Analysis of ^{1}H MRSI data of brain tumours using *LCModel* and whole tissue representations

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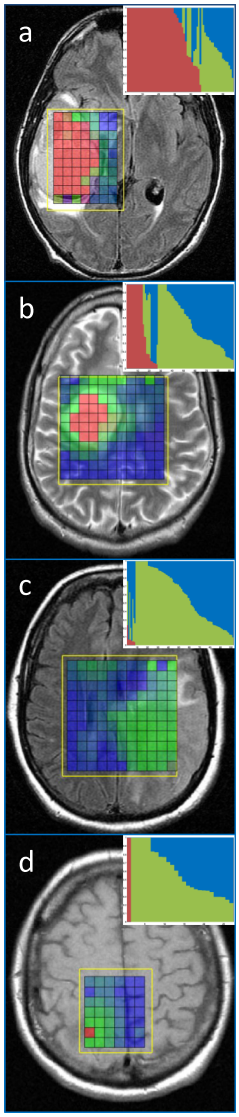

Figure 1: Colormaps and histograms showing tissue proportions fitted by *LCModel* (G4 red, G3 green, blue NWM) to each voxel for a glioblastomas (a), Anaplastic Astrocytoma (b), Gemistocytic astrocytoma (c) and G2 Astrocytoma.

Introduction: There is still a need for an automated and easy to use analysis tool for ^{1}H MRSI data that could return estimated tissue proportions for each voxel to assess glial brain tumour grade, heterogeneity and infiltration. This would be valuable information for biopsy planning to find regions corresponding to the highest tumour grade present or surgery and radiotherapy planning by finding areas of infiltrative growth beyond abnormal regions shown on standard MRI. In this study we apply a recently published novel methodology for the classification of single voxel ^{1}H MR brain tumour spectra [1] to 2D short echo MRSI data of WHO grade II (G2), III (G3) and IV gliomas (G4). The widespread analysis tool *LCModel* [2] is used to fit mean spectra (*M*) of different tumour grades and normal white matter (NWM) instead of individual metabolite spectra. To account for tumour heterogeneity within each tumour grade and white matter variation, a variability term (*V*) was calculated for each tissue type and added into the analysis. *LCModel* then gives an estimate of proportions of the tissue spectra for each MRSI voxel. Previous studies have shown that G3 gliomas share spectral characteristics with both G2 and G4 [3]. Therefore, for simplicity of the proof-of-principle method we only include G2 and G4 representations in the *LCModel* analysis calculated from single voxel data used in ref. [1]. The results are displayed in RGB colormaps and histograms showing the fitted tissue proportions for each MRSI dataset.

Methods: **Subjects** Informed consent was given by 29 brain tumour patients according to local ethics procedures for research MRI. Tumour diagnosis was subsequently confirmed histologically from biopsy or resected tumour tissue samples as six diffuse (G2) astrocytomas, three gemistocytic astrocytomas, four anaplastic (G3) astrocytomas, two G2 oligoastrocytomas, an anaplastic oligoastrocytoma, 12 glioblastomas, and one gliosarcoma. One diffuse astrocytoma had only a clinical and radiologic diagnosis [4]. **Data acquisition** Data was acquired at 1.5 T with the GE PROBE-SI protocol (TR/TE=2000/30ms), outer volume suppression and a 16x16 phase-encoded matrix with nominal voxel size of (13.75x13.75x15)mm. **Data preparation** Data was zero filled to a 32x32 matrix and voxels within the excitation region were analysed with *LCModel* using a NWM, G2 and G4 basis set calculated from the training set of single voxel spectra (PRESS, TR/TE=2000/30ms) used in ref. [1]. A Cramér-Rao Lower Bound cut-off criterion of 35% was used for accepting an *LCModel* output. For visualization, the sum of the estimated tissue proportions was normalized for each voxel and the results displayed as a RGB color map overlayed on corresponding flair or T2 imaging slices with blue representing NWM proportions, green G2 and red G4 [4]. Histograms were created for each data set showing the fitted tissue proportions in vertical lines with red representing G4, green G2 and blue NWM. Histograms are sorted from left to right from highest G4 to lowest G2 contributions. Voxels containing NWM only are not included, thus the histogram represents visual characterisation of only the "abnormal" tissue region.

Results: **Figure 1** shows examples for the resulting colormaps and histograms for G4 (a), G3 (b), G2 (c,d) with abnormal voxels reaching within normal appearing brain in all cases. The gliosarcoma and all of the 12 glioblastomas show high G4 proportions fitted in the centre of the tumour and a mixture of G4/NWM around the edges to 'normal' appearing brain. G4/G2 and G2/NWM proportions are mainly fitted to areas showing oedema. Six of the 11 low grade gliomas show clear G2 components with decreasing G2/NWM ratio towards the 'normal' appearing brain. Two other low grade MRSI sets show one voxel each with only G4 components fitted. Individual examinations of the spectra reveal bad fits with a very distorted baseline and high residual. Additionally the histograms of those cases show no G4 tissue 'gradient' with mixed proportions of NWM or G2 but instead a sharp cut-off as shown by one example in **Figure 1 (d)**. Two low grade MRSI sets show G4 components which on inspection were found to be fitted to cystic regions with high lactate. One gemistocytic astrocytoma shows clear high grade characteristics according to both the colormap and histogram (survival=376d consistent with a more high-grade tumour). Three of the five G3 gliomas show a high similarity to G4 while the other two have a lower G4 contribution fitted.

Discussion: In this study we present a novel method for the analysis of MRSI data of gliomas using *LCModel* to estimate proportions of G2 and G4 tumour tissue and NWM. Short echo MRS data is used to maximize the metabolic information available. Colormaps and tissue histograms show clear differences between G2 and G4 gliomas. G3 gliomas are not clearly distinguished but show G4 characteristics. An additional G3 basis set might improve the differentiation. Throughout the analysis there seems to be a diffuse fitting of low ratios G2/NWM beyond the regions of apparent tumour growth and contralateral brain. Longitudinal studies are needed to evaluate the validity of actual infiltrative tumour. Alternatively there may be larger metabolite variations in normal brain than currently expressed by our *M* and *V* of NWM, which is thus corrected for by fitting small G2 proportions to NWM. In few occasions fitting problems with large lactate peaks were found leading to non valid fits. However histogram continuity appears to be an indicator for voxels with abnormal fits and tissue proportions. Further work is needed to understand the variability within different tumour and tissue types and including additional components in the basis set and correlation of the results to other MR modalities such as DTI and DWI and patient outcome. Additional investigations need to focus on how well *LCModel* is able to separate mixed tissue proportions of different magnitudes and types using simulated spectra with changing SNR levels and CRLB cut-off criteria. This information could be used to evaluate minimal true tissue proportions that can be estimated using *LCModel*.

References

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