluorination of cyclooctene precursor. After HPLC purification, ^{18}F-TCO was mixed with *s*-tetrazine-RGD to provide the final product ^{18}F-TCO-*s*-tetrazine-RGD. microPET imaging of ^{18}F-TCO-*s*-tetrazine-RGD was performed in U87MG tumor-model to evaluate its *in vivo* targeting