Ongoing Dual-Angle Measurements for the Correction of Partial Saturation in 31P MR Spectroscopy

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Introduction

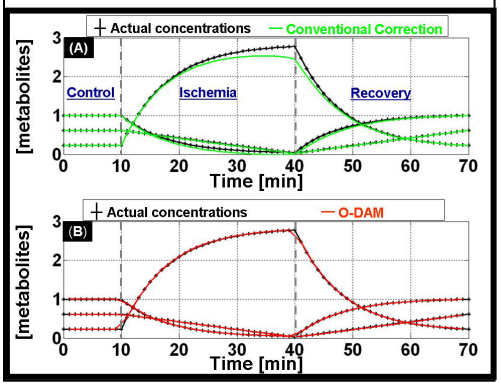
Interventional studies using ^{31}P Magnetic Resonance Spectroscopy (MRS) are typically designed to detect changes in the levels of metabolites integral to tissue bioenergetics, namely, adenosinetriphosphate (ATP), phosphocreatine (PCr) and inorganic phosphate (Pi). Use of a repetition time (TR) similar to, or shorter than, metabolite T1's is common in ^{31}P MRS of biological samples and living systems in order to improve signal–to–noise ratio. However, spectral resonances acquired with short TR values exhibit saturation effects that are generally corrected using saturation factors measured with a longer TR at the control phase of an intervention (1,4). Such corrections may lead to large errors in quantification in the presence of chemical exchange or if T1's change throughout the experiment. We describe an approach to quantification in the setting of such chemical-kinetic changes which is based on performing ongoing dual–angle measurements (O-DAM) throughout an experiment.

In particular, the goal of the present work was to analyze the ability of O-DAM to provide correct metabolite measurements in the setting of changing metabolite levels, chemical exchange rates, and T1's. O-DAM is a local-in-time saturation correction method based upon use of an apparent T1 calculated at sequential pairs of steady-state data acquisition time points acquired with different flip angles, α and β (2,3). Here, we extend this by evaluating the effects of changes in metabolite levels, T1's, and reaction rates, and compare the results with those obtained using the conventional correction for partial saturation. We use parameters appropriate to the perfused rat heart as our model system.

Methods

For definiteness, the metabolic time course of cardiac hypoxia was modeled as a process in which [PCr] and [ATP] decreased from baseline, with a corresponding increase in [Pi] (Figure 1). T1's and reaction rates were constrained to change linearly from a control to an end-ischemia value. Recovery was also simulated similarly. The one-pulse experiment was simulated, incorporating chemical exchange effects, at each time point using flip angles of α = 15° (α period) followed by a flip angle β = 60° (β period) (4). Input parameters (Mo's, T1's, and reaction rates) were defined for the α and β periods from the prescribed time courses of these parameters. Quantification according to O-DAM and the conventional correction for partial saturation was performed separately for each (α, β) pair (3). Literature parameters were used for the analysis: Mo(PCr) = 1.00, Mo(β-ATP) = 0.62, Mo(Pi) = 0.23; T1(PCr) = 2.78s, T1(γ-ATP) = 0.64s, T1(Pi) = 2.40s; $k_{(PCr\rightarrow\gamma\text{-}ATP)}$ = 0.70s $^{-1}$, $k_{(PCr\rightarrow\gamma\text{-}ATP)}$ = 0.20s $^{-1}$; and during the ischemic phase: Mo(PCr) = 0.05, Mo(β-ATP) = 0.03, Mo(Pi) = 2.78; T1(PCr) = 2.22s, T1(γ-ATP) = 0.50s, T1(Pi) = 3.60s; $k_{(Pi\rightarrow\gamma\text{-}ATP)}$ = 0.37s $^{-1}$, $k_{(Pi\rightarrow\gamma\text{-}ATP)}$ = 0.11s $^{-1}$, with TR = 0.25 s (5). Quantification errors were expressed as percent departures from the known input metabolite concentration values.

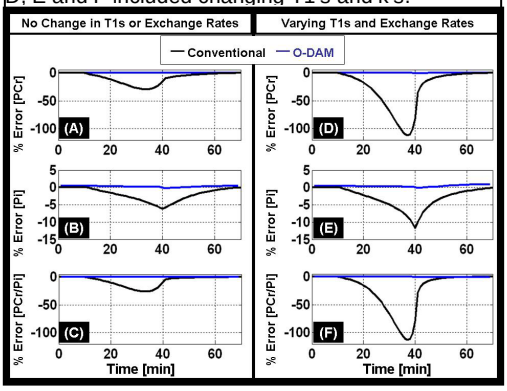
Figure 1. A) Conventional vs. B) O-DAM correction of simulated hypoxic intervention.



Results

The accuracy of the correction for partial saturation using the O-DAM and conventional corrections for the simulated cardiac hypoxia experiment are shown in Figure 1. As seen, the O-DAM correction resulted in substantially improved quantification accuracy as compared to the conventional correction, particularly as hypoxia progressed. In contrast to the case with conventional correction, varying M_0's, T1's, and reaction rates throughout the course of the experiment had little effect on the performance of the O-DAM correction (Figure 2). Figure 3 shows the signal intensity of PCr obtained from ^{31}P MRS of a perfused rat heart, with and without O-DAM correction; note alternation of signal intensities, reflecting use of alternating flip angles.

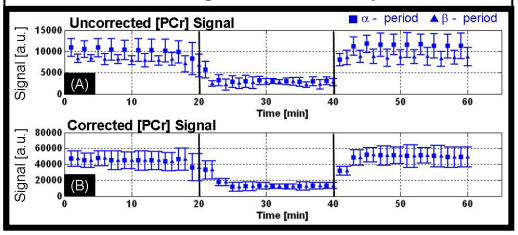
Figure 2. Percent error in metabolite levels resulting from conventional vs. O-DAM correction. A, B, and C simulated with no change in T1's or k's; whereas D, E and F included changing T1's and k's.



Discussion

Metabolite quantification is of importance in ^{31}P studies of tissue bioenergetics and has formed the basis of innumerable studies of cellular, tissue, and organism response to metabolic stress, and of bioenergetic baseline differences between groups. Comparison of the time course of metabolite changes in intervention protocols between experimental groups defines relative sensitivity to stress and capacity for energy repletion after e.g. reflow, reoxygenation, or discontinuation of stimulation. Partial saturation effects in these experiments have traditionally been corrected by use of saturation factors measured during a control period; however, this approach does not account for the chemical exchange exhibited in biological systems nor for changes in reaction rates and T1's (4). Our simulations indicate that the O-DAM correction can lead to markedly improved quantification accuracy in dynamic experiments in which these chemical-kinetic parameters vary. These results can readily be extended to other ^{31}P studies of other organ systems, including skeletal muscle and brain. In conclusion, the O-DAM correction procedure permits accurate monitoring of metabolite concentrations even in the setting of chemical exchange and changing chemical-kinetic parameters.

Figure 3. O-DAM correction of experimental [PCr] measurements in a perfused rat heart by 31P MRS.



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