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Methods for the assessment of the treatment dose using micro-PET/CT suitable for NCT Treatment Planning Systems in experimental animal models.

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Purpose

To evaluate and optimize strategies for BNCT dose calculation in an animal model, by using a Monte Carlo-based treatment planning system working on co-registered μPET/CT images.

Introduction

The present study explores the possibility to include the small animal PET data into a specific ***B*oron *D*istribution *T*reatment *P*lanning *S*ystem (BDTPS)**, integrating CT-based and PET-based Regions of Interest (ROIs) functionality in the same framework.
In a previous work, we validated the BDTPS with PET data using a heterogeneous phantom (HEBOM: *Heterogeneous Boron Model*), already used in previous BNCT researches [1]. In this second step, the animal model with implanted F98 glioma has been developed in order to simulate the tissue dose distribution.

Animal model of F98 glioma

^{18}F-FET extraction was determined after the second week (18th day) after tumor implantation in rat [2]. All the animals have been anaesthetized during the intervention following an authorized protocol in compliance with the Italian regulatory statements on animal experiments.

Why ^{18}F-FET-PET?

The pharmacokinetics of ^{18}F-BPA is assumed to be similar to that of BPA, but this has been only verified *ex-vivo*. In this work, an alternative to ^{18}F-BPA-PET has been studied to predict the BPA extraction with O-(2-18F-fluoroethyl)-*D,L*-tyrosine (^{18}F-FET, more commonly FET), probably the more promising candidate among the aromatic aminoacids [2].

^{18}F-FET demonstrated high in vivo stability in patients [3] , fast brain and tumour uptake kinetics, low accumulation in non-tumour tissue and ease of synthesis. FET–PET was already proposed to be appropriate for accurate RT-planning [4]

Spatial correlation between FET and BPA has been confirmed by ex vivo neutron radiography analysis at the Pavia Research Reactor: high-resolution quantitative Neutron Capture Radiography (NCR) was used as reference methodology to compare the μPET data for ^{10}B mapping in the corresponding slice. Even though NCR and μPET have different spatial resolution, they can be spatially correlated within few mm^2 [5].

TPS workflow

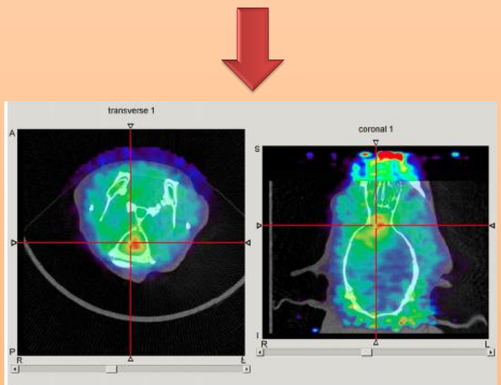
1. Micro-PET/CT Imaging

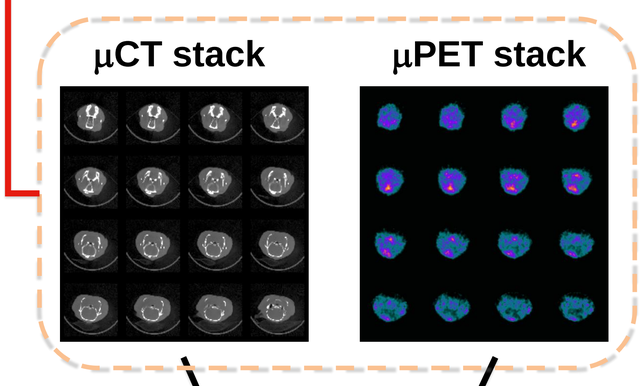
^{18}F-FET extraction was determined after the second week (18th day) after tumor implantation. Each animal (n=3) has been injected with ^{18}F-FET (150kBq/g of body weight) and ^{10}B-BPA (300 mg/Kg BPA-fructose complex b.w.). The images were acquired with the Xalt micro-CT scanner [6] and the YAP-(S)PET scanner (ISE srl, Italy) [7].

The focal uptake of ^{18}FET by the tumor is clearly visible, thus allowing a reliable definition of the Region of Interests (ROI) [2].

The PET and CT images have been co-registered and resampled to have the same voxel size (0.23x0.23x1.0 mm^3), and then they have been sent to BDTPS, where the ROIs were drawn.

Xalt$_{HR}$ + YAP-(S)PET II (ISE Ingegneria dei Sistemi Elettronici)



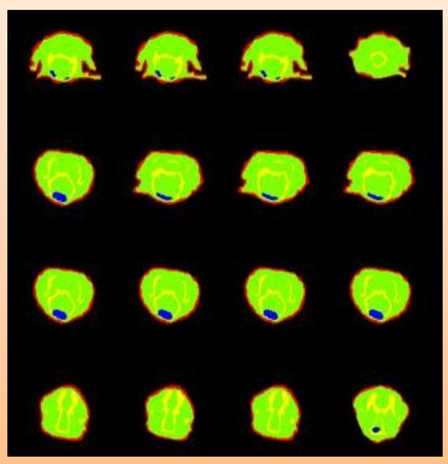


2. Definition of the ROIs

BDTPS implements a specific tool for manual outlining the ROIs on PET and CT slices. More specifically, the following regions have been defined in this study:

1. **Skin (external surface)**
2. **Soft tissues**
3. **Bones**
4. **Tumor**

ROIs from 1 to 3 have been defined on CT slices, whereas the tumor has been delineated from the PET slices.



3. Results

BDTPS is a ***pre- and post-processing system*.** It prepares the MCNP input through an ***integrated environment*** where CT and PET (but also MRI, if needed) are combined in a single 3D model for the dose and fluence calculations.
PET data have been normalised, being the maximum FET concentration value equal to ~30 ppm (as acquired by neutron radiography). Quantification of boron uptake by PET with [^{18}F]FET in future studies will requires the introduction of parameters, that could corrects the different affinity between BPA and FET to aromatic amimoacid transporters.
In post-processing, BPTPS shows the isodose and isofluence surfaces, reading through the MCNP output. The data evaluation is in progress, but the preliminary results show that FET-BNCT could be a reliable methodology for a successful treatment.

Conclusions

- Due to its high specificity to brain tumour cells and its affinity to BPA, FET has a high potential as a PET tracer for the delineation of target volume in BNCT treatment planning.
- Our approach could lead to the use of dose evaluation in tumour and healthy tissues in an experimental animal models before the animal irradiation.

References

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