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Introduction

Metabolic imaging with hyperpolarised [1-13C]pyruvate (Pyr) has great potential for in vivo diagnosis of tumours and other disorders. One of the main constraints is the non-quantitative nature of current spectroscopic imaging approaches, yielding metabolite images in arbitrary units. One partly quantitative approach is looking at the ratio of the downstream metabolites (lactate (Lac), alanine (Ala) or bi-carbonate (BC)) to Pyr, which is still dependent on timing and other variations. A more quantitative approach is trying to extract the metabolic exchange rate constants, usually by fitting time-resolved spectra to the kinetic exchange rate model. Recently, we proposed a saturation-recovery approach, where downstream metabolites are excited spectrally and spatially selective with 90° [1]. In this work we introduce several improvements to this approach: (a) new spectral-spatial (SPSP) pulses are designed with a novel, fully 2D fitting approach; (b) SNR is improved by a spiral trajectory and apodisation matched to T2* and (c) optimised sequence parameters. The metabolic-exchange rate imaging approach was validated in 4 rats bearing subcutaneous MAT BII tumours.

Methods

Saturation Recovery Principle: The metabolic conversion $k_{PX}$ of Pyr into downstream metabolite X (Lac, Ala or BC) can be modelled by a simplified two-site exchange model [2] $\frac{dM_X}{dt} = k_{PX} M_P - M_{X,eff} T_{1,X}^{-1} [\text{Eq. 1}], where $M_P$ and $M_X$ denote the magnetisation of X and Pyr, respectively. For sufficiently short metabolite repetition times $t_m$, the relaxation term $M_X T_{1,X}$ is small as compared to the conversion part and can be neglected. Exciting X selectively with a $\theta=90^\circ$ spectral-spatial pulse yields high signal for imaging, while at the same time saturating the existing magnetisation of X. With the detected signal intensity $S = M \sin \theta$, the metabolic conversion is thus directly given by $k_{PX} = \frac{S_X}{t_m \cdot (S_P + \alpha)}$, where $\alpha$ denotes a regularisation parameter to avoid division by zero or very small values of $S_X$.

SPSP pulses (Fig. 1) suitable for exciting all four resonances with minimal contamination from other peaks were designed directly in the two (i.e. spectral and spatial) dimensions using the small-tip-angle approximation by linear least-squares optimisation. This 2D approach helps to minimise (or in case of flyback completely eliminate) the sidelobe artefacts normally occurring with a separable design. Three types of pulses with different properties were designed: (1) main excitation lobe shifted to the first side lobe; (2) centred main lobe with bi-directional and (3) flyback gradient modulation. For image encoding, the SPSP pulse is followed by a single-shot spiral readout [1,3].

The spiral trajectories were SNR optimised by matching the readout with the expected T2*. The spiral starts in the centre of k-space at the beginning of the FID, where the signal level is maximal. The highest spatial frequencies are encoded towards the end of the spiral readout. The readout duration is typically longer than T2* and the signal already disappeared into the noise. The SNR is optimised during the reconstruction by apodising with a matched filter [4].

The sequence parameters were optimised by simulating the signal evolution with Eq. 1 with the Pyr curve shown in Fig. 2 with different values of $k_{PX}$ (0.01, 0.02, 0.03, 0.05 1/s), $T_{1,X}$ (10, 20, 30 s), $t_m$ (0.1,0.1,1.15 s) and $\theta$ (0.1-90°) (shown in Fig. 3 for $k_{PX}$=0.02 1/s, $T_{1,X}$=20s). For saturation-recovery ($\theta=90^\circ$), $t_m=4$ s was identified as good compromise between SNR while exhibiting only 10% error in $k_{PX}$ due to omitting the $M_X T_{1,X}$ term in Eq. 1.

Experimental: Each of the 4 Fischer rats with subcutaneous MAT BIII tumours received two injections of 2.5 ml/kg of [1-13C]Pyr (maximum or cross-section) in combination with the Pyr spectrum.

Results and Discussion

Metabolic exchange rate images for Lac of all four rats are shown in Fig. 4. All four tumours show an elevated lactate turnover $k_{LC}$, clearly separating the tumours from the other tissue. This is in contrast to the pure Lac images, where signal is often visible in the abdomen as well. However, Pyr is increased there as well, indicating that there is no increased metabolic exchange activity present. The exchange rate images (bottom in Fig. 4) are scaled to $k_{PX}$=0.08 1/s, whereas the Pyr and Lac images are in arbitrary units. The tumours are highlighted by white arrows.

References


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