Using *LCModel* and whole tissue representations for the classification of single voxel ^{1}H spectra of paediatric brain tumours

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Introduction: In this study we apply a recently published novel methodology for the classification of adult brain tumour ^{1}H MR spectra [1] to paediatric brain tumours. We evaluate classification of Medulloblastoma (MDB), Astrocytoma (AG) and Ependymoma (EPD), which is an important clinical question since the appropriate treatment planning can vary considerably [2]. The widespread analysis tool *LCModel* [3] is used to fit mean spectra (*M*) of the tumour types instead of individual metabolite spectra. To account for tumour heterogeneity, a variability term (*V*) was calculated for each tumour type and added into the analysis. *LCModel* then gives an estimate of the proportions of mean tumour spectra and the highest tumour proportion is used as a classifier. Representations *M* and *V* of normal spectra of the cerebellum (NCB) were included in the analysis to investigate possible improvements in classification by accounting for partial volume with adjacent brain. Because of the relatively small sample sizes a leave-one-out (LOO) analysis was used to evaluate the classification performance. Additionally the effect of different Cramér-Rao Lower Bounds (CRLB) cut-off criteria for accepting an *LCModel* output as a true component of the whole tissue analysis was investigated.

Methods: **Data acquisition** The same dataset is used as in ref. [4] and is comprised of 18 MDB (age 7.0±3.9), 5 EPD (age 2.0±1.1) and 13 AG (age 7.4±3.9) single voxel spectra acquired on a 1.5 T scanner with PRESS localisation and short echo time (TE=30ms, TR=1500ms). Diagnosis was confirmed by histopathology after surgical resection. 4 spectra from the non-involved cerebellum NCB were acquired of four children (age 6.8±4.0) who were treated for a posterior fossa tumour. **Data preparation** 1 EPD and 1 AG spectra were excluded from further analysis due to low SNR and poor shimming, and 1 AG spectrum has been excluded because of poor water suppression. Spectra were apodized, phased, referenced to choline peak at 3.2 *ppm*, truncated to a range 4.0 *ppm* to 0.2 *ppm* and normalized by setting the area under each spectrum over this limited *ppm* range to unity. The mean *M* and variability term *V* were then calculated for each tumour type using PCA [1]. The LOO analysis was performed by excluding one spectrum of each tumour type from the calculation of the tumour representations *M* and *V* for every iteration (MDB vs. AG - 198 iterations; MDB vs. AG vs. EPD - 792 iterations). The training set classification accuracy is determined from all spectra that have been used to calculate the representations *M* and *V* while the ones left out are used to evaluate the test set classification accuracy.

Results: **Figure 1** shows the *M* and *V* components and the variability as a linear combination of the two for one random iteration taken from the LOO analysis. The highest classification accuracies in discriminating MDB vs. AG and MDB vs. AG vs. EPD are shown in **Table 1** and are compared to those of previously published work achieved for the same dataset using *LCModel* metabolite estimations and a linear discriminant analysis (LDA) [4]. Including NCB in the basis set gave similar classification accuracies however a higher CRLB cut-off had to be set to achieve this. The standard deviation of the overall classification accuracy across the different CRLB cut-off criteria was 1.2% and 0.4% with and without including NCB in the analysis respectively. One of the four EPD spectra is consistently misclassified in the test set throughout the LOO analysis giving a constant 75% EPD classification accuracy while the accuracy in the training set is higher with 91%. Overall, the correct classifications are very confident with on average more than 80% of the corresponding tumour proportion fitted whereas misclassified spectra showed a more equal distribution of contributions from all tumour spectra types.

	MDB vs. AG				**MDB vs. AG vs. EPD**			
	Training Set		Test Set		Training Set		Test Set	
values in [%]	*CRLB*	avg.	*CRLB*	**avg.**	*CRLB*	avg.	*CRLB*	**avg.**
Excl. NCB	*100*	98.5	*20*	**100.0**	*30*	94.7	*25*	**87.7**
Incl. NCB	*100*	98.8	*35*	**97.5**	*100*	94.6	*100*	**86.9**
Ref. [4]	-			**93.1**				**92.9**

Table 1: Shown are the best overall classification accuracies and the corresponding CRLB cut-off criteria with and without NCB in the analysis.

Discussion: After showing proof-of-principle that the *LCModel* can be used for the direct classification of common adult brain tumour ^{1}H MR spectra using whole tissue representations [1] we now successfully applied this method to the paediatric brain tumours MDB, AG and EPD. The achieved classification results compare well to previously published work [4]. Due to the small size of the EPD dataset of four spectra, reliable representations of *M* and *V* could not be calculated throughout the LOO analysis resulting in the low EPD classification accuracy. An EPD classification accuracy of 91% in the training set promises better results for a larger dataset. The influence of the CRLB cut-off criteria on the classification accuracy is low while the additional NCB representations did not improve the overall classification accuracy but increased the uncertainty in the *LCModel* fits. This study further confirms the potential use of *LCModel* as a fast and easy classification tool with the flexibility to represent different tissue types in the basis set with similar classification accuracy as specialized pattern recognition analyses.

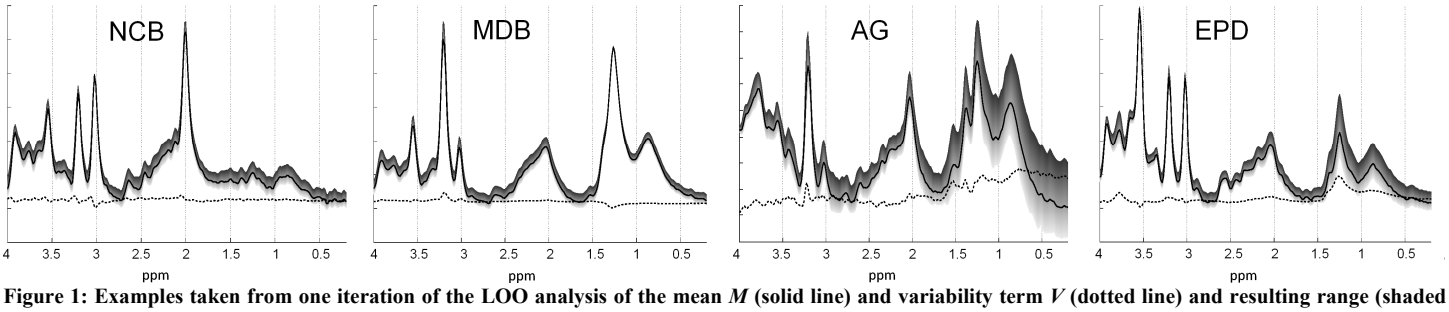

Figure 1: Examples taken from one iteration of the LOO analysis of the mean *M* (solid line) and variability term *V* (dotted line) and resulting range (shaded area) as defined by *LCModel* 'soft constraints' for the different tissue classes. Note that NCB was not part of the LOO classification analysis.

References
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