Saturation-Recovery Metabolic Exchange Rate Imaging with Hyperpolarised [1-13C]Pyruvate using Spectral-Spatial Excitation

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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 much 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 BIII tumours.

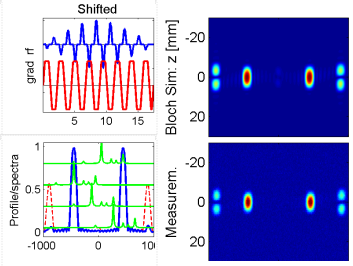

Fig. 1: SPSP pulse (top left), its 2D profile (right) and its profile (maximum or cross-section) in combination with the Pyr spectrum.

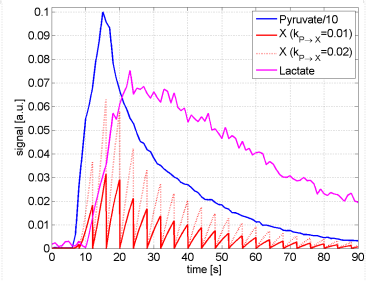

Fig. 2: Signal evolution for the saturation-recovery experiment. Pyr and Lac are measured typical curves (blue and magenta). The saturation-recovery effect is simulated with Eq. 1 for typical values of $T_{1,X,eff}$=20s, tm=4s and k_{PX}=0.01 1/s (red solid), k_{PX}=0.02 1/s (red dotted).

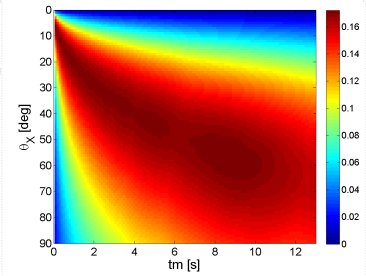

Fig. 3: SNR using two-site exchange model simulations as shown in Fig. 2, plotted over flip angle θ_X and metabolite repetition time tm. The plot shows the averaged signal level, attained by averaging the SNR-optimal number of points.

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] $dM_X/dt = k_{PX}M_P - M_X/T_{1,X,eff}$ [Eq. 1], where M_X and M_P denote the magnetisation of X and Pyr, respectively. For sufficiently short metabolite repetition times tm, the relaxation term $M_X/T_{1,X,eff}$ is small as compared to the conversion part and can be neglected. Exciting X selectively with a θ_X=90° 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 $k_{PX} = S_X \sin\theta_P / tm \cdot (S_P + \alpha)$, where α denotes a regularisation parameter to avoid division by zero or very small values of S_P.

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_{PL} (0.01, 0.02, 0.03, 0.05 1/s), $T_{1,X,eff}$ (10, 20, 30 s), tm (0.1:0.1:15 s) and θ_X (0:1:90°) (shown in Fig. 3 for k_{PL}=0.02 1/s, $T_{1,X,eff}$=20s). For saturation-recovery (θ_X =90°), tm=4s was identified as good compromise between SNR while exhibiting only 10% error in M_x due to omitting the $M_X/T_{1,X,eff}$ term in Eq. 1.

Experimental: Each of the 4 Fischer rats with subcutaneous MAT B III tumours received two injections of 2.5 ml/kg 80mM pyruvate prepared with a HyperSense DNP polariser. Measurements were performed on a GE 3T HDx scanner equipped with a volumetric, dual-tuned rat coil. Sequence parameters: tm=4s, θ_P=15°, θ_X=90°, half-shifted pulse, excitation iterating through Lac, Pyr, BC and Ala; spiral: FOV=8cm, 32×32 nominal,16×16, real resolution, 45ms duration.

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_{PL}, 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_{PL} = 0.08 1/s. This demonstrates the quantitative nature of the proposed method. Some of the tumours were already necrotic, while some were still fairly small. High tumour activity was detected despite this variability.

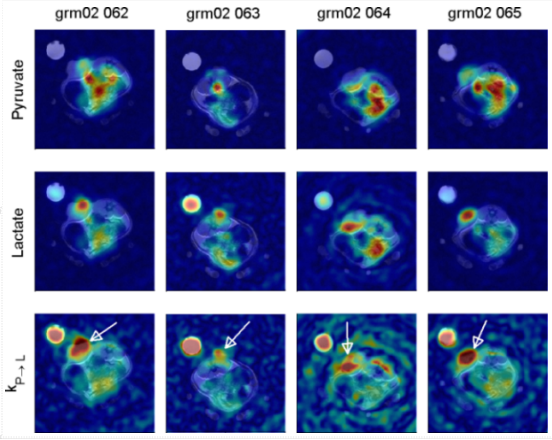

Fig. 4 (left): Pyr, Lac and turnover (k_{PL}) images of all four measured rats of the 4th time step. The colourmap for k_{PL} is scaled to 0.08 1/s, whereas the Pyr and Lac images are in arbitrary units. The tumours are highlighted by white arrows.

References

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