Comparison of methods for quantitative in-vivo 31P and 1H MRS in human brain

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Methods

The following four ^{31}P and ^{1}H spectra were acquired twice from each one of six volunteers:

For all three calibration strategies: The classical in-vivo ^{1}H metabolite spectrum was acquired with a head coil, water-suppression, 128 averages, 9 ml PRESS VOI, 135 ms T_E and 5 s T_R. The ^{31}P spectrum was obtained with the same double-tuned head coil, 64 averages, 150 ml ISIS VOI and 12 s T_R. All ^{1}H and ^{31}P spectra were fully relaxed and T_2-effects of ^{1}H were taken into consideration. In order to find the most robust calibration strategy, we implemented and compared three different methods for both, ^{31}P and ^{1}H MRS:

1) Tissue water was used as an internal homonuclear reference for ^{1}H MRS and as an internal heteronuclear standard for ^{31}P MRS, since the water concentration is well-known and stable in human brain (about 74 % according to the literature). For ^{1}H MRS, the calibration-water spectrum was then acquired with the same parameters, VOI-size and VOI-location as the 1H-metabolite spectrum, but single-shot and of course no water-suppression. For ^{31}P MRS, the calibration-water spectrum was obtained with the same VOI-size and VOI-location as the 31P-metabolite spectrum. Since tissue water is a heteronuclear standard for ^{31}P MRS, the ^{1}H/^{31}P-conversion factor was determined experimentally by measuring the ^{31}P reference bottle (^{1}H level of 111'000 mM; ^{31}P level of 75 mM KH_2PO_4).

2) Reference bottles filled with a calibration solution served as an external standard. We used a 1 liter bottle of 50 mM creatine for ^{1}H MRS and an identical bottle of 75 mM KH_2PO_4 solution for ^{31}P MRS. Both bottles were placed on top of the head. The spectra of the bottles were acquired with the same coil, VOI size and measurement parameters as the tissue spectra but, of course, with different VOI centers, with only 8 averages and with a long T_R of 40 s.

3) Replacement phantoms filled with the calibration solutions mentioned before, but measured instead of the volunteer, were finally used as an additional external calibration standard. A spherical 3-liter container simulated the head. The in-vitro coil loadings were interactively adjusted to the in-vivo loadings using a saline bottle, placed at a well-defined distance to the rf-coil. After removal of the volunteer and installation of the phantom, its spectrum was finally obtained with the same coil and parameters, but with only 8 averages and with a long T_R of 40 s.

Results

As can be seen in Table 1, the concentrations of creatine and ATP correspond best to literature values for the replacement phantom method, which is reasonably accurate and produces very small systematic errors (no more than 5 %), once the coil-load-adjustment problem is solved. The intra-individual statistical errors are small for the replacement phantom method (about 8 %). The reference bottle method is clearly less accurate than the replacement phantom method. Finally, the internal water method produces acceptable results for ^{1}H but not for ^{31}P MRS.

Table 1	Concentration mmol/l = mM	**Statistical Errors** Intra-individual Stand. Dev.	**Systematic Errors** Deviation from Literature
^{1}H Measurements of Creatine			Creatine: Literature ≈ 7.7 mM
Tissue Water (internal, homonuclear Standard)	7.4 ± 0.8	11 %	4 %
Reference Bottle (external, homonuc. Standard)	9.3 ± 1.8	19 %	21 %
Replacement Phantom (external, homonuc. St.)	7.6 ± 0.6	8 %	2 %
^{31}P Measurements of ATP			ATP: Literature ≈ 2.8 mM
Tissue Water (internal, heteronuclear Standard)	2.1 ± 0.9	43 %	25 %
Reference Bottle (external, homonuc. Standard)	3.1 ± 0.7	22 %	11 %
Replacement Phantom (external, homonuc. St.)	2.7 ± 0.2	7 %	4 %

Discussion

Each method has its own systematical advantages (positive points: +) and disadvantages (negative points: -):

1) Tissue water for ^{1}H MRS is a reasonably **good** method.
   + a) equal coil load, b) equal coil-sensitivity area, c) equal amount of VOI contamination.
   - a) concentration of really free water is not exactly known, b) water-suppression sequence could lower the metabolite signal, c) dynamic problems (water is approx. 10'000 times more concentrated than the metabolites).

   Tissue water for ^{31}P MRS is a **bad** method.
   - a) heteronuclear standard requires a ^{1}H/^{31}P-conversion factor, which is different for each measurement, coil load and sensitivity area, b) different proportion of contamination of the VOI (because of different frequencies).

2) Reference bottles for ^{1}H and ^{31}P MRS are **not optimal**.
   + a) equal coil load.
   - a) different proportion of contamination of the VOI (bottle smaller than head), b) different coil-sensitivity regions.

3) Replacement phantoms for ^{1}H and ^{31}P MRS are **the best** method.
   + a) equal coil-sensitivity area, b) equal amount of VOI contamination
   - a) potentially different coil loads (load of the calibration measurement has to be matched to the in-vivo measurement).

Because the coil-load problem of the replacement phantom method can easily be solved by quick individual adjustment of the calibration coil load, the **replacement phantom method is the most accurate strategy** with respect to systematic errors (i.e. deviation from the mean in the literature) and statistical errors (i.e. differences between the two measurements of the same volunteer).