Chemical Shift Selective Imaging of Hyperpolarized $^{13}$C Using Variable Phase Balanced Steady-State Free Precession

A. K. Grant$^1$, E. Vinogradov$^1$, X. Wang$^1$, H. Wang$^1$, P. K. Seth$^1$, V. P. Sukhatme$^2$, D. C. Akop$^1$, and R. E. Lenkinski$^1$

$^1$Radiology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, United States, $^2$Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, United States

**Introduction:** $^{13}$C spectra acquired using hyperpolarized pyruvate show a relatively sparse collection of spectral lines. Typically, spectra are dominated by pyruvate and lactate, with smaller signals from alanine, pyruvate hydrate, and bicarbonate. Several imaging strategies have been proposed to exploit the sparsity of hyperpolarized $^{13}$C spectra, including spiral CSI [1], multi-echo techniques [2-4], and compressed sensing [5]. Here we demonstrate that chemical-shift selective images can be obtained by acquiring a series of balanced steady-state free precession (bSSFP) images with a variable RF phase advance. Similar imaging strategies make use of variable TR have been proposed previously for proton imaging [6,7].

**Theory:** In the bSSFP steady state, the magnitude and phase of the transverse magnetization depend on the chemical shift $\Delta$ relative to the center frequency of the acquisition. The steady state has singular points at chemical shifts $\Delta_{k}=(k+1/2)/TR, k=0, \pm 1, \pm 2, \ldots$. The transverse magnetization increases and changes sign at each of singular point as illustrated in Fig. 1. In the idealized limit of a small tip angle $\alpha$, a short TR, and very long $T_1$ and $T_2$, the transverse magnetization has a relatively weak dependence on $T_1$ and $T_2$. The location of the singular points can be shifted by modifying the phase advance $\phi$ between successive RF pulses. In standard bSSFP imaging the phase advance is set to $\pi$ radians to obtain a series of pulses with tip angles $+\alpha, -\alpha, +\alpha, -\alpha, \ldots$. For other values of $\phi$, the singular points are shifted to $\Delta_{k}=(k+\phi^{2}/2\pi)/TR, k=0, \pm 1, \ldots$ (Fig. 1b). These properties of the steady state can be exploited to obtain spectrally selective images of multiple metabolites by acquiring images at several values of $\phi$. Fig. 1c shows the signal from a single metabolite as a function of the RF phase advance, illustrating a singular point at $\phi=\pi/2$. The location of the singular point, which is different for each metabolite, can be used to separate signals from different metabolites. For suitable values of TR, each metabolite will have a distinct profile, and images of each metabolite can be reconstructed by fitting the image intensity as a function of $\phi$ to a sum of profiles like the one shown in Fig. 1c.

**Images in Phantoms:** A bSSFP pulse sequence (Bruker Corporation, Billerica MA) was modified to incorporate a variable RF phase advance. A total of 100 images were continuously acquired in 10 blocks of 10 images each, and each block was acquired with a successively larger value of the phase advance to cover the range from 0 to $2\pi$. An $\alpha/2$ preparation pulse was applied prior to each block, and a crusher gradient was applied after each block. Fig 2a shows a proton image of two phantoms containing $^{13}$C labeled acetate and t-butanol acquired in a 4.7T scanner (Bruker Biospec). Fig 2b shows $^{13}$C images acquired at increasing values of the phase advance using TR=2.208ms and a small ($\sim 5^\circ$) tip angle. For this choice of TR, the signals from acetate and t-butanol can be readily distinguished through their dependence on the phase advance. The measured signal intensity from the acetate phantom is shown in Fig. 2c. Fig 2d shows images of acetate and t-butanol obtained by fitting the data of Fig. 2b to profiles of the type shown in Fig. 1c.

**In Vivo Images:** These techniques can be applied to metabolic imaging of pyruvate and lactate in vivo. Figure 3 shows proton, pyruvate, and lactate images acquired in the kidneys of a normal mouse 40 seconds after administration of 250 micromolars of 80mM hyperpolarized pyruvate solution. Techniques for animal preparation and administration of pyruvate have been described previously [8]. The Institutional Animal Care and Use Committee approved all methods. Scan parameters were 5cm FOV, 8mm slice, 32x32 matrix, TR=2.448ms, 32kHz bandwidth, 10° tip angle, 7s scan time. Note that the total scan time is set by the use of 10 images per phase advance block; the acquisition could be shortened by up to a factor of 10. The pyruvate signal is heavily concentrated near the renal pelvis, while uptake and metabolism results in a more uniform distribution of lactate. These techniques can be extended to three spectral lines. t-butanol has been proposed as a freely diffusible perfusion agent [9]. Pyruvate and t-butanol can be polarized and administered in a single bolus to obtain simultaneous images of perfusion and metabolism. Fig. 4 shows proton, pyruvate, lactate, and t-butanol images acquired in a TRAMP mouse 45 seconds after administration of a solution containing 80mM pyruvate and approximately 2% t-butanol by volume. Imaging parameters were as in Fig. 3, except that TR=2.22ms was chosen to optimize separation of pyruvate, lactate, and t-butanol. The proton image shows a soft tissue mass, possibly a tumor, in the vicinity of the prostate. This mass also shows high lactate signal, in accordance with the findings of Ref. [10]. The chemical specificity of these images is validated by the signals seen in the phantoms on each side of the image, which contain t-butanol (right) and acetate ($\sim$43Hz from lactate) on the left.