The Effect of Signal to Noise Ratio and Linewidth On 4T Short Echo Time 1H MRS Metabolite Quantification

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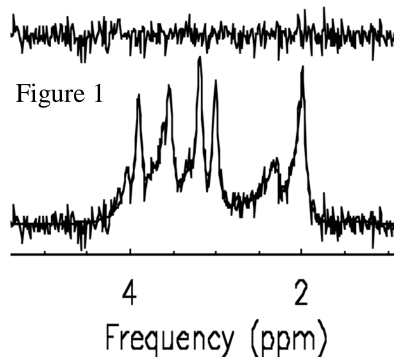
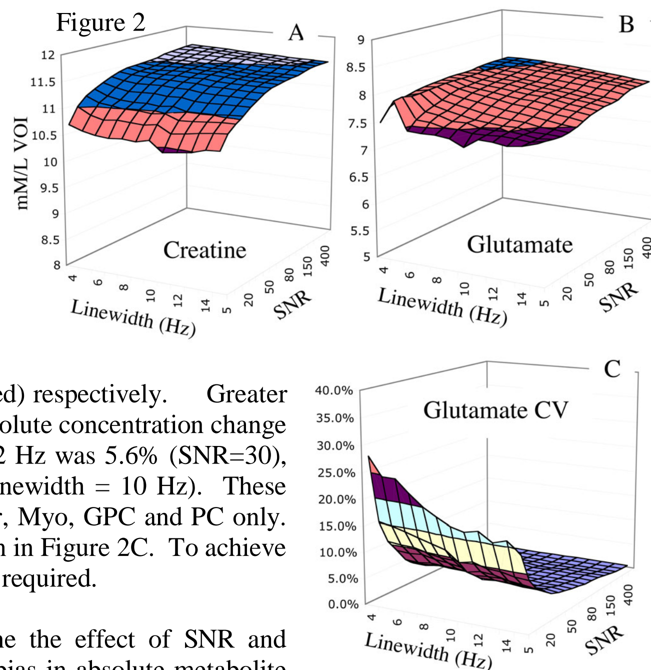
Introduction: Recent advances in the fitting (1) and/or measurement and subtraction (2) of the macromolecule baseline in short echo-time (TE) ^{1}H MR spectra (MRS) reduce the uncertainty associated with metabolite level measurements. At high field, in-vivo single-voxel ^{1}H MRS can detect more than twenty different metabolites (3), however the quantification of metabolite levels involves careful optimization of acquisition methods (including outer volume saturation and shimming), proper post-processing to remove eddy current artifacts, and complete modeling of spectral information. In addition to these considerations, previous studies have shown that both spectral signal to noise ratio (SNR) and linewidth (reflecting magnetic field homogeneity within the voxel) can alter measured metabolite levels (4, 5). Therefore, the purpose of this study was to measure the effect of both SNR and linewidth on metabolite levels quantified from 4T short echo-time spectra assuming macromolecule signals were removed (2), and to determine whether the range typically encountered in-vivo (SNR: 15-50:1, linewidth: 8-12Hz) increases the variance associated with measured group means.

Methods: LASER (6) localized (TR/TE 3200/46) in-vitro spectra of 19 different metabolites including N-acetylaspartate (NAA), glutamate (Glu), glutamine (Gln), creatine (Cr), myo-inositol (Myo), and choline containing compounds (GPC, PC), were acquired on a 4T Varian (Palo Alto, Ca) whole body MRI with Siemens (Erlangen, Germany) Sonata gradients. Spectra were processed to remove lineshape distortions (7) and modeled as previously described (5). Each noiseless model spectrum was scaled to represent the concentration of the corresponding metabolite in the human hippocampus (2), line broadened to 4 Hz full width half maximum (FWHM), and added to simulated an in-vivo MR spectrum. The simulated spectrum was then added to 100 randomly generated Gaussian noise spectra and scaled to produce a SNR (measured as the intensity of the NAA_{CH3} peak divided by the root mean square (RMS) of the noise) of 5:1. Additional simulations were produced at SNR = 10, 15, 20, 30, 40,50, 60, 70, 80, 90, 100, 150, 200, 300, 400, and 500:1. The process was repeated to characterize the effect of decreasing magnetic field homogeneity (shim) by further line broadening the spectrum up to 15 Hz FWHM in steps of 1 Hz. Therefore in total 204 simulated data sets were generated, each consisting of 100 spectra. Each spectrum was fit in the time domain using fitMAN software (2) incorporating prior knowledge of the 19 metabolite lineshapes used to generate the simulations. Plots of metabolite level as a function of SNR and linewidth were produced to demonstrate the variability in metabolite measurements.



Results: Figure 1 depicts a simulated 4T LASER TE=46ms spectrum with SNR = 20:1 and 12 Hz linewidth. Superimposed on the data is the fit result with the residual shown above. Figures 2 A, B show the variation in quantified metabolite level as a function of SNR and linewidth for creatine (11.6 mM/L VOI expected) and glutamate (8.0 mM/L VOI expected) respectively. Greater variation occurred as a function of SNR than linewidth. The average absolute concentration change for *all* metabolites associated with a linewidth increase from 8 Hz to 12 Hz was 5.6% (SNR=30), and that associated with a SNR decrease from 50 to 15 was 12.4% (linewidth = 10 Hz). These values decreased to 0.7% and 2.9% respectively for NAA, Glu, Gln, Cr, Myo, GPC and PC only. Variation in the % standard deviation (CV) of Glu measurement is shown in Figure 2C. To achieve a CV of <10% for Glu in spectra with 8-12 Hz FWHM , a SNR ≥ 15:1 is required.



Discussion: Short TE ^{1}H spectra were simulated and fit to determine the effect of SNR and linewidth on metabolite quantification. Results demonstrated a larger bias in absolute metabolite level measurement associated with low SNR compared to large linewidth. These results suggest that when compiling group means, care must be taken to exclude spectra acquired with insufficient SNR and/or excessive linewidth. However, within the range of linewidth and SNR typically encountered in-vivo, average metabolite levels (including all 19 metabolites) are within 6% and 12% of their expected values respectively when the macromolecule baseline is not a factor.

Acknowledgements and References: Funding provided by the Robarts Research Institute. The author wishes to thank Chandrew Rajakumar for data compilation. (1) Kanowski et al, Magn Reson Med 2004; 51: 904-912, (2) Kassem and Bartha, Magn Reson Med 2003; 49: 918-927, (3) Pfeuffer et al, J Magn Reson 1999; 141: 104-120, (4) Kries and Boesch, ISMRM 2003 Proceed. Abstract 264, (5) Bartha et al, NMR Biomed 1999; 12: 205-216 (6) Garwood and DelaBarre. J Magn Reson 2001; 153: 155-177, (7) Bartha *et al*, Magn Reson Med 2000; 44: 641-645.