SNR improvement by frequency correction and timepoint addition in dynamic 3D imaging of pre-polarized ^{13}C metabolites

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Introduction: Hyperpolarized ^{13}C substrates have become a promising tool to study real-time metabolic processes *in vivo*. Metabolic imaging using 13C-labeled compounds pre-polarized using DNP-dissolution [1,2] has been shown to characterize prostate, heart and cancer metabolism noninvasively using chemical shift imaging (CSI) techniques [1]. Time-resolved imaging is advantageous for imaging DNP compounds because the transport of the substrate to the tissue is variable, as is the time-course of substrate conversion to metabolic products. Previously, a rapid spectral-spatial echo-planar imaging (ss-epi) pulse sequence was developed [3] for time-resolved 3D metabolic imaging with correction for the spatial shifts that occur in practice due to field inhomogeneities. However, the temporal resolution comes at the expense of low SNR for most of the timepoints. In this work, an automated method was developed to create higher SNR images by correcting the spatial shifts and summing k-space data from multiple time points above a set SNR threshold.

Methods: *In vivo* studies were performed using a GE MR750 3 T scanner (GE Healthcare, Waukesha, WI) and a micro-strip dual-tuned 1H-13C rat coil (Magvale, San Francisco, CA). All animal experiments followed a protocol approved by the local institutional animal research committee. A HyperSense DNP polarizer (Oxford Instruments, Abingdon, UK) was used to polarize neat (99% purity) [1-13C] pyruvic acid for 1 hour following previously described methods [1]. Tail-vein injections of 2.0mL/80mM of pre-polarized [1-13C] pyruvate were performed in RNU nude rats (n=3) implanted with U87 tumors in the flank. The injections were 10 seconds, with data acquisition started at the beginning of the injection. A spectral-spatial excitation pulse was designed with 18.2 ms pulse duration, giving a 120 Hz spectral passband width (FWHM). Time resolved 3D images of pyruvate, lactate and a urea reference were acquired with 5 s temporal resolution over a minute duration in each study, acquiring images of 5 mm isotropic spatial resolution, field of view: 8 cm A/P, 8 cm R/L and 6 cm S/I.

The images were acquired by reversing the k-space trajectory for every other time point obtaining a spatial shift of reversed direction between time points as described previously [4]. A script was programmed in Matlab (The MathWorks Inc., Massachusetts, USA) to automatically find the timepoints with SNR better than a threshold (i.e. SNR > 2), calculate the spatial shifts between timepoints using mutual information [5], correct for the resulting mis-registration with a phase ramp in the k-space data, and finally adding the selected timepoint images obtaining a higher SNR image as described in the flow chart in Fig. 1.

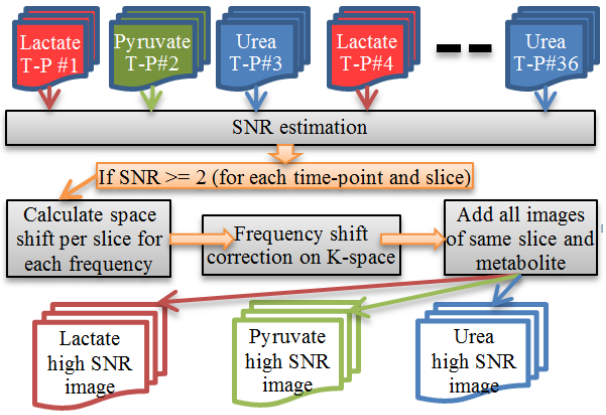

Figure 1. Flow chart of the image processing script.

Results: Representative images of Lactate resulting from the pulse sequence are shown in Fig. 2. The left panels are the highest SNR time point for each slice (t=50s for A, t=64s for C, t=85s for F). Note the excellent correspondence between ^{13}C signal and anatomical detail in the T2-weighted images. Table 1 shows Lactate SNR of single time points and after addition of all time points for each rat and respective slices. For almost all slices the SNR increased by a factor of 2 or more, the least SNR improvement was 60% as in the case of the kidneys slice in rat #1. Even though temporal information is lost by summing the timepoints, this method gives important information about relative signal (lactate) levels over different regions of the entire tumor or organ (e.g. kidneys) and can be especially useful when spatial resolution is increased resulting in low SNR in the time-resolved images.

Conclusions: This study demonstrated that it is possible to obtain hyperpolarized ^{13}C maps of the substrate and metabolites of higher SNR and excellent contrast by correcting the spatial shifts and summing k-space data from acquisitions of temporally resolved metabolic imaging data with modest SNR. With this technique we can still use the temporal resolution of the dynamic images and then create a higher SNR image for better depiction of the metabolites. The tradeoffs between spatial-temporal resolution and image quality inherent in this technique will be explored further in future studies.

Acknowledgments: Funding from the Heart and Stroke Foundation of Ontario NA7074 and the Ontario Institute for Cancer Research

References

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Table. 1: Lactate SNR of single time points and after addition of all time points for each rat and respective slices

		Max SNR single time point	SNR after time points addition
Rat #1	Tumor slice1	13.2	25.7
	Tumor slice2	8.7	18.1
	kidneys	9.1	15.5
Rat #2	Tumor slice1	10.4	20.8
	Tumor slice2	6.8	12.9
	kidneys	15.9	30.3
Rat #3	Tumor slice1	14.4	27.5
	Tumor slice2	9.8	19.3
	kidneys	18.2	33.8

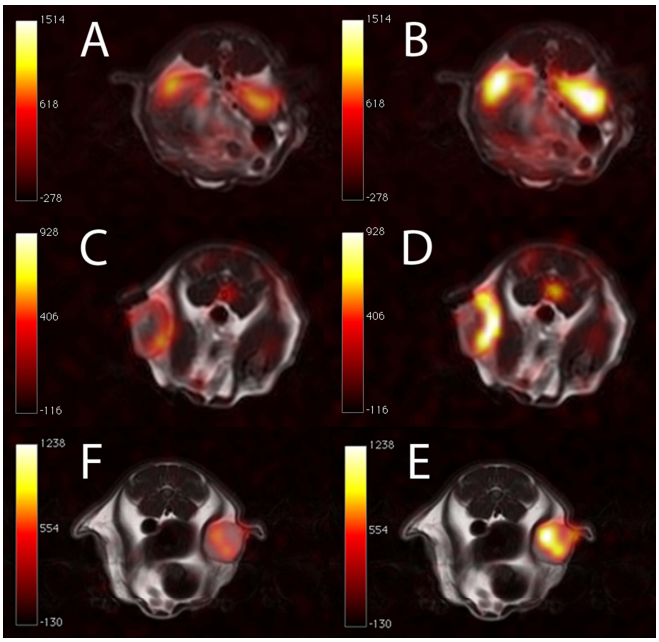

Figure 2: Lactate within the rat kidneys (A and B). A is the highest SNR time point. B is the result of adding all time-points together. Similarly C, D, F and E are Lactate images of a tumor for 2 different rats. C and F are the highest SNR single time-points. D and E are the result of adding all time-points together.