Metabolic Exchange Rate Imaging with Hyperpolarised [1-13C]Pyruvate

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Introduction

Hyperpolarising and injecting [1-13C]pyruvate (Pyr) enables imaging the enzymatic conversion to lactate (Lac), alanine (Ala) and bi-carbonate (BC) minimally invasive. A current trend in the field is going towards more quantitative methods, mainly by fitting metabolic exchange rates to the acquired time-resolved data. Recently, we proposed two methods to detect metabolic exchange rates spatially localised: saturation-recovery [1] and frequency-domain modelling [2]. In this work we use the frequency-domain approach to derive a saturation-recovery quantification utilising the complete dataset. Both approaches are compared in a MAT BIII tumour study.

Methods

Frequency-domain metabolic modelling: The metabolic conversion k_{PX} of P (Pyr) into its downstream metabolites X (Lac, Ala or BC) can be modelled with the simplified two-site exchange model [3] $dX(t)/dt = +k_{PX}P(t) - R_{X,eff}X(t)$ [Eq. 1]. This expression can be Fourier transformed into the frequency-domain $i\omega x(\omega) = +k_{PX}p(\omega) - R_{X,eff}x(\omega)$ [Eq. 2]. It is possible to obtain a physical interpretation of the commonly used ratio $\frac{\int X(t)dt}{\int P(t)dt} = \frac{x(0)}{p(0)} = \frac{k_{PX}}{R_{X,eff}}$ [Eq. 3], by evaluating this expression at zero-frequency (ω=0). Including Eq. 3 in Eq. 2 leads to the following analytical expression for the metabolic exchange rate $k_{PX} = i\omega \frac{x(\omega)x(0)}{p(\omega)x(0) - x(\omega)p(0) + \alpha}$, where α denotes a regularisation parameter to avoid division by values close to zero.

Saturation-recovery principle: Analysing the metabolic conversion (Fig. 1 and Eq. 1), one can see that the initial part of the curve is dominated by conversion and the later part by relaxation. When exciting metabolites with sufficiently short metabolite repetition times tm, the relaxation term $R_{x,eff}X(t)$ 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 $k_{PX} = {S_X \sin\theta_P}/{tm \cdot (S_P + \alpha)}$.

The saturation-recovery effect is repeating itself every metabolite repetition time tm. In [1], the best time-step in terms of highest SNR was chosen. One possibility to use more of the available information is to average k_{PX} over several time steps. However, this leads to large errors because values close to zero in the denominator amplify the error, particularly considering the fact that many time steps have poor SNR. While it is not obvious from the time-domain description, it is possible to derive a quantification utilising the whole time-series via the frequency domain modelling approach. The $R_{x,eff}$ term contains relaxation effects and back conversion as well as depletion due to flipping X into the transverse plane. In case of saturation-recovery, relaxation is neglected, but every time step the magnetisation of X is completely depleted by flipping into the transverse plane; hence, yielding $R_{x,eff}=1/tm$. Evaluating this again at ω=0 as in Eq. 3 gives $k_{PX} = {\sum S_X \sin\theta_P}/{tm \cdot (\sum S_P + \alpha)}$.

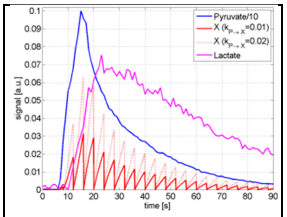

Fig. 1: Signal evolution for the saturation-recovery experiment. Pyr and Lac are measured, typical curves (blue and magenta). The saturation-recovery effect is simulated with Eq. 1 for typical values of $R_{X,eff}$=0.05s^{-1}, tm=4s and k_{PX}=0.01s^{-1} (red solid), k_{PX}=0.02s^{-1} (red dotted).

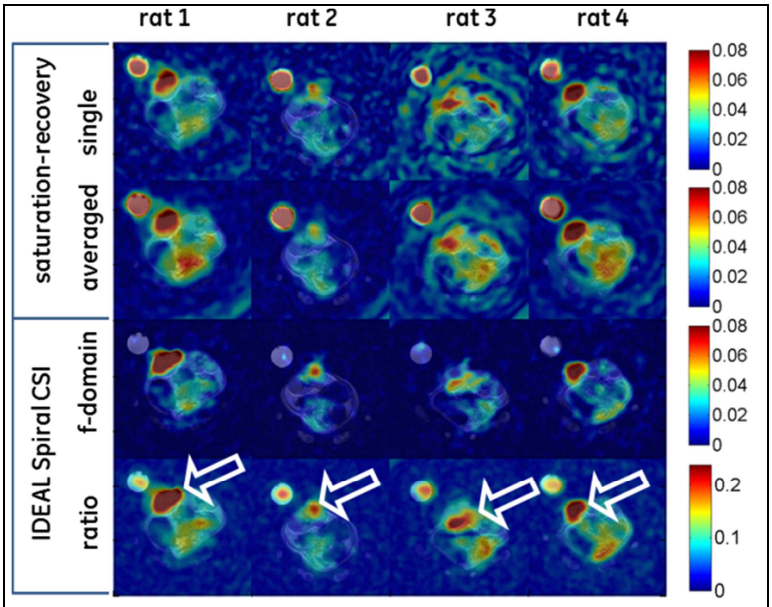

Fig. 2: Metabolic exchange rate images k_{PL} (scaled to 0.08 s^{-1}) of the slice through the tumour (marked with the white arrow). For the saturation-recovery approach, the fourth time step is shown (top) and the averaged turnover (below). For the acquisition with IDEAL Spiral CSI (second injection), k_{PL} is obtained via frequency-domain fitting and also compared to the ratio of sums (bottom).

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. Both injections used the same spiral trajectory acquiring 4 slices with FOV=8cm, 32×32 nominal matrix size and 45ms duration, leading with an SNR-optimal matched filter to a real matrix size of 16×16 [1]. First injection: spectral-spatial excitation with half-shifted pulse, excitation iterating through Lac, Pyr, BC and Ala; TR=1s, tm=4s, θ_P=15°, θ_X=90°. Second injection: IDEAL Spiral CSI [4] encoding with nTE=7, ΔTE=1.12ms, θ=10°, TR=0.5s, tm=4s.

Results and Discussion

Metabolic exchange rate images k_{PL} of the conversion from Pyr to Lac obtained with the different methods are shown in Fig. 2. All tumours in the four rats show an elevated conversion to Lac k_{PL}, thus clearly separating the tumours from the other tissue. Using all time-steps acquired with saturation-recovery increases the SNR of the measurement (Fig. 2; row 2).

All exchange rate images show the same turnover pattern, even when comparing the two different acquisitions from separate injections. All developed methods require no user interaction, performing in a simple and robust manner, which will be of paramount importance for a possible clinical application of this technique.

References

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