A novel Bloch-McConnell simulator for perfused hyperpolarized substrates

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TARGET AUDIENCE

This work may be of interest to investigators that are focused on developing methods for acquiring and/or processing MR data from hyperpolarized agents.

PURPOSE

Recently, the dramatic signal increase resulting from dynamic nuclear polarization has been leveraged for real time ^{13}C MRS in-vivo[1]. Specifically, the conversion of hyperpolarized [^{13}C]pyruvate to [^{13}C]lactate has been shown to correlate well with cancer presence, stage, and response to therapy[2]. Hyperpolarized (HP) signal differs from conventional MRI; magnetization is non-renewable, thus relaxation processes and depletion of longitudinal magnetization during RF excitations represent a permanent loss of signal. Detection and processing of HP data differs from conventional acquisition strategies, and requires careful optimization to maximize data quality. In this work, we describe a novel simulation environment that couples pharmacokinetic modeling of substrate delivery with enzyme kinetics and basic spin physics, enabling systematic study of sequences and acquisition strategies using numerical HP phantoms that mimic biological systems via kinetic models. We used this environment to determine the effects of perfusion on the accuracy of measurements made using a basic pulse-acquire sequence with a range of repetition times (TR) and excitation angles (FA).

METHODS

Custom software was developed using Matlab to process the Bloch equations coupled with kinetic models for enzyme activity and substrate delivery. The Bloch equations were defined using the formalism developed by McConnell[3] for two exchanging spin pools. In the case of a perfused system, pyruvate delivery was modeled by a gamma variate function. For the closed (non-perfused) system, pyruvate was assumed to be present at its maximum concentration at the start of data acquisition (Figure 1). Simulations of closed and perfused systems were performed for a pulse-acquire sequence with a range of FAs and TRs. Signal from the resulting dynamic FIDs were calculated by HHFW integration of metabolite peaks yielding metabolite concentration curves. The curves were fit to muti-compartment models using a least squares algorithm. The resulting exchange constant for pyruvate to lactate (k'_{pl}) were compared to the exchange constant assumed in the numerical phantom to determine the accuracy of the detection and modeling strategy.

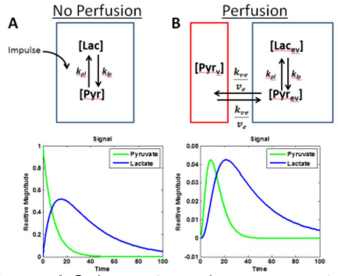

Figure 1 Schematic and representative Signal from a non-perfused system (left) and perfused system (right)

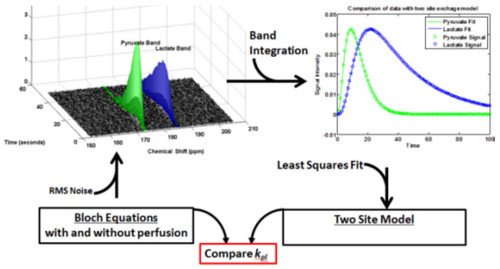

Figure 2 Schematic of the Simulation, processing and modeling procedure.

RESULTS

Surface plots of accuracy across a range of FAs and TRs are shown in figure 3. For the closed system, measurements recapitulate k_{pl} across a range of TRs and FAs (Fig 3.a). The accuracy of measurements using the perfused system was much more sensitive to FA and TR, yielding a band of sequence parameters that yield accurate measurements.

DISCUSSION

Model-based analysis of the closed system begins to perform poorly at very low FAs where there is not enough signal or very high FAs where the entire signal is expunged before significant lactate conversion. While the perfused system was similarly impacted by low FA measurements, it was much more sensitive to TR. Long repetition times would miss much of the pyruvate input thus hindering the ability to accurately fit the data. At higher FAs the fresh pyruvate flowing in compensates for the drastic signal loss at each excitation, yielding more accurate fitting.

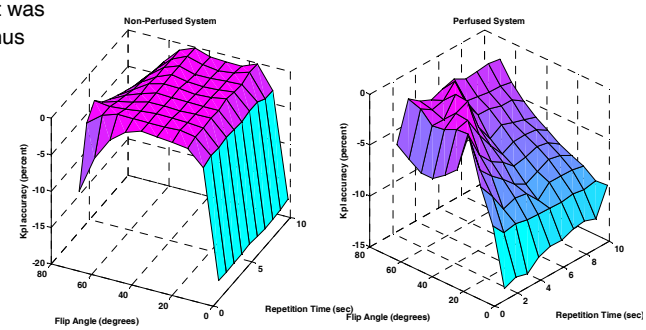

Figure 3 Accuracy of measured exchange constant (k_{pl}) for non-perfused (left) and perfused (right) systems across a range of FAs and TRs.

CONCLUSION

Using a novel Bloch simulator we were able to explore the effect of sequence parameters on the measured exchange rate for two different models of hyperpolarized label delivery. While the pulse acquire studies simulated were simplistic, the results show that sequence parameters can significantly impact results. The platform described was built to accommodate a wide range of biologic and kinetic models as well as advanced pulse sequences. It is critical to understand the effect of sequence parameters and modeling assumptions on measurements the use of HP agents enters clinical trial. This system will be ideally suited to elucidate those relationships and guide investigators toward efficient and accurate use of sequences, models, and reconstruction algorithms.

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