Feasibility of Using Predicted Cramer Rao Lower Bounds for the Design of Optimized In Vivo MR Spectroscopy Sequences Targeting Multiple Metabolites

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Introduction

Quantitation of metabolites by ^{1}H MRS is fundamentally complicated by signal overlap. Fitting short TE spectra with the use of prior knowledge of metabolite spectra (linear combination model fitting, LCMF) is one way to ease this problem. The use of editing sequences for exclusive recording of signals from single metabolites is an alternative route to gain more accurate metabolite information. The former approach does not achieve the accuracy of the latter, where signal overlap for selected parts of the metabolite spectrum is eliminated as much as possible. The second approach has the significant disadvantage that information on most metabolites is sacrificed for accuracy on a single one. The achievable accuracy in fitting can be judged by the Cramer-Rao minimum variance bounds (CRB), which depend entirely on the fit model (i.e. constituting metabolites and their relative concentrations as well as the type of MR experiment) and the signal to noise, but not the actual experimental spectrum. It is therefore possible to compare the achievable accuracy for any metabolite in any MR experiment without ever implementing and performing it if the spectra can be simulated and we have a reasonable idea of tissue composition. In this work we demonstrate the feasibility of using CRB for design optimization of localized ^{1}H MR sequences. This has been done previously in other areas of MR (e.g. high resolution NMR [1], diffusion MR [2]). As a simple demonstration example it was tested which parameter setup in PRESS and STEAM experiments would be best for optimal accuracy of glutamate (Glu) and glutamine (Gln).

Methods and Subjects

Spectra were simulated using the framework of GAMMA [3] for STEAM and PRESS sequences with ideal pulses, as previously implemented in the GAVA interface [4]. The dependence of CRB for Gln and Glu amplitudes on two parameters was investigated for 3 field strengths (1.5T, 3T, 7T). For PRESS, 1st and 2nd echo times were incremented from 0 to 288 ms. For STEAM, TE and TM were varied. Following Ref [5], CRB were calculated for LCMF of Glu and Gln at equal concentrations, specific linewidths and SNR, which was made TE dependent using T_2's from the literature.

Results & Discussion

CRB can be calculated in the available parameter space of a given MR sequence, as illustrated in Fig. 1 for Glu and Gln in PRESS. In this example, longer TE yield generally higher CRB because of T_2 signal decay. But the graphs show that ridges are followed by troughs with relatively better performance. In specific editing sequences the T_2 decay will not dominate the overall minimum and optimal parameters can be chosen to minimize CRB for selected metabolites. Fig. 2 shows spectra for the same overall TE where the simulations predict much better performance for area estimation in one parameter combination than the other. The examples show that it is indeed feasible to optimize experiments for detection of specific metabolites using spectral simulation and CRB as criterion. This approach is promising for both optimization of general experiments, and also specific editing methods that can be combined with LCMF, where CRB will yield a criterion for optimal detection based on the full spectrum, not selected regions - as usually targeted in editing [6].

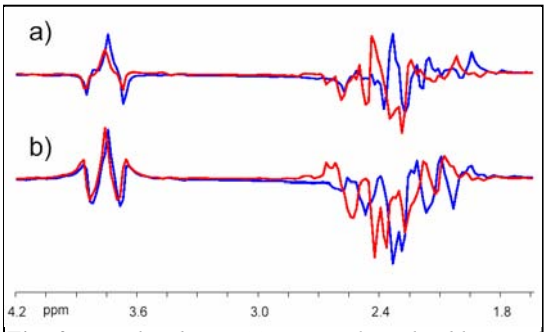

Fig. 2: *Simulated PRESS spectra for Glu (blue) and Gln (red), at TE 288, but different TE1 and TE2 combinations to obtain minimum (a, 38%, TE1 198ms , TE2 90 ms) and maximum (b, 60%, TE1 72ms , TE2 216 ms) CRB for Gln (similar behavior for Glu).*

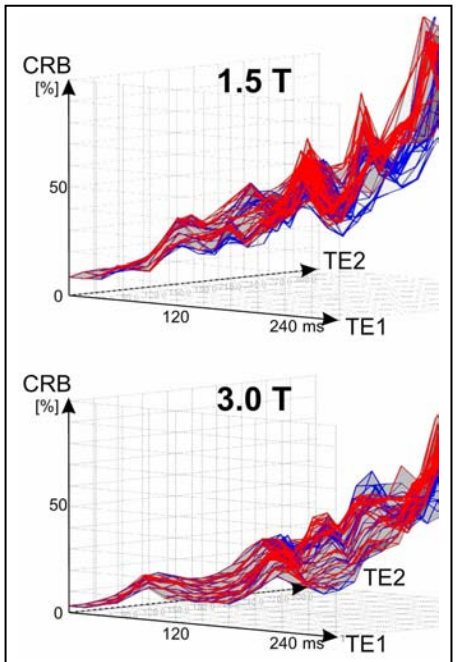

Fig. 1: *CRB for Glu (blue) and Gln (red) amplitudes in idealized PRESS spectra as function of TE1 and TE2 at 1.5 and 3 T in % of amplitude at 1.5 T (assuming smaller T_2 and linear increase of SNR at 3 vs. 1.5T)*

This work clearly provides a proof of principle only for the design of new experiments and the examples serve as illustrations. Useful new experiments can be obtained after removing the severe restrictions that have not been addressed here. Shortcomings in the current implementation include: 1) Use of ideal experiments (RF bandwidth, flip angles), 2) Only 2 metabolites considered, 3) Neglect of baseline, which can severely affect calculation of CRB [7]. Further extensions will also include more sophisticated experiments, like use of MQ filters, selective pulses, or 2D experiments.

Conclusion

CRB provide design criteria for optimized in vivo MRS scans using complete metabolite spectra in combination with LCMF. This should yield higher accuracy for ranges of targeted metabolites without complete loss of information on other compounds.

References

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