Investigating the effect of spectral linewidth on metabolite measurement bias in short-TE MRS

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Introduction. It has been shown previously that in-vivo metabolite concentration estimates derived from short-TE MRS data are strongly dependent on the spectral linewidth (LW) of the data. Specifically, Kreis et al. [1,2] observed that when LCModel [3] is used for spectral quantification, increasing spectral LW resulted in a decrease in the estimated concentration of several major metabolites. However, the source of these systematic errors is not clearly understood. The primary aims of this study are i) to reproduce the findings of Kreis, and ii) to investigate the underlying cause of the strong dependence between spectral LW and LCModel measurement bias. These investigations are achieved through LCModel analysis of a large number of simulated MRS datasets with varying LW.

Methods. A complete set of metabolite basis spectra was simulated using an in-house implementation of the density matrix formalism. Metabolites were simulated under the influence of a spin-echo sequence at 3 Tesla with a TE of 8.5 ms to approximate the ultrashort-TE SPECIAL technique [3]. Macromolecule signals and residual water basis spectra were also simulated. All basis spectra were line broadened using an exponential filter to achieve the desired LW, and the simulated spectrum was generated by combining all basis spectra in approximate in-vivo concentrations. Normally distributed random noise was then added to the simulated spectrum to achieve the desired signal-to-noise ratio (SNR). For a given SNR and LW, 500 simulated spectra were generated using different noise seeds. The above procedure was then repeated again for different values of LW and SNR. In all, 11 different LW values were simulated (ranging from 2 Hz to 12 Hz, in integer steps), and SNR values of 50, 100, 200 and 400 were simulated. Each simulated spectrum was then processed twice in LCModel, once using LCModel's default baseline model, and once with an approximately flat baseline model (vitro='T' option). For each set of SNR and LW values, the measurement bias was assessed by taking the fractional difference between the estimated and the actual metabolite concentrations, and taking the average across all 500 spectra. The effect of spectral LW on the LCModel baseline was also investigated. This was achieved by saving the baseline signal estimates from LCModel outputs. The shape of the baseline signal as well as the total baseline power (the integral of the baseline signal) was investigated as a function of spectral LW.

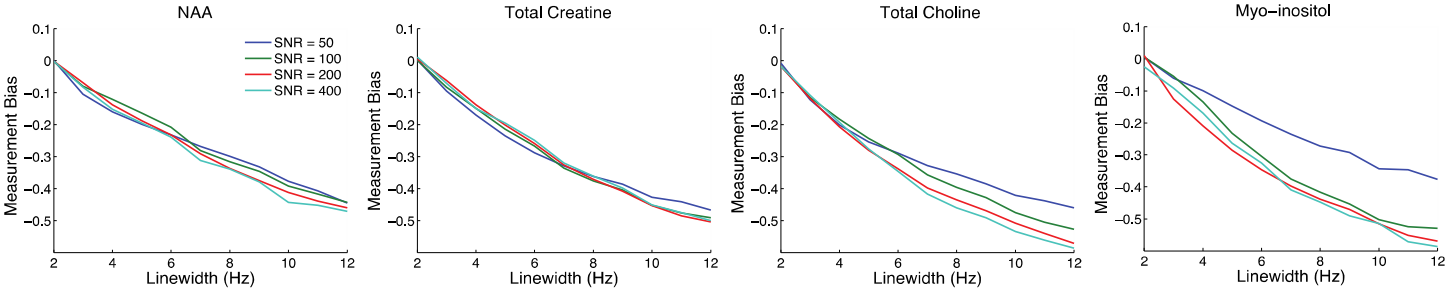

Figure 1. Metabolite measurement bias as a function of spectral linewidth for (left to right) NAA, total creatine, total choline, and myo-inositol with SNR values of 50, 100, 200, and 400. Metabolite concentration estimates decrease as linewidth increases.

Results. Figure 1 shows measurement bias as a function of LW for NAA, total creatine, total choline and myo-inositol when the default LCModel baseline is used. Very similar trends were observed when the vitro='T' baseline option was used (results not shown). Regardless of the baseline model or the SNR, the estimated concentration decreases as LW increases, as observed previously [1,2]. Figure 2 shows baseline signals from LCModel analyses of simulated spectra with LW ranging from 2 to 12, and SNR =100 using the default baseline (a) and the vitro='T' baseline (b) options. For both models, there is a trend of increasing baseline amplitude as the spectral LW increases. Finally, Figure 3 shows the total baseline power plotted vs. spectral LW. Once again, for both models, the baseline power increases as a function of spectral LW.

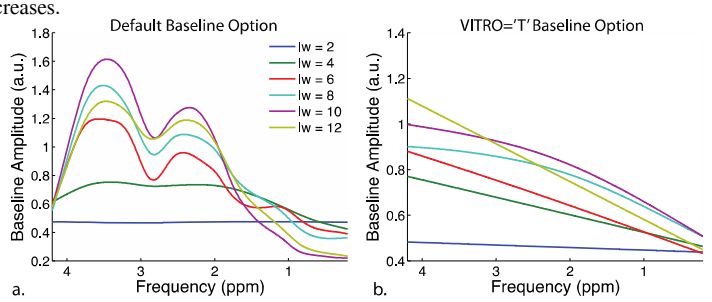

Figure 2. Baseline signals as a function of LW for a) default LCModel baseline option, and b) VITRO='T' baseline option.

Discussion. This study confirms the earlier observation by Kreis [1] that short-TE LCModel MRS measurements of major metabolites are inversely proportional to spectral LW. Based on the results of this study, the most likely cause of this relationship is an increase in the LCModel baseline component as a function of spectral LW. As the estimated baseline component increases, metabolite concentrations must necessarily decrease in order to maintain small residuals. This study has several limitations. Firstly, the simulated spectra were generated using exactly the same basis spectra that were used to fit the data in LCModel. Secondly, the simulated spectra contained no added baseline component. And finally, the effects of non-exponential line broadening were not considered. Despite these limitations, this study reproduces the dependency between spectral LW and metabolite concentration estimates that was previously observed in real in-vivo data. These results reinforce the importance of controlling the spectral LW of datasets within an MRS study, especially if the study involves LCModel analysis of short-TE MRS data. The major hurdle for accurate short-TE MRS measurements at arbitrary spectral LWs appears to be accurate estimation of the spectral baseline. This study suggests that improved baseline models are needed.

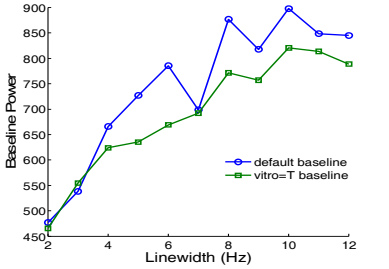

Figure 3. Baseline power as a function of LW.

References. [1] Kreis R et al. Proc Intl Soc ISMRM 11:264 (2003). [2] Kreis R. NMR Biomed 17:361-381 (2004) [3] Provencher SW, Magn Reson Med 30: 672-679 (1993) [4] Mekle R et al. Magn Reson Med 61:1279-1285 (2009).