Extended Cramér-Rao Lower Bounds: Background Accommodation

H. Ratiney[1], S. Cavassila[1], D. van Ormondt[2], D. Graveron-Demilly[1]

[1]CNRS UMR 5012, Université Claude Bernard Lyon1-CPE, Villeurbanne, France, [2]Faculty of Applied Physics, Delft University, Delft, P.O Box 5046, Netherlands

Synopsis

Quantitation of ^{1}H short echo-time signals is often hampered by a background signal originating mainly from macromolecules and lipids. While the model function of the metabolite signal is known, that of the macromolecules is often partially known. As a consequence, we use a semi-parametric approach to estimate the metabolite amplitudes. Because error-bars for the amplitudes are of paramount importance for diagnosis reliability, we propose in this work, to extend the traditional Cramér-Rao lower bounds to account for the uncertainty caused by the background and give a better insight into the quantitation performance.

Method

An *in vivo* MRS signal, contaminated by a nondescript background *e.g.* – macromolecule, water residue, etc -- signals, can be written as

where $\hat{x}_{\mathrm{Met}}$ is the metabolite part whose model function is known, b the background signal whose model function is unknown, and e a Gaussian-distributed noise. The nuisance parameters θ of the background are obtained by a nonparametric *preprocessing* procedure. The wanted parameters p of the metabolites are estimated by a time-domain non-linear least squares quantitation algorithm.

The errors are usually calculated by estimating the Cramér-Rao lower bounds (CRBs) [1]. The latter exist only if the model function is known. If part of the model function is not available, the CRB calculation is incomplete, and resulting bounds are too low. We extended the traditional CRB calculation by applying the theory of estimation in the presence of 'nuisance parameters' proposed in [2].

For the metabolites -- model functions known -- the CRBs are usually computed from the Fisher information matrix $\boldsymbol{F_p}$.

$$F_p = \frac{1}{\sigma_m^{\,2}} \Re(D^H D)$$

where σ_m is the standard deviation of the measurement noise, $\Re$ denotes real part, the superscript ^{H} denotes Hermitian conjugate. D is the derivative matrix $\frac{\partial \hat{x}_{\mathrm{Met}}}{\partial p}$. To account for the effect of imprecise knowledge of the nuisance parameters θ on estimation of the metabolite parameters, we added a correction term to the information matrix. The extension was estimated from an estimate of the nuisance model $\hat{b}(\theta)$ and the corresponding covariance matrix F_θ^{-1}. The global covariance matrix is then estimated from

$$F_{\mathrm{Met}}^{-1}(p,\theta) = F_p^{-1} + \frac{1}{r} D_\theta F_\theta^{-1} D_\theta^T$$

where $D_\theta = \frac{\partial p}{\partial \theta^T}$ is the derivative matrix and the superscript ^{T} denotes transposition. The coefficient r reflects the confidence on the background model. The derivatives D_θ are obtained by estimating p for the estimated values of θ and $\theta + \Delta\theta$, and then applying a finite-difference method. The extended CRBs on the standard deviations of the metabolite model parameters p now become

$$\sigma_{pl} \geq CRB_{pl,\theta} = \sqrt{(F_{\mathrm{Met}}^{-1}(p,\theta))_{ll}}$$

Results

A ^{1}H short echo-time signal at 1.5T was simulated. It contains: 1) signals of twelve metabolites, with amplitudes corresponding to *in vivo* concentrations of a normal adult human brain, see Table, 2) a simulated version of a true macromolecule signal, see Fig.1, 3) noise. The metabolite signal was quantitated with a non-linear least squares algorithm after background removal. The CRBs were estimated by using the traditional and extended CRB formulae. The extended CRBs of myo-Inositol (m-Ins) and Glutamate-Glutamine (Glx) better approach the true error.

Discussion

At 1.5T, extended CRBs enable to better conclude on the precision of quantitation. We recommend to use them to avoid misleading conclusions for metabolites which are strongly correlated with the background such as Glx, m-Ins and, NAA and choline in tumours.

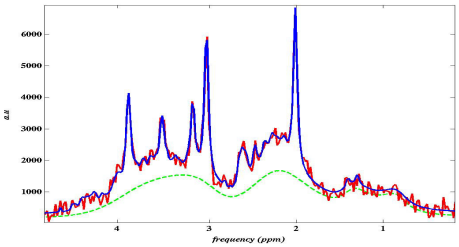

Fig.1. Fourier transform of x (red), $\hat{x}_{\mathrm{Met}} + b$ (blue) and b (green)**.**

Metabolites	True Amplitude	Estimated Amplitude	Traditional CRB	Extended CRB
NAA	13	11.90	0.34	0.83
Cr/Ppcr	6	6.67	0.2	0.31
Cho	2	2.19	0.18	0.48
Glx	6	4.02	0.3	1.34
m-Ins	5.5	4.55	0.46	1.55

Table: True and estimated amplitudes, conventional and extended CRBs.

Acknowledgements

This work is supported by Philips Medical Systems, Best, NL.

References

[1] Cavassila S., Deval S., Huegen C., van Ormondt D., and Graveron-Demilly D., NMR in Biomedicine, vol. 14, pp. 278--283, 2001.

[2] Spall J.C. and Garner J.P., IEEE Transactions on Aerospace and Electronic Systems, vol. 26, no. 6, pp. 992--998, 1990.