Apparent T_2 of ^{13}C-labeled Metabolites *In Vivo*

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Introduction

Apparent T_2 relaxation time (T_{2a}) of ^{13}C-labeled metabolites was measured for the first time in animals, following an injection of hyperpolarized ^{13}C-pyruvate solution. The measurement was made on a 20mm slice on rat kidney, TRAMP tumor, and dog prostate, using a CPMG sequence that acquired spectra at every spin echo for total of 8-10 seconds. Metabolites such as pyruvate, lactate, alanine and bicarbonate were observed in the spectra. Multi-component curve fitting was performed to fit the T_2-decay curves and the results are reported here.

Method

***Animal and Experimental Setup*:** Healthy Sprague-Dawley rats, TRAMP mice, and a healthy adult male beagle were used in the studies. Preparation and physiological monitoring of animals followed the protocol approved by the UCSF Institutional Animal Care and Use Committee. A typical dose consists of pyruvic acid/EPA mixture dissolved in TRIS/EDTA NaOH solution. For rats and mice, 3mL and 0.3mL of 79mM concentration was injected, respectively. For the dog, 19mL of 250mM concentration was injected. Custom-made dual tuned $^1H/^{13}C$ coils [1,2] were used. All experiments were performed on a 3T GE Signa system.

***Pulse Sequence*:** The CPMG sequence consists of 90° slice-selective excitation pulses, followed by a train of slice-selective 180° refocusing pulses. The 90° RF pulse is a minimum-phase SLR pulse [3] of 2060Hz bandwidth and the 180° pulse a linear SLR pulse [3] of 800Hz bandwidth. A 20mm axial slice was acquired on rat kidney, TRAMP tumor, or dog prostate. A 20.8kHz bandwidth spectrum of 646 points was acquired on spin echo every 42 ms. Total scan time was 8-10 s. This FSE signal time curve is a combination of the T_2 decays of all tissue types within the selective slice and therefore is termed 'apparent T_2' curve here.

Data Analysis: The spin-echo signals were Fourier transformed to the frequency domain. The magnitude peak height of each metabolite was plotted as a function of time. The noise baseline was determined from the magnitude signal at a frequency away from any metabolite peaks, averaged over all echoes. The noise baseline was subtracted from the T_2 curves prior to fitting. Curve fitting was performed using Nelder-Mead method in Matlab using the formula: $S = C(1)\cdot e^{-t/T_{2a}(1)} + C(2)\cdot e^{-t/T_{2a}(2)} + C(3)\cdot e^{-t/T_{2a}(3)}$, where T_{2a}'s are the apparent T_2 variables and C's are the corresponding weighting factors.

Results

Figure 1: Apparent T_2 data (color symbols) and curve fitting (black lines) results of rat kidney (left), TRAMP tumor (middle) and dog prostate (right). The blue line indicates the absolute noise baseline.

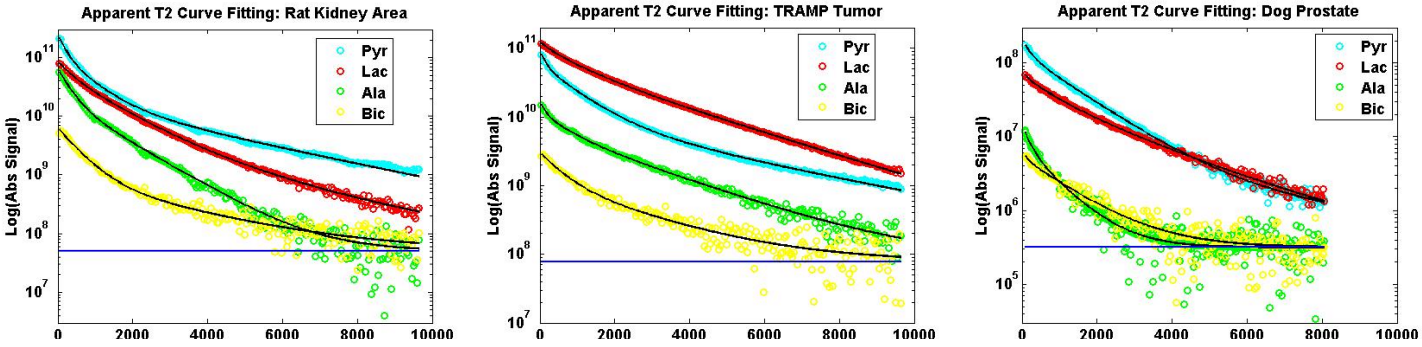

Table 1: T_2 value and percentage weight of the three components from curve fitting results.

	Rat Kidney						TRAMP Tumor						Dog Prostate					
Metabolite	T2a(1)	T2a(2)	T2a(3)	W(1)%	W(2)%	W(3)%	T2a(1)	T2a(2)	T2a(3)	W(1)%	W(2)%	W(3)%	T2a(1)	T2a(2)	T2a(3)	W(1)%	W(2)%	W(3)%
Lactate	0.35	1.10	2.80	37	56	7	0.25	0.93	2.57	12	40	48	0.11	0.80	2.27	17	38	45
Alanine	0.31	1.17	N/A	70	30	N/A	0.14	0.64	2.27	32	29	39	0.20	0.82	N/A	52	48	N/A
Pyruvate	0.20	0.69	3.17	53	40	8	0.14	0.88	3.77	37	52	11	0.22	1.24	4.71	35	63	2
Bicarbonate	0.53	2.48	N/A	86	14	N/A	0.54	2.19	N/A	63	37	N/A	0.13	1.22	N/A	23	77	N/A

Discussion and Conclusion

Because each slice is composed of various tissues including vasculature, the multiple T_2 components are expected. The apparent T_2 curves of lactate and pyruvate are best described by a three-component fit. For those fitted the best with two components (bicarbonate curve of all animals and alanine curves of rat kidney and dog prostate), their signal to noise ratios are worse than others as well and therefore, it is unknown whether those curves also contain a third T2 component or not. Lactate of rat kidney has stronger weights on the short and intermediate components, whereas lactate of tumor and prostate weigh more heavily on the long component. Pyruvate has stronger weight on short and intermediate components for all tissue types measured in this work. The *in vivo* T2 results presented here are valuable for future sequence and study designs in ^{13}C metabolic imaging applications. The T2 values and their weight distribution may vary between healthy and diseased tissues. Method for voxel-selective, tissue specific T_2 measurement will be important for the understanding of the origins of these components.

Reference:

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