# *In vivo* $T_2$ mapping of hyperpolarized [1-$^{13}$C] pyruvate using an indirect method

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**Target Audience** Scientists and engineers interested in hyperpolarized $^{13}$C and $T_2$ relaxation time of $^{13}$C metabolites.

**Introduction** $T_2$ relaxation time is an important consideration in metabolic imaging. However, *in vivo* $T_2$ relaxation time of $^{13}$C metabolites in hyperpolarized $^{13}$C study is still not well investigated. Recently, apparent *in vivo* $T_2$ relaxation times of hyperpolarized [1-$^{13}$C] pyruvate and its downstream metabolites were reported in several studies, which were measured from whole slice or single voxel using a spin-echo based methods [1, 2, 3]. In this work, we propose a $T_2$ estimation method for hyperpolarized $^{13}$C metabolites which utilizes the $T_2'$ information of water proton and $T_2^*$ of the $^{13}$C metabolites from a conventional chemical shift image (CSI).

**Methods** ***Theory - Relationship between $T_2'$ of $^1$H and $T_2'$ of $^{13}$C:*** When the $B_0$ field change inside a voxel volume can be modeled as being linear, the external decay rate due to the field contribution $R_2'$ (= $R_2^* - R_2$) can be approximated as $\gamma\Delta B$ where $\gamma$ is the nuclear gyromagnetic ratio and $\Delta B$ is the average B0 inhomogeneity across the voxel [4, 5]. Therefore $R_2'$ of $^1$H and $^{13}$C can be written as $R_2'_H = \gamma_H \Delta B$ and $R_2'_C = \gamma_C \Delta B$ respectively if following two conditions are satisfied: (i) water proton and $^{13}$C spins of a specific metabolite coexist with very similar distribution and (ii) field inhomogeneity in each voxel can be assumed to change linearly with an average field inhomogeneity $\Delta B$. In this case, $R_2'_C$ can be indirectly estimated by $R_2'_C = (\gamma_C/\gamma_H)\cdot R_2'_H$ if $R_2^*{}_H$ and $R_{2H}$ are measured a prior (Fig. 1).

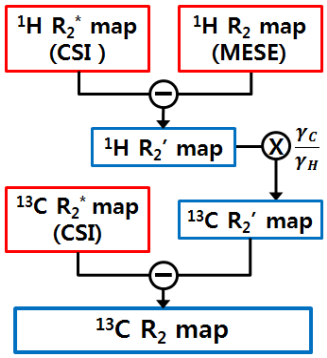


**Figure 1** Schematic diagram of $^{13}$C $R_2$ map estimation method. Red and blue boxes indicate measured and derived results, respectively.

***Experiments:*** Using this indirect estimation scheme, experiments were performed from a female Sprague-Dawley (SD) rat with $1\times10^4$ C6 glioma cell implanted in the brain. *In vivo* experiments were performed on a 9.4T Bruker BioSpec (Bruker BioSpin, Germany) equipped with $^1$H-$^{13}$C dual-tune coil. Local shim for ROI in brain parenchyma was performed before imaging experiments. A $T_2$ map of water proton was acquired using multi-echo spin-echo (MESE) sequence over 4mm slice including brain tumor with 30mm*30mm FOV and matrix size of 24*24. To measure $T_2^*$ maps of $^1$H and hyperpolarized $^{13}$C, pulse-and-acquire CSI of $^1$H and $^{13}$C were sequentially acquired with the same FOV and resolution as MESE. For hyperpolarized $^{13}$C experiments, [1-$^{13}$C] pyruvic acid doped with 15mM Trityl radical and 1.5M Dotarem was polarized and dissolved using HyperSense DNP polarizer (Oxford Instruments, UK). The rat was injected with a 2.5ml of 75mM [1-$^{13}$C] pyruvate bolus through a tail vein catheter. All procedures were approved by the Animal Care and Use Committees.

***Data Processing:*** To obtain $T_2$ or $T_2^*$ relaxation time constant (TC) from the acquired data, least-square nonlinear fitting was performed using mono-exponential decay function with DC bias: $S=C\cdot e^{-t/TC}+A$. $T_2$ and $T_2^*$ maps of water proton were fitted using 16 echoes from MESE image and spatially encoded FID signal from CSI acquisition, respectively. For $T_2^*$ mapping of [1-$^{13}$C] pyruvate, inverse Fourier transformed signal of extracted pyruvate peak from $^{13}$C CSI was used for fitting. $^{13}$C CSI data was apodized in time domain by multiplying a decaying exponential function with time constant of 50ms and the spectra of pyruvate were extracted by Gaussian window with full width at half maximum of 240Hz. The fitted $T_2^*$ values were corrected with the apodization taken into account. By taking reciprocal of these TC maps, $^1$H $R_2$ and $R_2^*$ maps and $^{13}$C $R_2^*$ map were obtained. $^1$H $R_2'$ map was calculated by subtracting $^1$H $R_2$ map from $^1$H $R_2^*$ map and finally $^{13}$C $R_2$ map was obtained by $R_{2C} = R_2^*{}_C - (\gamma_C/\gamma_H)\cdot R_2'_H$ (Fig. 1).

**Results** The *in vivo* experiment results are shown in Fig. 2. The $T_2$ map of [1-$^{13}$C] pyruvate (Fig. 2 (e)) shows localized longer $T_2$ values on tumor region were observed and its mean value was 228ms. Mean $T_2$ value of other normal region in ROI was 64ms. These values are close to the range of the short $T_2$ component (100~250ms) previously reported in the whole-slice studies with multicomponent $T_2$ analysis [2, 3].

**Discussion and Conclusion** *In vivo* $T_2$ map of [1-$^{13}$C] pyruvate were estimated indirectly using the relationship of $T_2'$ of two different nuclei. This method does not use any 90° or 180° pulse allowing conservation of the hyperpolarized magnetization. Therefore it can estimate localized $T_2$ values from multiple voxels and can potentially be used with time resolved fast CSI sequences to gather additional information such as conversion rates. To verify the accuracy of the estimated $T_2$ value, additional $^{13}$C phantom experiments should be performed. Also, the ability to obtain $T_2$ maps from downstream metabolites should be further investigated.

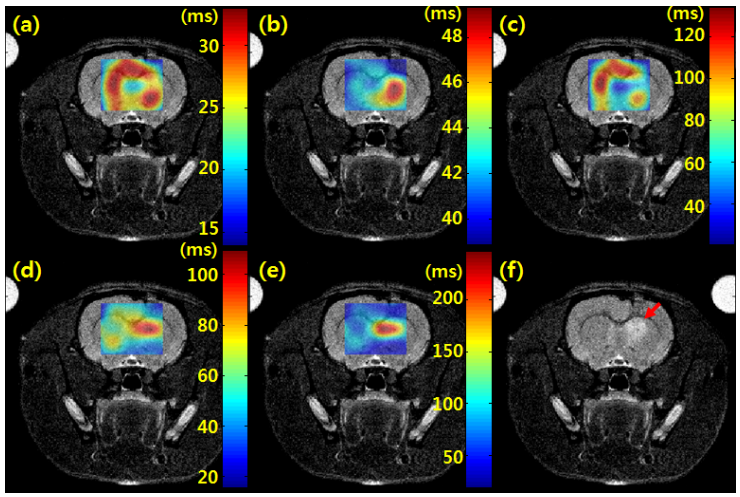


**Figure 2** (a) $T_2^*$ map, (b) $T_2$ map and (c) calculated $T_2'$ map of water proton. (d) $T_2^*$ map and (e) estimated $T_2$ map of [1-$^{13}$C] pyruvate. (f) $T_2$ weighted scout image (the red arrow indicates tumor).

**References** [1] Yen *et al.* NMR Biomed 23: 414-423, 2010. [2] Kettunen *et al.* MRM 63: 872-880, 2010. [3] Yen *et al.* In Proceedings of the 16th ISMRM, p1747, 2008. [4] Yablonskiy *et al.* MRM 32: 749-763, 1994. [5] Haacke *et al*, Magnetic resonance imaging, New York: Wiley-Liss; 602-604, 1999.