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Potentiality of ^{18}F-FDG easyPET-3D studies in mouse solid tumours

F. Ribeiro[1], *M. Lapo Pais*[2,3,4], *A. C. Santos*[3,5,4], *C. Ramos*[2], *A. Parma*[6], *A. L. M. Silva*[1,7], *I. F. Castro*[1,7], *P. M. M. Correia*[1,7], *P. M. C. C. Encarnação*[1], *N. C. Ferreira*[8], *D. A. Sá*[9], *I. Mohammadi*[1,10], *C. Nicolucci*[11], *D. Priolli*[11], *J. F. C. A. Veloso*[1,7];
[1]*University of Aveiro, Institute for Nanostructures, Nanomodelling and Nanofabrication (i3N) - Department of Physic, Aveiro, PORTUGAL,* [2]*Faculty of Sciences and Technology of University of Coimbra, Coimbra, PORTUGAL,* [3]*Institute of Biophysics of University of Coimbra, Coimbra, PORTUGAL,* [4]*Institute for Clinical and Biomedical Research (iCBR), Coimbra, PORTUGAL,* [5]*Faculty of Medicine, University of Coimbra, Coimbra, PORTUGAL,* [6]*Università degli Studi di Padova, Padova, ITALY,* [7]*RI-TE Radiation Imaging Technologies, Lda, Ílhavo, PORTUGAL,* [8]*Faculty of Medicine, Institute for Clinical and Biomedical Research (iCBR), Coimbra, PORTUGAL,* [9]*University of Coimbra, Institute of Nuclear Sciences Applied to Health (ICNAS), Coimbra, PORTUGAL,* [10]*Department of Basic Sciences, Faculty of Medicine, Sari Branch, Islamic Azad University, Sari, IRAN, ISLAMIC REPUBLIC OF,* [11]*Multidisciplinary Research Laboratory, São Francisco University, Bragança Paulista, BRAZIL.*

Aim/Introduction: The study of human diseases and the initial development of new drugs and therapeutics is often done using animal models. Preclinical PET scanners dedicated to small animal imaging allow evaluating the total period of radiopharmaceutical biodistribution. The same animal can be studied along time, representing its own control (inter-subject variability eliminated). In this context, the main application is oncology: to determine if the subject is a candidate for the study and to assess the response to therapy in tumoural models. Since glucose has a high uptake in certain organs and in tumours, ^{18}F-FDG has been one of the most used radiotracers for cancer imaging. However, the access to preclinical PET scanners is usually a problem for research centres mainly due to the high cost of the equipment and infrastructural requirements, associated to limited research budgets. EasyPET technology (a patented axial microPET system) represents a solution, since it allows a significant reduction in the number of components and thus in the final equipment cost, while achieving good sensitivity and state of the art spatial resolution in all the FOV. In addition, easyPET is highly portable and compact, requiring minimal lab space. The purpose of this study was to assess the potentiality of easyPET system to image mouse solid tumours with ^{18}F-FDG. **Materials and Methods:** In total, 35 BALB/c-nu/nu mice were used for scanning: 21 males were inoculated (subcutaneously) on the right flank with WiDr cells (human colon cancer, 2-3-wks. inoculation) and 14 females with MCF-7 cells (human breast cancer, 4-7-wks. inoculation). ^{18}F-FDG (8-26MBq/0.2-0.5mL) was intraperitoneally (i.p.) administered. 40 min latter, the animals were anaesthetized (i.p.) with a mixture of ketamine/largactil (3:1) diluted in saline. A scan with 10^6 counts was performed approximately 60 min after ^{18}F-FDG injection. PET images were reconstructed with the 3D MLEM-OSEM algorithm. **Results:** EasyPET was able of detect and characterize tumours in a very early stage (1-1.5mm), as well as to monitor their size through time, with its anatomopathology confirmed by histological studies. **Conclusion:** EasyPET technology was for the first time applied for in-vivo preclinical studies and showed great potential for applications in oncology. This study showed that easyPET scans provided an early diagnosis of tumours originated by human colon and breast cancer cells, all confirmed by histology. By detecting tumours before any external signs, easyPET allows an earlier treatment. Furthermore, easyPET allows a direct molecular assessment of treatment effects by follow-up imaging. **References:** None.

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Radiofluorinated gases as regional ventilation markers: Application to a rat model of acute lung inflammation

J. Llop Roig, *V. Gómez-Vallejo, U. Cossío, A. Lekuona;*
CIC biomaGUNE, San Sebastian, SPAIN.

Aim/Introduction: Imaging methods visualizing local areas of impaired ventilation may become a powerful tool in the early/differential diagnose of lung diseases, as well as for the development of new therapeutic approaches. Currently, ventilation studies in the clinical arena are performed with single photon emission computerized tomography (SPECT) using radiolabelled aerosols [1]. However, these show central airway deposition and peripheral "hotspot" formation in patients with obstructive lung diseases. Moreover, SPECT has limitations in terms of sensitivity, spatial resolution and image quantitation. Recently, we have developed a fast an efficient method for the production of the radiofluorinated gases [^{18}F]SF_6 and [^{18}F]CF_4, which proved efficient in the visualisation of lung ventilation in healthy rodents using Positron Emission Tomography (PET) [2]. Here, we describe the investigation of [^{18}F]CF_4 as a ventilation marker in an animal model of impaired lung ventilation and correlate the results with [^{18}F]FDG-PET. **Materials and Methods:** [^{18}F]CF_4 was produced by a double irradiation process as recently reported [2]. Ventilation studies were carried out in a rat model of lung inflammation induced by intratracheal administration of lipopolysaccharide (LPS). Dynamic 10-min [^{18}F]CF_4-PET images were obtained in list mode at t=4 hours after administration of LPS, during inhaled administration of the radiofluorinated gas. [^{18}F]FDG-PET static images were also obtained for each animal 30 minutes after the finalisation of the first imaging study. Ventilation images were reconstructed by OSEM-3D iterative algorithm and voxel-by-voxel analysis was carried out to determine the coefficient of variation as a surrogate indicator of non-uniformity of gas distribution. [^{18}F]FDG-PET images were analysed to determine Standard Uptake Values in the lungs. **Results:** Ventilation studies in control groups showed uniform distribution of the radiofluorinated gas and fast elimination of the radioactivity after discontinuation of the administration. For LPS rats, the coefficient of variation was significantly higher than that obtained in the control group. Compared to controls, the mean [^{18}F]FDG uptake in the lungs of LPS rats was almost 2-fold greater at 4h. **Conclusion:** Our results suggest that [^{18}F]

CF_4 is an appropriate marker of regional lung ventilation and may find application in the early diagnose of acute lung disease. **References:** [1] Burch WM, Sullivan PJ, McLaren CJ. Nucl. Med. Commun. 1986, 7(12), 865. [2] Gómez-Vallejo V, Lekuona A, Baz Z, Szczupak B, Cossío U, Llop J. Chem Commun. 2016, 52(80), 11931.

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A Computational Phantom of the Adult Labrador for Use in Preclinical Nuclear Medicine Dosimetry Studies

W. Bolch[1], *M. Sands*[1], *R. Milner*[1], *I. Dormehl*[2];
[1]*University of Florida, Gainesville, FL, UNITED STATES OF AMERICA,* [2]*University of Pretoria, Pretoria, SOUTH AFRICA.*

Aim/Introduction: With the completion of the canine genome project, dogs have been proven be an ideal species for pre-clinical investigations of both molecular imaging agents and therapy radiopharmaceuticals. There is thus an expressed need to establish computational anatomic models of dogs of different species to support the associated organ radiation dosimetry for these studies. In this work, we present a comprehensive hybrid computational anatomic and dosimetric model of the adult Labrador. This species is known to present with high incidence of osteosarcoma that is both genetically and phenotypically similar to human bone cancer. **Materials and Methods:** NURBS and polygon mesh models were constructed from high-resolution CT images of a 1.5-year Labrador imaged prior to euthanasia under an approved animal research protocol at the University of Florida. Bone samples from the skeleton were harvested and ex-vivo CT imaged at sub-millimeter resolution to obtain volume fractions of cortical bone, spongiosa, and medullary cavity space. Next, spongiosa bone cores were taken from 30 skeletal sites and subjected to microCT imaging at 30 micrometer resolution. The microCT images were segmented to assess volume fractions of trabecular bone and total marrow space of spongiosa. Voxel retagging procedures were applied to establish bone microstructures at varying marrow cellularities. Paired-image radiation transport was performed to assess values of monogenetic electron specific absorbed fractions across the canine skeletal sites. **Results:** A database of specific absorbed fractions (SAFs) has been assembled for both monoenergetic photons and electrons emitted within 32 different source tissues of the adult male Labrador phantom. Values of energy deposition to active marrow and skeletal endosteum were obtained via energy-dependent integration of the volumetric photon fluence in regions of trabecular spongiosa and newly developed canine-specific fluence-to-dose photon response functions. Canine-specific S values are presented for several key radionuclides used in diagnostic and therapeutic nuclear medicine. **Conclusion:** Dosimetric applications of the Labrador model are presented for model osteosarcoma tumors treated with ^{153}Sm-EDTMP or ^{153}Sm-PEI-MP. Based upon the ^{153}Sm S values established in this model, and a six-compartment biokinetic models of each agent (to include blood, urinary bladder content, kidneys, trabecular bone surfaces, cortical bone surfaces, and tumor), model tumor doses ranged from 16 to 50 Gy for ^{153}Sm-PEI-MP and from 8 to 25 Gy for ^{153}Sm-EDTMP. **References:** Biodistribution and pharmacokinetics of variously sized molecular radiolabelled polyethyleneiminomethyl phosphonic acid as a selective bone seeker for therapy in the normal primate model. Arzneimittelforschung 2001; 51, 258-263.

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In vivo imaging of ^{68}Ga-labelled NOTA-EGFRvIII aptamer

J. Park, *Y. Cho, J. Chae, W. Kang;*
Yonsei University College of Medicine, Seoul, KOREA, REPUBLIC OF.

Aim/Introduction: Aptamers are synthetic single-stranded oligonucleotides that bind to a target molecule with high affinity and specificity. Glioblastoma is the most aggressive primary malignant brain tumors. Epidermal Growth Factor Receptor Variant III (EGFRvIII) is a most common extracellular EGFR mutation in glioblastoma. EGFRvIII has been considered as a promising target in cancer diagnosis and therapy because EGFRvIII is expressed only in tumor cells [1,2]. Herein, we investigate the biological characteristics of ^{68}Ga-NOTA- EGFRvIII aptamer as potential glioblastoma imaging agents. **Materials and Methods:** Ga-68 was concentrated using a NaCl-based ^{68}Ga eluate concentration method and labeled with NOTA conjugated EGFRvIII aptamers. Flow cytometry was performed on DKMG/EGFRvIII and U87-MG cell lines to confirm the expression of EGFRvIII. In vitro binding specificity of EGFRvIII aptamers was evaluated using confocal microscopy. In vivo PET/CT imaging of the ^{68}Ga-NOTA-EGFRvIII aptamer were determined in DKMG/EGFRvIII tumor-bearing nude mice. **Results:** ^{68}Ga- NOTA-EGFRvIII was prepared in 96-98% RCYs (decay-corrected, n = 10) with radiochemical purity above 98%. High levels of EGFRvIII expression was found in DKMG/EGFRvIII; however, EGFRvIII were not detectable in U87-MG cells. Confocal fluorescence microscopy images showed that Cy5-EGFRvIII aptamer bound specifically to EGFRvIII expressing DKMG/EGFRvIII cells, however, not bound to U87-MG cells. DKMG/EGFRvIII tumors were clearly visualized by microPET imaging in a tumor-bearing mouse at 60 after injection. **Conclusion:** NOTA EGFRvIII aptamer conjugate was successfully labeled with Ga-68. In vitro data showed that the EGFRvIII aptamer was selectively bound to target tumor cells. In addition, DKMG/EGFRvIII tumor xenografts in mice were clearly visualized on microPET imaging. Our study demonstrated that EGFRvIII may be a useful target molecule for the imaging of glioblastoma **References:** 1) Sampson JH, et al. Tumor-specific immunotherapy targeting the EGFRvIII mutation in patients with malignant glioma. Semin Immunol. 2008;20:267-275. 2) Bakas S, et al. In Vivo Detection of EGFRvIII in Glioblastoma via Perfusion Magnetic Resonance Imaging Signature Consistent with Deep Peritumoral Infiltration: The φ-Index. Clin Cancer Res. 2017;23:4724-4734.