Comparison between internal and external validation of in vivo 31P MRS quantification

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Introduction:

Quantification of MRS signals is possible with an internal or external reference. The ^1H_2O signal has commonly been used as an internal reference for ^{1}H MRS data (e.g. in LCModel). Unlike ^{1}H MRS, ^{31}P MRS does not have a reliable internal reference; therefore external references have been generally used [1]. However, it is difficult to validate the result of an external reference. In this work, we propose to use phosphocreatine (PCr) concentration, obtained from *in vivo* ^{1}H MRS in LCModel, as an internal reference for ^{31}P metabolites quantification and compare it with the results determined by using the external reference of inorganic phosphate (Pi). Our goal is to validate quantification of ^{31}P metabolites using Pi phantom data, thus eliminating the need for *in vivo* ^{1}H scans while still affording the same capabilities of ^{31}P metabolite quantification.

Methods:

All MR studies were performed on a Varian 4T whole-body MR system using a ^{31}P-^{1}H dual head coil. Five healthy volunteers were consented and participated in the study. The region of interest for this study was an 8 ml and 12 ml voxel from the anterior cingulate (ACG) for ^{1}H and ^{31}P MRS, respectively. The ^{1}H spectra were obtained using the single-voxel PRESS sequence (2 x 2 x 2 cm voxel size) and the ^{31}P spectra were acquired using a one-pulse 3D MRSI sequence with a three-dimensional spherical sampling scheme (13 x 13 x 13 data matrix, 24 x 24 x 24 cm FOV). A 3D MDEFT image was also acquired for the determination of tissue contents within MRS voxels and the voxel positioning. Analysis of the ^{31}P data was performed by the single voxel reconstruction method, which allows spatial positioning of the center of the ^{31}P spectral voxels to be the same as that of the ^{1}H MRS voxels. *In vitro* ^{31}P phantom data were ascertained from a 50mM Pi solution using the same sequence and coil as the *in vivo* ^{31}P MRSI studies. For comparison, two methods were used for data analysis: the first method relies on PCr levels of *in vivo* ^{1}H data while the second method uses Pi levels of *in vitro* ^{31}P phantom data for the reference to determine the *in vivo* ^{31}P metabolites concentration.

For method 1, ^{1}H MRS data were analyzed by LCModel with water-suppressed and water-unsuppressed ^{1}H MRS data. The concentration of PCr can be determined by using the ^1H_2O signal as a reference from the water-unsuppressed MRS at the same voxel. Then, one can use the determined PCr concentration as an internal reference to estimate all other ^{31}P metabolite concentrations with ^{31}P MRS spectra. All *in vivo* data (^{1}H and ^{31}P) were quantified and accounted for tissue volume (compartmentalization), receiver gain, and relaxations. Here, we assume that the "partial volume" effect of these two voxels (8 *vs.* 12 ml) is negligible.

Method 2 used a two-liter spherical phantom containing a 50 mM Pi solution as an external reference to determine the *in vivo* ^{31}P metabolite concentrations. The phantom ^{31}P MRS data were collected temporally adjacent to the subject acquisition. The *in vivo* ^{31}P MRS data were also adjusted for tissue volume, receiver gain, and T1 relaxation when using *in vitro* Pi signal as a reference. All ^{31}P MRS data were analyzed by using JMRUI software.

Results:

Figure 1 is a plot of Pearson correlation for all phosphorus metabolite concentrations (PCr, P_i, α-, β-, and γ-ATP, PME, and PDE) as determined by methods 1 and 2. A fitted line reveals a slope of 0.937 with an R^2 value of 0.925, indicating an approximate 1:1 relationship between these two methods. In addition, all metabolite concentrations are well within reasonable and expected physiological values.

Discussion:

Healthy subjects receiving both ^{1}H and ^{31}P MRSI scans has proven valuable in obtaining important bioenergetic information (e.g., ADP level) and the absolute concentration of high-energy phosphate metabolites [1], but the lengthy protocol may not be practical for patients with mental disorders or other physical conditions. The replacement of *in vivo* ^{1}H scans with *in vitro* ^{31}P scans will drastically reduce the amount of time that subjects spend inside the scanner, which is of particular benefit to clinically oriented studies. The slope of nearly one and high R^2 value indicate that phantom calibrated metabolite quantification is a very promising method. It should be noted that both methods are slightly limited in that ^{31}P T_1 and T_2 corrections cannot be made specific to gray and white matter content due to no such T_1 and T_2 data available, however both methods yield concentrations well within physiological ranges. Our results demonstrate that using the *in vitro* Pi signal as a ^{31}P external reference can be reliable and practical for the quantification of *in vivo* high-energy phosphate metabolites concentration.

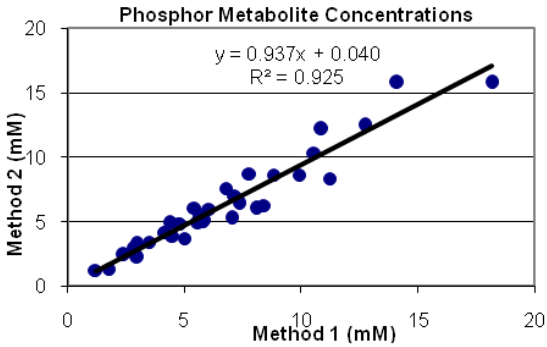

Fig 1. Comparisons of ^{31}P concentrations between two methods.

References: 1) Pan JW and Takahashi K. Ann Neuro 2005;57:92-97