Integrating Diffusion Kurtosis Imaging, Dynamic Susceptibility-Weighted MR imaging and short echo time Chemical Shift Imaging for grading gliomas.

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Aims and objectives

Several studies, using advanced MR techniques to grade gliomas have been published with different setups and mixed results, indicating a widespread interest in the topic, with most of the reported results demonstrated on a group level.

In order to find acceptance in clinical practice, prospective grading of gliomas should be performed on an individual patient level with sufficient accuracy. Moreover, combining different modalities has the potential to increase diagnostic accuracy, as the different advanced MR techniques yield complementary information.

In this study, it was our aim to assess the separate diagnostic performances of diffusion kurtosis imaging (DKI), perfusion MRI using dynamic susceptibility-weighted MR imaging (DSC-MRI) and short echo time chemical shift imaging (CSI) for grading gliomas, and to examine if a multimodal approach could be used to improve diagnostic power of the individual methods, leading to a diagnosis of glioma grade on an individual patient level.

Methods and materials

In this prospective study, thirty-five patients with cerebral gliomas underwent DKI, DSC and CSI on a 3T MR scanner. Diffusion parameters - mean diffusivity (MD), fractional anisotropy (FA), mean kurtosis (MK) -, perfusion parameters - mean relative regional cerebral blood volume (mean rrCBV), mean relative regional cerebral blood flow (mean rrCBF), mean transit time (MTT) and relative decrease ratio (rDR) - and twelve CSI metabolite ratios- were compared between 22 high grade gliomas and 14 low grade gliomas (Mann-Whitney-U, p<0.05). The classification accuracy was determined with a linear discriminant analysis for each MR modality independently. Furthermore, the performance of a multimodal analysis, using a decision-tree rule which combines the statistically significant DKI, DSC-MRI and CSI parameters with the lowest p value, is reported. The proposed classifiers are furthermore validated on a set of subsequently acquired data from 19 clinical patients.

Results

While MK was significantly higher, MD was significantly lower in high grade compared to the low grade gliomas (p<0.001 and p=0.003, respectively). FA did not significantly differ between high and low grade glioma (p=0.195).
Mean rrCBV, mean rrCBF and rDR were significantly higher in high grade glioma than in low grade glioma (p<0.001 for all three parameters). MTT did not show statistically significant differences between tumor grades (p=1).

Lips/tCho, Lips/Cre, Myo/sum and Cre/sum showed statistically significant differences between high and low grade glioma (p=0.002, p=0.004, p=0.02, p=0.004, respectively). Lips/tCho and Lips/Cre increased with higher tumor grade, whereas Myo/sum and Cre/sum were lower in high grade compared to low grade gliomas. Normalized tCho/NAA and tCho/Cre and NAA/tCho, NAA/sum, tCho/sum, NAA/Cre, tCho/Cre and Glx/sum did not significantly differ between tumor grades (p=0.328, p=1, p=0.16, p=0.13, p=0.37, p=0.15 and p=0.42, respectively).

DSC-MRI proved to be the modality with the best performance, when comparing modalities individually.

We propose a decision-tree rule based on the ROC curves, determined for the statistically significant diffusion, perfusion and MR spectroscopic parameters. These ROC curves with the corresponding area under the curve values (AUC) are shown in Fig 1. We consider the parameter of each modality with the lowest p value in each modality; mean rrCBF for DSC-MRI, MK for DKI and Lips/tCho for CSI.

The performance averaged over 100 runs of the proposed decision tree was 86%; i.e. 86% of the cases were correctly classified, 5% of the cases were misclassified and for 9% of the cases diagnosis was not reached, since all the considered parameters were within the low-confidence interval. We also observed that 75% of the cases were classified at the first decision-tree level (based on mean rrCBF) out of which 74% of cases were correctly classified; 11% of the cases were classified in 2nd decision-tree level based on MK, out of which 9% were correctly classified; 5% of the cases were classified in the 3rd step based on Lips/tCho, out of which 3% were correctly classified. In Figure 2 we demonstrate the decision-tree, by presenting the rules extracted from a randomly selected run within the cross-validation step. Based on the ROC analysis, the mean rrCBF low-confidence interval for the current dataset was 1.45 -1.96. The low-confidence interval for MK was 0.44 to 0.53 and for Lips/tCho 0.63 to 3.40. The combination of a high mean rrCBF, a high MK and high Lips/tCho was indicative for high grade glioma (see Fig 3).

Furthermore, the proposed combination and cut-off values of imaging parameters of the decision tree rule were validated on subsequent acquired data coming from 19 new patients. Sixteen out of 19 cases were correctly classified. In three out of 19 cases, no final diagnosis could be made, and therefore the cases were classified as undecided. None of the cases was miss-classified.

Images for this section:
Fig. 2: A-B-C, Receiver operating characteristic curves indicating the sensitivities and specificities of mean rrCBF-based, MK-based and the Lips/tCho-based differentiation between low and high grade gliomas, respectively. The two indicated points show the range where misclassifications can occur in this specific study population. The cutoff values indicated on the ROCs are an example obtained during a validation run randomly selected in the leave-one-out cross-validation. D, Decision tree to distinguish low from high grade glioma in our study population based on the ranges of possible misclassification of mean rrCBF, MK and Lips/tCho obtained for the leave-one-out cross-
validation. The percentage of undecided cases after each decision step is indicated at each level. Nine percent of cases could not be classified, using the proposed decision algorithm.

![Fig. 3: T2-weighted MR image, mean rrCBF, MK and Myo/sum maps of a 71-year old female patient with a glioblastoma multiforme in the left parietal lobe (panel A) and a 35-year old male patient with a grade II pilocytic astrocytoma in the left temporal lobe (Panel B). The mean rrCBF and MK maps display the tumoral area in detail as indicated on the T2-weighted MR image with the purple box. Notice the high mean rrCBF and MK values in the high grade glioma (top row) compared to the low grade glioma (bottom row). The VOI of the CSI (green box) is superimposed on the T2-weighted images showing Lips/tCho ratios per voxel. The tumoral area is indicated with white arrows. Lips/tCho ratios are higher in high grade glioma compared to low grade glioma. Notice that only the center voxels are displayed in the color map for the sake of clarity as the outer rows are affected by the chemical shift displacement error (CSDE). This CSDE can be defined as the difference in location of the center of the excitation or refocusing slices of two resonances with a different chemical shift, i.e. Lips (0.9 and 1.3 ppm) and the carrier frequency of the water suppressed spectrum (2.2 ppm). Intensities of Lips/tCho are equally scaled in the parameter maps of the low and high grade glioma patient.](image-url)
Fig. 1: ROC curves and AUC values for MK and MD (panel A), mean rrCBV, mean rrCBF and rDR (Panel B) and Lips/tCho, Lips/Cre, Myo/sum and Cre/sum (Panel C) in solid tumor in order to differentiate between low and high grade glioma.
Conclusion

Combining information from DKI, DSC-MRI and CSI increases diagnostic accuracy to differentiate low from high grade gliomas, possibly providing diagnosis for the individual patient.

Personal information

References


