In vivo biochemical imaging of HCC tumor bearing rats using hyperpolarized [1-13C]pyruvate and 18F-FDG

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Introduction

Hyperpolarized [1-13C]Metabolic MR imaging using [1-13C]pyruvate (Pyr) allows for real-time in vivo detection of energy metabolism, i.e. mitochondrial PDH activity and LDH activity in healthy and tumor bearing animals [1]. Recently [2, 3] proposed to use IDEAL spiral CSI in combination with single-shot spiral acquisition to simultaneously encode position, time and spectrum to study metabolic processes in vivo. In this study we evaluated the comparison of a group of 23 male Buffalo rats with subcutaneous HCC tumor of varying grade of necrosis and size, which received both 18F-FDG PET and hyperpolarized [1-13C]pyruvate.

Methods

Subcutaneous tumours were induced by injection of 1 Mio Mca-RH7777 HCC and grown until they reached 1 cm diameter. FDG PET and IDEAL spiral CSI [2] of hyperpolarized pyruvate were performed on two consecutive days under isoflurane anaesthesia. Animal experiments were approved by the local governmental agency. 3D PET data was acquired for 60 min (list mode) using Irive small animal PET/CT scanner (Siemens, Knoxville, USA) starting with injection of [18F]FDG (6.09 - 22.45 MBq). PET data was reconstructed using an OSEM3D81 algorithm (normalized and corrected for randoms, dead time, decay, but not for attenuation or scatter).

[1-13C]pyruvic acid was hyperpolarized using a HyperSense DNP (Oxford Instruments, Oxford, UK) dissolved in physiological pH and temperature (liquid state polarization 19-31 %) and 5 ml/kg was injected with 0.17 ml/s into the tail vein of the tumor bearing rats (~215 g). Anatomical T1 reference images and 13C-IDEAL spiral CSI data sets were acquired on a GE Signa Excite 3T scanner (GE Healthcare, Milwaukee, WI, USA) of a 10 mm thick, transversal slice through the tumor with a 10° flip angle, using a dual-tuned (13C-1H) quadrature coil. Data reconstruction was performed according to [2] resulting in 32 consecutive 13C metabolite images. Images acquired with both methods (18F-PET and 13C metabolic MR) were visually assessed for signal strength in target tissue. Regions of interest (ROIs) were placed over tumor and dorsal muscle according to anatomical proton MR images. Additional ROIs were placed of the gastrointestinal tract (GIT) and the vena cava in the CS images. From the ROIs in the PET images the standardized uptake value (SUV) and tumor to muscle ratio (TMR) were calculated and from CS images the maximum peak (MP), TMR and lactate to pyruvate ratio (LPR).

Results and Discussion

In this study we evaluated a group of 23 rats with subcutaneous HCC tumors regarding CS measurements of hyperpolarized [1-13C]-pyruvate and its metabolites [1-13C]-lactate and [1-13C]-alanine. [18F]-FDG-PET imaging verified that all tumors were metabolically active, had comparable uptake and were easily distinguishable from surrounding tissue by eye. Further analysis of a subgroup showed that the tracer delivery to the tumor during the first two minutes of PET imaging was comparable in all tumors analyzed (data not shown).

Visual assessment of integrated [1-13C] metabolite maps, on the other hand, presented high variability of contrast between [1-13C]-pyruvate, [1-13C]-lactate and [1-13C]-alanine. [18F]-FDG-PET imaging verified that all tumors were metabolically active, had comparable uptake and were easily distinguishable from surrounding tissue by eye. Further analysis of a subgroup showed that the tracer delivery to the tumor during the first two minutes of PET imaging was comparable in all tumors analyzed (data not shown).

Conclusion:

In PET images all tumors showed high signal intensities, whereas in pyruvate images less than half (40 %) and in lactate images only 2/3 (70 %) showed visible signal in tumors. No correlation could be found between TMR from PET and from CS images or between SUV and LPR. Analysis of the MPs revealed that a higher proportion of the pyruvate that could be detected in the blood vessel reached the GIT than the tumors. But in tumors turnover of pyruvate to lactate and alanine was higher than in the GIT. This effect of compartmentalization of [1-13C]pyruvate and its downstream metabolites demands a more sophisticated data analysis than simple integration of the metabolite signal curves for visual display, which captures the individual dynamic rather than the absolute signal. This may be achieved by kinetic modeling [6].

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References