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

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Introduction

The use of repetition times (TR) which are short relative to metabolite T_1's is common in NMR spectroscopy of biological samples. Spectral resonances acquired with short TR values exhibit saturation effects, which must be corrected when accurate quantification of metabolite concentrations is required. However, correcting for saturation effects can be problematic when chemical parameters change, such as during intervention procedures, e.g. ischaemia/reperfusion or hypoxia. These issues have been discussed in previous studies, with no suitable approach to correct for saturation effects emerging besides the use of a lengthy TR (1).

In this work, we describe an approach to metabolite quantification in the setting of changing metabolite concentrations which is based on a recently proposed continuous dual–angle method (2). Apparent T_1 values obtained from each pair of dual–angle measurements are used to correct the resonance amplitudes observed during that pair of measurements for the effects of saturation. Simulations appropriate to a hypoxic intervention experiment in the heart were performed. We find that accurate metabolite concentrations can be determined when metabolite changes are modest, and that more accurate results are obtained from corrections applied to the smaller of the two angles in the dual-angle measurement.

Methods

The method was evaluated using parameters appropriate to the isolated perfused heart. Additionally, a hypoxic intervention experiment was simulated using a model in which phosphocreatine (PCr) decreased from baseline with a corresponding increase in inorganic phosphate (Pi). The one-pulse experiment at steady-state was simulated (3) for a data acquisition using a flip angle α (α period) followed by data acquisition with flip angle β (β period). The TR was taken to be the same during both periods. Input parameters (M_0's, T_1's, and reaction rates) were prescribed for the α period, and are referred to as α parameters. Similarly, a set of β parameters was prescribed. For a stable system, the α and β parameters would be identical, while for an intervention experiment, they are all subject to change. In the current study, only the M_0's were allowed to vary. Observed magnetizations were calculated according to the model for steady-state resonance amplitudes incorporating the effects of chemical exchange (3). An apparent T_1 of a given metabolite was calculated from the ratio of the simulated magnetizations for the two different flip angles (4), and then used to correct observed magnetizations for saturation effects. The concentration of ATP was taken as constant throughout, as was the sum of PCr and Pi, so that a change in PCr was accompanied by a corresponding opposite change in Pi. This pattern of metabolite change is commonly seen in bioenergetic experiments. The change in M_0's between α and β periods was described by the fractional decline (*f*) in PCr that occurs between α and β periods. Furthermore, percent errors resulting from this procedure were determined over the time course of a simulated experiment. We present results using flip angles of 15° and 60°, and TR = 0.25 s.

Results

Figure 1 shows the net effect of errors in the individual metabolites on the ratio of PCr/Pi. The error during the β-period rapidly becomes unacceptable, even for relatively small changes in PCr. In contrast, the error during the α-period remained within 10% for a fractional change in PCr of up to 0.05, and within 20% for *f* up to 0.1. As expected, the results demonstrate that a greater degree of accuracy can be achieved for smaller fractional changes in PCr. Figure 2 shows the actual vs. corrected magnetization values for a simulated time course of PCr and Pi during an intervention protocol (e.g. cardiac hypoxia and normoxia). The % error plot indicates that the errors in corrected concentrations are greatest during the periods of most rapid metabolite change. Nevertheless, the errors in the values obtained by correcting the data acquired during the smaller of the two flip angles in the dual-angle measurement are reasonably small (< 20%).

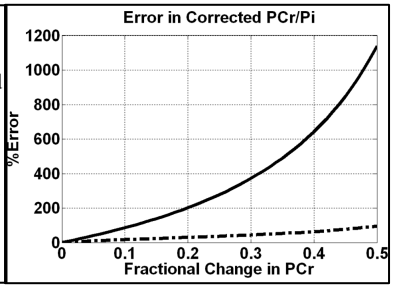

Figure 1: Percent error in corrected PCr/Pi for α (dotted line) and β (solid line) periods as function of a fractional decline, *f*, in PCr.

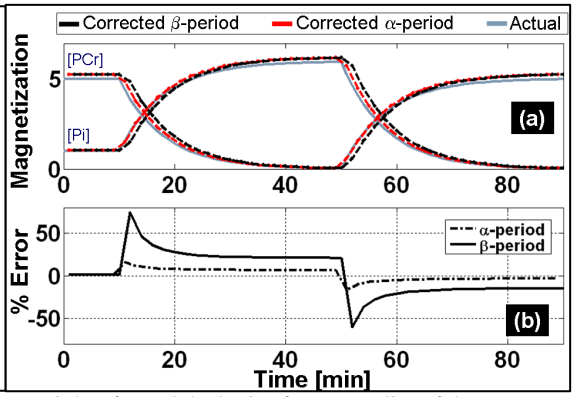

Figure 2: A) Actual vs. corrected values in PCr and Pi concentration derived from the α and β periods, respectively, during a simulated intervention experiment. B) Percent error in PCr/Pi.

Discussion

Accurate metabolite quantification is of importance in ^{31}P studies of tissue energetics, hence, it has formed the basis of many studies of the response to metabolic stress in the heart, muscle, and brain. One of the recently recognized issues in correcting metabolite concentrations through use of saturation factors is the effect of chemical exchange (3). The present work indicates an approach to performing this correction by collection of data at two flip angles alternately throughout the experiment. The goal was to determine whether accurate metabolite measurements could be performed using partially saturated spectra, given the effect of metabolite concentration changes on saturation factors in the presence of chemical exchange. We were able to establish general properties of the dual-angle correction method and obtain results which are applicable to actual experimental situations. While calculation of the saturation corrections uses data acquired at both the smaller and larger flip angles, we find that correction for partial saturation can be accomplished for a much greater range of metabolite variation when it is applied to the data acquired for the smaller of the two flip angles. In conclusion, this work demonstrates the feasibility of using continuous dual–angle data collection to correct for partial saturation of metabolite resonances in bioenergetic experiments.

References

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