Single-shot, 2D and 3D Dynamic Imaging of Hyperpolarized 13C Biomarkers In Vivo at 14.1 Tesla

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MRSI using hyperpolarized (HP) ^{13}C biomarkers can provide novel biochemical and physiological information and has been used to detect and characterize tumors in mouse models (1). For example, $^{13}C_1$ pyruvate and its byproducts are commonly used biomarkers in murine studies. Due to the dynamic nature of the system, time course images need to be acquired with high temporal resolution to better understand the kinetics (2). The rapid loss of the HP signal due to spin relaxation (T_1), RF pulse saturation, and tissue metabolism require special pulse sequences to acquire the magnetization rapidly and efficiently. In this project we developed single-shot imaging methods based on the echo-planar/fast-spin-echo hybrid (GRASE) imaging sequence (3) for acquiring 2D and 3D dynamic data at 14.1T. Using mouse models, images were acquired in about 154ms and provided excellent temporal and spatial resolution for our preliminary dynamic studies.

Experimental Methods and Materials

The experiments were done using a vertical, 14.1T Varian (Agilent) 600WB micro-imaging system equipped with 55mm 1000mT/m gradients and 40mm diameter proton and carbon RF coils. The mice were placed in a temperature controlled animal holder and anesthetized using a mixture of isoflurane/oxygen. An animal monitoring system (SA Instruments) was used to monitor respiration and trigger the scanner during all protocols. The proton coil was used for shimming and anatomical imaging and then the carbon coil was used for ^{13}C imaging. $^{13}C_1$ pyruvate was polarized using an Oxford Hypersense™ DNP instrument and 400ul of the resulting dissolution mixture containing 80mM pyruvate was administered via a jugular vein catheter. 3D images were acquired using the echo-planar based (GRASE) (3) pulse sequence shown in Figure 1, where the RF pulses are frequency selective for acquiring metabolite specific images during a time course study. For the 2D dynamic study, the 180° pulse was replaced with a slice selective pulse and the second phase encode gradients were omitted. The signals from the EPI trains were co-added to improve the SNR of the final image.

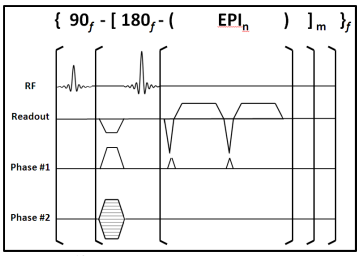

Fig. 1 - ^{13}C 3D Imaging sequence

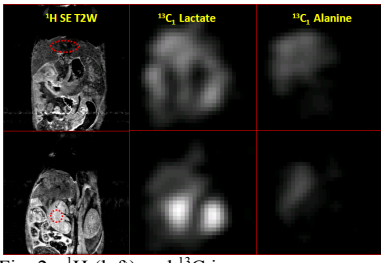

Fig. 2 - ^{1}H (left) and ^{13}C images

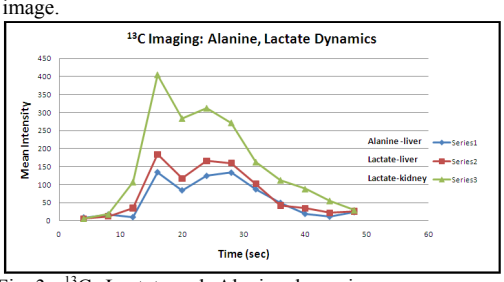

Fig. 3 - $^{13}C_1$-Lactate and -Alanine dynamics

Results and Discussion

3D single shot images of $^{13}C_1$-lactate and -alanine were acquired every 4s over a period of 48s, following the injection of $^{13}C_1$ pyruvate into a normal mouse. ^{13}C slices extracted from one of the 3D image is shown in Fig. 2, along with the ^{1}H reference image. Pyruvate is converted to alanine and lactate by the enzyme-catalyzed reaction of lactate dehydrogenase (LDH) and alanine transaminase (ALT) respectively. The images indicate lactate and alanine generation in the liver. High lactate signals are also detected in the kidneys. The lactate and pyruvate generation is better visualized in Fig. 3 where the mean signal from the liver and kidney regions (see Fig. 2) are plotted as a function of time. Since we used 90 degree excitation pulses the plot represents the rate of lactate and alanine generation during the time course experiment. Following the injection of HP $^{13}C_1$ pyruvate, its signal is rapidly depleted by metabolism and T_1. Figure 4 shows an axial, proton, reference image from a transgenic mouse prostate cancer (TRAMP) model with a large tumor along with a $^{13}C_1$ lactate (color overlay) image taken from a 2D dynamic study. After injection of HP $^{13}C_1$ pyruvate, high levels of lactate signal is detected in tumors with negligible signals from the other byproducts. Even though the tumor appears fairly uniform in the proton image, the lactate image shows a heterogeneous distribution due to differences in metabolism and perfusion (Fig. 4, 5). Dynamic plots from four regions in the tumor (Fig. 6) clearly show large differences in the rate of lactate generation. The necrotic region (series 4), for example, shows low perfusion and decreased lactate signal.

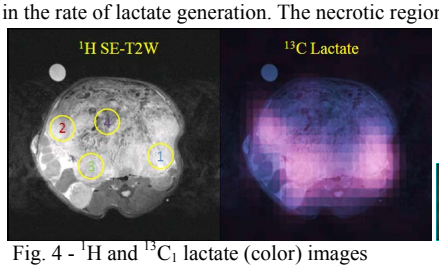

Fig. 4 - ^{1}H and $^{13}C_1$ lactate (color) images

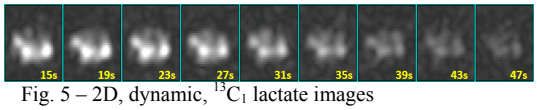

Fig. 5 – 2D, dynamic, $^{13}C_1$ lactate images

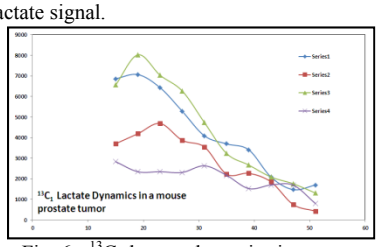

Fig. 6 - $^{13}C_1$ lactate dynamics in tumor

Summary and Conclusion

We have demonstrated, novel, single shot, imaging methods for obtaining 2D and 3D dynamic metabolic images *in vivo* at 14.1T. The pulse sequences were specially designed to acquire HP signals efficiently with high temporal resolution and SNR. The frequency selective excitation pulses and multiple refocusing pulses help to minimize some of the limitations associated with high field systems, such as, wide spectral widths and T_2* effects. Dynamic metabolite imaging is helpful in understanding the kinetics of tumor metabolism and may help, for example, to monitor and characterize tumors during drug therapy.

Acknowledgments

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References

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