Reproducibility of ^{1}H MRS measurements as a function of SNR

I. Hancu[1], S. Adak[2], E. Hutchison[3], R. Hurd[4]

[1]GE GRC, Niskayuna, NY, United States, [2]GE GRC, Bangalore, India, [3]Union College, Schenectady, NY, United States, [4]GE ASL, Menlo Park, CA, United States

Introduction

Longitudinal MRS studies to assess the progress of a disease [1] or the efficacy of a drug [2] are increasingly common. For these studies it is of utmost importance that the MRS measurements are extremely reproducible, in order for any small deviation from the baseline to be associated with the effect of the disease or drug. Literature documents factors contributing to the measurement variability, such as biological variation or voxel repositioning [3]. Since any quantitative MRS measurement involves curve fitting for the determination of metabolite concentration, it has usually been assumed that the (limited) SNR of a spectrum is also contributing to the overall variability [4]. We present here the results of a study designed to help understand the impact of the SNR on MRS data reproducibility.

Methods

All in vivo and in vitro experiments described below were done at 3T, using PRESS (TE/TR=35/2000). Three normal volunteers underwent 15 scanning sessions each during 6 months. A high-resolution localizer (1.15/1.15/2mm for x/y/z resolutions) was acquired at the beginning of the scanning sessions, and then 480 spectra were collected from 8cc voxels in the posterior cingulate gyrus of each volunteer. Care was taken repositioning the voxel in the repeat scans. Spectra were then partitioned into 4 blocks, containing 32, 64, 128 and 256 spectra (labeled as SNR bin 1, 2, 3 and 4, respectively). The spectra in each block were contiguous, and no single spectrum from the initial scan belonged to more than one block. The ordering of the blocks was random, to get rid of the possible effects of non-linear scanner instabilities or motion biases (more significant at the end of a long scan). Figure 1 presents a graphical depiction of the data partitioning: here, the 480 spectra were split in the order 32, 64,128,256 for the first scan, and 256, 64,128, 32 for the second scan shown.

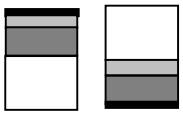

Figure 1: *Graphical depiction of partitioning of the 480 spectra*

Twenty five scans were also performed during the course of 6 months on a typical brain phantom [5]. 30 spectra were collected each time, then partitioned into 4 bins, containing 2,4,8 and 16 spectra (referred to, as SNR bin 1,2,3 and 4, respectively). The average SNR of each bin (matched for the in vivo and in vitro acquisitions) is displayed in Table 1.

SNR bin	1	2	3	4
In vivo SNR	42	57	75	101
In vitro SNR	39	55	76	107

Table 1: *SNR values for the bins*

For each scan, the spectra in each bin were averaged together and then fit, using both SAGE and LCModel. Metabolite concentrations and ratios were then recorded and binned together as a function of SNR. Standard deviations were then calculated per SNR bin for each metabolite for the phantom and each volunteer considered separately), and a homogeneity of variance test (Levene's test with the Brown-Forsythe modification) was performed to compare variances as a function of SNR bin. A Kruskal-Wallis test was also performed to estimate the impact of the SNR on the means of the metabolites.

Results and discussion

A consistent decrease of the variance is observed for the in vitro measurements as SNR increases, indicating that the SNR is an important source of the overall variability. No such significant variance decrease is noted in vivo, however, where the variance of most metabolite concentrations and metabolite concentration ratios, obtained through both fitting programs, stays constant. For illustration, Figure 2 presents the Cr and Glx variance as a function of SNR bin for the phantom and one of the volunteers (data analyzed with LCModel). Out of the 3 volunteers studied, a single one presented 2 metabolites (Cho and mI) whose variance went down as the SNR increased. In that case, post-hoc comparisons using the Bonferroni correction indicate that variance is significantly lower in the SNR 3 bin as compared to the SNR bin 1, but it increases as SNR further increases (possibly due to motion).

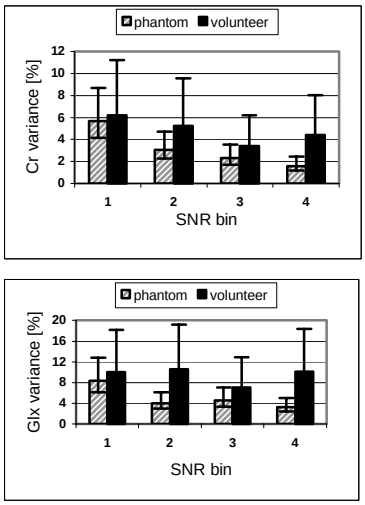

Figure2: ***a)*** *Cr and* ***b)*** *Glx variance as a function of SNR bin*

The impact of the SNR on the metabolite means was also quantified. The one-way Kruskall-Wallis test for the phantom indicate that neither SAGE, nor LCModel yield mean metabolite concentrations which are a function of SNR The same test for each volunteer analyzed separately indicate that, while metabolite means obtained with SAGE are not a function of SNR, LCModel yields some metabolite concentrations or ratios which decrease as a function of SNR. For each of the 3 volunteers, there was as little as one metabolite (Glx), and as high as 3 metabolite and metabolite ratios (NAA, Cho and Glx, and their ratios to Cr) that decreased as SNR increases. This fact can be attributed to the difference between the flat and curvy baselines between the low SNR and high SNR spectra, and leads to the conclusion that no comparison should be made (on an individual or class basis) for spectra having different SNR's.

Conclusions

The impact of the signal to noise ratio on the repeatability of the 1H MRS spectra has been studied. While data sets collected from a phantom confirm the intuitive trend, ie that a increase in the number of averages leads to a decreased variability, in vivo spectra do not obey the same trend. No significant decreases in the variance of fitted metabolite concentrations have been linked to an increased number of averages, suggesting that other sources of variability found in vivo are much more important. Unless these additional sources of variability are properly controlled (through automatic voxel repositioning, eg), the higher SNR of a scan (obtained though increased averaging) does not decrease variance for the typical metabolites (Cr, NAA, Cho, mI, Glx). Moreover, it was also discovered that the means of some in vivo metabolites obtained with LCModel are a function of SNR, therefore no comparisons should be made between 2 studies acquiring data with different SNR's.

References

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