Real-time feedback paradigm for functional and metabolic imaging using a combined PET/MR scanner: proof of concept

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OBJECTIVE

To illustrate the concept of a real-time feedback paradigm for using complementary data from a PET/MR scanner in the functional studies of biological processes and demonstrate this concept in a preliminary study of tumor metabolism.

INTRODUCTION

The study of biological processes in-vivo is vital to their proper elucidation. Positron Emission Tomography (PET) and Magnetic Resonance (MR) offer complementary functional and anatomic information [1] that provide unique windows into such processes. Previous studies have shown that PET and MR data combined retrospectively show correlations between information garnered from the individual modalities [2]. Despite the use of careful registration techniques, it can be difficult to analyze multimodal data that are temporally and spatially different. The combined PET/MR scanner [3] overcomes these problems by allowing simultaneous imaging using both modalities. Apart from integrating datasets in space and time, PET/MR offers the potential to perform real time analysis of multi-modal data that can feedback to direct further studies in a single imaging session. The high spatial resolution capabilities of anatomical MRI provides the base upon which PET and other MR imaging methods such as MR spectroscopy (MRS) and angiography can be performed. The latter methods can be analyzed immediately to determine the appropriate timing windows and regions of interest (ROI) to pursue. A diagram illustrating this concept is shown in Figure 1. In this study, we demonstrate the feasibility of this paradigm. Mice implanted with tumor cells were imaged simultaneously with PET/MR. Functional data derived from the PET was then used as a basis for MR spectroscopy studies of tumor heterogeneity.

METHODS

Animal: Mice with MC-38 tumor cells injected into the left groin two weeks prior to imaging were anaesthetized with isoflurane. A catheter was inserted into the tail vein for [18F]-FDG administration. The mice were secured in a plastic holder and positioned using a computer controlled device (Aerotech) at the center of the magnet and thus also of the PET insert. Normal body temperature (37ºC) was maintained with an air heating system; respiration was monitored with a transducer coupled to a respiration pillow (BIOPAC). *Experimental*: Imaging was done on the combined 7T Bruker Biospec MR/PET system. Prior to animal imaging, a glass phantom containing [18F]-FDG was imaged simultaneously with PET/MR to obtain a calibration control. [18F]-FDG (200µCi) in 0.2mL sterile saline solution was injected as a short infusion over 15 seconds. One hour post injection, a high resolution MRI anatomical image (RARE TR/TE: 2000/12ms, 0.137x0.137x0.75mm voxel size) was obtained simultaneously with PET (0.28x0.28x.75mm reconstructed voxel size, 5minute scan duration). After analysis of results, MRS was performed on the tumor. ROIs were defined by [18F]-FDG activation in the tumor environment. Spectra were taken in three regions: i) ROI of the tumor with high [18F] FDG uptake, ii) ROI of the tumor with low uptake, iii) area of muscle on the contra-lateral leg (PRESS TR/TE: 1685/10ms, 3mm^3 voxel with water suppression). *Analysis*: In house software written in MATLAB was used to automatically calibrate all images in real time.

RESULTS AND DISCUSSION

Figure 2 shows a PET/MR superimposed image along with the corresponding MR spectra for all ROIs.

Anatomical MRI was used to identify the tumor mass and thus define the FOV for PET/MR imaging. Immediate analysis of the PET/MR data showed high uptake of FDG in the medial-ventral region of the tumor mass. To compare the metabolic profile of this region with other regions of the tumor mass, we acquired MRS data over different tumor regions. A muscle spectrum was obtained as a control. Previous studies have demonstrated high choline levels in tumor cells due to high membrane turnover [4]. In Figure 2, MRS of the high FDG uptake area showed a choline/creatine ratio of 2.1 vs. 0.8 in the area of low uptake. This correlates well with the notion that high FDG activity is an indication of high metabolic activity. Choline was not detectable in the muscle spectrum. In both tumor spectra, broad peaks in the region of 3-4ppm were observed. While many metabolites may resonate in this region, making a definitive assignment is difficult. It is likely that a portion of the peaks can be attributed to glucose, as the glycolytic rate in the tumor is presumably high. A similar broad peak was not observed in muscle. Also of interest are the peaks around 2-2.5ppm. Colorectal cancer cells have been described to have abundant glutamate receptors [5]. Thus, it is conceivable that the peaks around 2-2.5ppm may reflect high levels of glutamate in the tumor. In the anatomical scan, a small lesion was observed in the low FDG uptake ROI, suggesting the presence of necrosis or abscess. High lipid peaks in the corresponding spectrum support this notion, although the expected increase in lactate is not seen. Although both the PET and MRS protocols can be further developed to obtain more refined data, it can be seen that the combined information provides a more complete picture of the tumor environment than either alone. Conceivably, each modality can guide the other in a variety of ways. For example, PET imaging can guide MRS studies to fully characterize regions of tumor cell turnover or hypoxia. Studies with fMRI or MRS could shed light on brain imaging data obtained by PET. The real time feedback capability offered by the PET/MR allows more finely tuned studies to be conducted.

CONCLUSION

A paradigm for real time feedback PET/MR experiments was presented and proof of concept was provided in a study of tumor metabolism. MR spectra taken over areas of high FDG uptake differed from other tumor regions. This illustrates the potential of this paradigm for exploring interesting temporal and spatially dependent biological questions using the PET/MR.

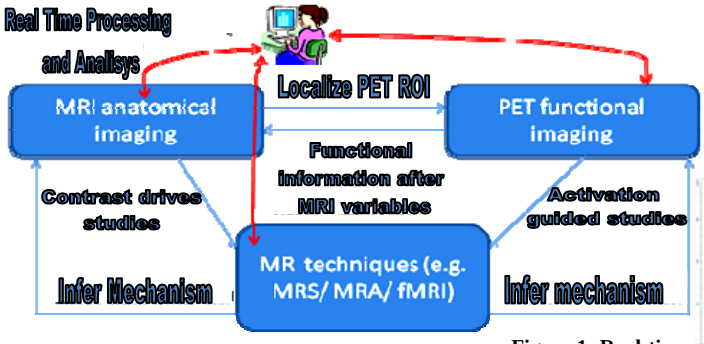

Figure 1: Real-time feedback paradigm with combined PET/MR scanner

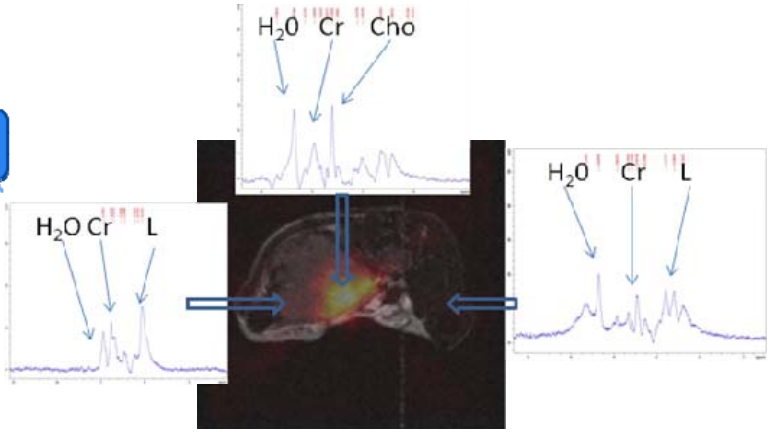

Figure 2: PET/MR of tumor with heterogeneous region spectra (Cr = Creatine, Cho = Choline, L = Lipids, Water is set at 4.7ppm)

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