Development and evaluation of a dedicated setup for co-registered PET/MRI abdominal imaging of the mouse

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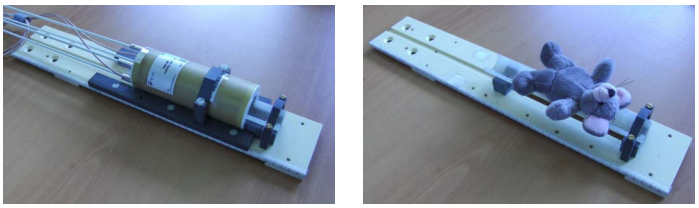
Introduction

The combination of the PET sensitivity with the imaging capabilities offered by MRI is of great interest to improve the detection and characterization of cancer tissues. One of the main challenges to fully exploit this complementary information, especially regarding pre-clinical studies, is to achieve perfect co-registration between both image types. The goal of this work was then to develop and evaluate a dedicated setup and processing for co-registrated PET/MRI abdominal images of the mouse acquired on two independent imaging systems based on external fiduciary markers. A first validation was performed on dedicated phantoms, followed by *in vivo* examinations using various mouse models of digestive tumors.

Material and Methods

A dedicated holder for abdominal mouse MR and PET imaging was designed and built to be compatible with two independent imaging systems: a Bruker 7T Biospec system (Bruker, Ettlingen, Germany) and a ClearPET system (Raytest GmbH, Straubenhardt, Germany). A non-magnetic and low attenuation plastic holder was designed to have a mouse (laid on a plastic bed) centered for both imaging systems (Fig. 1). The plastic bed was equipped with three non parallel fiduciary tubes of 1 mm inner diameter. Two identical holders were built to speed up the whole acquisition process and scan a second animal with MRI when the first animal underwant the PET examination. For MR examinations, fiduciary tubes were filled with a solution of $NiS0_4$. A 32 mm inner diameter quadrature birdcage coil (Rapid Biomedical, Würzburg, Germany) was used. Axial SE T1-weighted (TR/TE 550/12 ms) and RARE T2-weighted (TR/TE 6000/38 ms) were performed using the following geometric acquisition parameters: 3 cm FOV; 256x256 matrix; 0.5 mm slice thickness. On the liver, acquisitions were synchronized with breathing using the strategy described in [1] whereas no synchronisation was performed on the upper abdomen. Two rails guided the coil to be removed while keeping the anesthetized mouse untouched for PET imaging (Fig 1). The solution in the external fiduciary tubes was then replaced with ^{18}F-FDG without moving the animal to enable accurate depiction on PET images for image co-registrations. The *in vivo* PET imaging protocol consisted in injecting about 300 µCi of 18F-FDG, waiting for the radiotracer equilibrium state (about 30-45 minutes) and performing a static 20 minutes whole-body acquisition.

Phantom experiments were performed to assess the co-registration process using 1) a 70 mm long and 30 mm diameter plexiglass cylinder containing three spheres of variable diameters (5, 7, 9 mm) and 2) a resolution phantom from Bruker (Aufloesung 30 KIT G; model 1P T58930). *In vivo* animal examinations were performed under isoflurane anaesthesia. Just before introduction within each imaging system, 30 µl of an antispasmodic drug (Scoburene®, Renaudin, France) was administered. One mouse with a subcutaneous neuroendocrine tumor [1], two thioacetamide-induced fulminant hepatic failure (FHF) [2] and three 12 months old *Apc*1/1638N mice [3] were investigated. Acute liver injury was induced by i.p. injection of thioacetamide (100 mg/kg in phosphate-buffered saline). Following thioacetamide administration, animals rapidly (2-3 days) develop FHF characterized by severe liver function impairment, massive hepatocyte necrosis and apoptosis. *Apc* mice typically develop 5 to 6 tumors in the small intestine within the first year of life. In *Apc* mouse models, polyp formation is favoured in the small intestine, in contrast to human disease, which occurs predominantly in the colon. The pathological changes associated with *Apc* deficiency include increases in crypt size, cell proliferation and apoptosis. In addition, the cells in *Apc*-deficient crypts show reduced crypt to villus migration and differentiation.



a b

Fig. 1. Photographs of the dedicated bed in MRI (a) and PET (b) configuration.

Co-registration between PET and MR images were obtained using different strategies implemented in the BioImage Suite image analysis software developed at Yale University (www.bioimagesuite.org) including standard rigid and non-rigid transformations and a semi-automated method based on the external fiduciary markers.

Results

Fig. 2 shows the mean 18F-FDG intensity measured in the PET image of the Bruker phantom based on two ROIs drawn on the MR image at the center of the two inserted cylinders. This graph indicates that the semi-automated method and the non-rigid transform allowed the best co-registration corresponding to the highest radiotracer concentrations. Fig. 3 shows one example of co-registered and overlaid PET and MR transverse slices centered on the subcutaneous neuroendocrine tumor. The corresponding quantitative evaluation confirms that the semi-automated method driven by the fiduciary markers enabled the best co-registration. Visual analysis of the PET images of the *Apc* mice, developing spontaneous intestinal tumors, allowed in 2 out of the 3 mice, to detect tumors that were not localized by an experienced radiologist on the MR image only. PET, thus, helped guiding the MR image analysis.

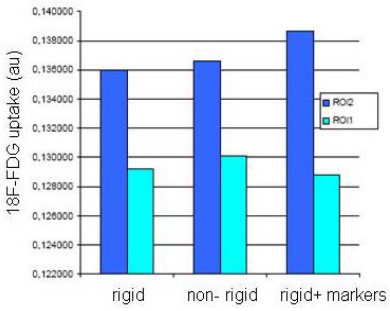


Fig. 2. Mean FDG value measured on the PET image of the Bruker phantom after co-registration to the MR image by the three evaluated strategies.

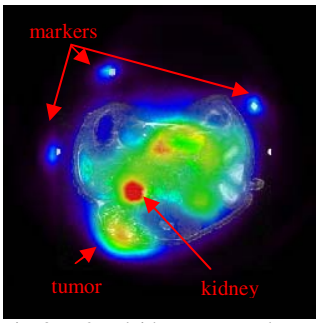


Fig. 3: Overlaid PET and MR transverse slices of a mouse with a subcutaneous neuroendocrine tumor.

Conclusions

The combination of a dedicated PET and MR compatible mouse holder associated with a system of fiduciary markers allowed accurate co-registration of these complementary anatomical and functional images acquired on separate systems. Further investigation on a larger number of animals is required to confirm these results. The interest of automatic registration methods that would account for the fiduciary markers will be further investigated.

References

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Acknowledgements

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