Sensitivity of hyperpolarized 13C kinetic modeling to flip angle and number of temporal samples

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INTRODUCTION Dynamic imaging of hyperpolarized ^{13}C with MRI provides metabolic kinetics with spatial localization *in vivo* [1] but is challenging because both T_1 decay and RF decay reduce the hyperpolarized signal throughout the experiment. A low flip angle and reduced number of RF excitations are typically used to mitigate RF decay. This enables acquisition of multiple time points at the sacrifice of image signal to noise ratio (SNR). Simulations presented in this study investigate kinetic modeling accuracy using a centric Cartesian trajectory in which flip angle and temporal sampling are traded off against SNR. A minimum SNR of dynamic images is then recommended to achieve reliable modeling accuracy of < 10% error.

METHODS A digital phantom for pyruvate and lactate was developed based on the two-site exchange model [2] with p_P=1/30s^{-1}, k_P=0.05s^{-1}, and k_L=0.03s^{-1} chosen to produce dynamics typically seen *in vivo*. RF decay of the signal was accounted for using $M_{z,n+1}=M_{z,n}*\cos(\alpha)$ where α is the flip angle. A Cartesian gradient echo dynamic imaging sequence was simulated by sampling the digital phantom with TR=48ms using centric phase encode ordering. Zero-mean Gaussian noise was added to the real and imaginary components of k-space to achieve an image SNR of ~50 for pyruvate at t=10s for a α = 5°. The initial image of all simulations was selected to be t_0=10s. The mean signal of the magnitude images was corrected for RF decay and subsequently fit to the two-site exchange model. A parameter space of flip angle (α =1°-20°) and temporal samples (2-12 images) was used to investigate the accuracy of the reconstructed metabolite images using a temporal resolution of Δt=5s and Δt=10s. Variations of the initial image timing (t_0) of ± 3s did not significantly affect the accuracy. The composite percent error, defined by the mean percent error of the model parameters, was plotted against SNR of the last image to investigate the lower bounds of image quality without sacrificing kinetic modeling accuracy.

RESULTS Simulation results are displayed in Figure 1. A temporal resolution of Δt=5 provides more robust modeling as indicated by the area of parameter space with error below 10%. Figure 1 (e-f) demonstrate that k_L is the most sensitive to acquisition parameters, most likely because its value is most sensitive to SNR as it is the lowest of the three parameters used to construct the phantom. Two parameter sets (arrows Figure 1) that produced a mean percent error of less than 3% of all three model parameters were compared in Table 1, demonstrating equivalent kinetic modeling accuracy using vastly different acquisition parameters. Figure 2a,b display the SNR of the last pyruvate and lactate images for the same parameter space shown in Fig. 1 a,c,e. As the SNR of the last image decreases, inaccurate modeling parameters result. Figure 2c compares the SNR of the last image to the composite percent error of the three model parameters, demonstrating the model accuracy suffers if the SNR falls below ~10. For any parameter set that produced a final pyruvate and lactate image SNR of greater than 15, the composite percent error was below 6%.

DISCUSSION This work explores the tradeoff between flip angle and acquired number of images for kinetic modeling of ^{13}C MRI. Simulations demonstrate that accurate parameter estimation can be made as long as the resulting SNR is sufficient (Figure 2c). These results suggest that accurate model fitting is relatively insensitive to flip-angle, temporal samples, and image timing. Even in the presence of noise, accurate kinetic parameters can be obtained from as few as 3 temporal samples with a moderately high flip angle (Table 1). A Cartesian acquisition was studied first because of wide availability and robustness to off-resonance artifacts. Future work will consider more time-efficient acquisition techniques like EPI [3] and spiral [4] trajectories that will allow even higher flip angles to be used because fewer RF-excitations are needed. For example, the SNR gain from using a higher flip angle can then be spent acquiring at a higher spatial resolution rather than increasing the number of temporal samples. Incorporation of independent flip angles for pyruvate and lactate with a spectral spatial pulse [5] may provide a further SNR advantage when used with a generalized kinetic model that incorporates flip angles for pyruvate and lactate species.

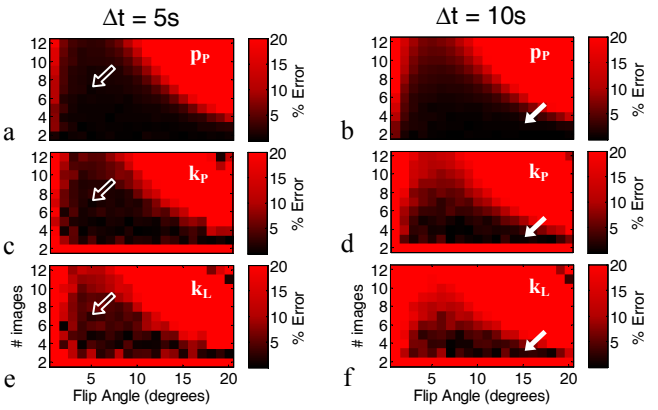

Figure 1. Number of acquired images and flip angle were simulated and fit to the two-site exchange model using a temporal resolution of Δt=5s (a,c,e) and Δt=10s (b,d,f), with the initial image beginning at t_0=10s, and 16 phase encodes. Maps display percent error of estimated model parameters p_P (a,b), k_P (c,d), and k_L (e,f) over 50 simulations with independent noise realizations with peak SNR of ~50. Arrows depict the experimental parameters used in Table 1 chosen based on a composite error of <3% for all parameters.

	Δt (s)	Flip	# samples	pP (s^{-1})	kP (s^{-1})	kL (s^{-1})
Truth				0.0333	0.0500	0.0300
1	5	5°	7	0.0331 ± 0.0004	0.0504 ± 0.0030	0.0308 ± 0.0029
2	10	15°	3	0.0331 ± 0.0004	0.0504 ± 0.0045	0.0307 ± 0.0053

Table 1. Sensitivity of simulated kinetic values for flip angle and sampling resulting in minimum composite error (<3% for all parameters) using a Cartesian acquisition (arrows in Figure 1) with 50 noise realizations.

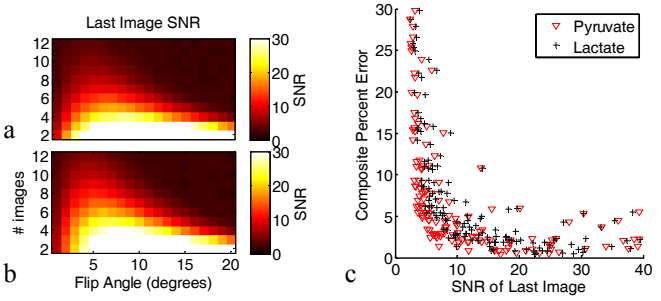

Figure 2. SNR of the last acquired (a) pyruvate and (b) lactate image with t_0=10s and Δt=5s temporal resolution over the same parameter space as in Figure 1a,c,e. (c) The composite percent error of the three kinetic model parameters plotted against the SNR of the last acquired pyruvate and lactate images over all parameter space. This display reveals the sensitivity of model accuracy if there is insufficient SNR. To achieve a mean percent error of less than 10%, SNR of the last metabolite images should exceed 15 for a temporal spacing of Δt=5s for both pyruvate and lactate.

References

[1] Golman *et al*., Acad Radiol. 2006;13(8).
[2] Day *et al*., Nat Med. 2007;13(11).
[3] Cunningham *et al.*, J Magn Reson. 2008;193(1).
[4] Mayer *et al*., J Magn Reson. 2010;204(2).
[5] Larson *et al.*, J Magn Reson. 2008;194(1).

Acknowledgements

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