Reproducible Quantitative Analysis of Corpus Callosum Infiltration and Contralateral Involvement Using a Probabilistic Mixture Model: Relevance in primary brain tumors

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Introduction

Diffusion Tensor Imaging (DTI) is evaluated for better delineation of tumor infiltration by primary brain tumors. First reports show conflicting results mainly due to difficulties in reproducible determination of DTI-derived parameters (1, 2). We used an improve version of a recently introduced method for ROI-analysis based on probablistic voxel classification (3) for a user independent analysis of DTI-derived parameters and tested this method in healthy controls and patients with primary brain tumors. We evaluated reproducibility of this method and we used the integrity of the Corpus callosum (CC) as a measure to evaluate the nature of ambiguous contralateral lesions seen on conventional imaging.

Methods

15 patients with supratentorial gliomas (WHO grades II-IV) were included in the study. To evaluate potential CC infiltration (CCI), patients were divided in three groups of five patients: patients without contralateral lesions (CLL) and no midline CC infiltration CLL-/CCI-), patients with contralateral lesions but no infiltration of the CC (CLL+/CCI-) and patients with contralateral lesions and CC infiltration on FLAIR imaging (CLL+/CCI+). We included a control group of 5 age-matched controls. We used a 1.5 T whole-body clinical scanner and a quadrature head coil (Magnetom Symphony, Siemens Medical Solutions, Erlangen, Germany). Gradient strength 40 mT/m, SSEPI, parameters: TR/TE 4700/78, FOV 240 mm, matrix of 96x96, 50 axial slices, thickness 2.5 mm, 6 gradient directions and two b-values (0 and 1000 s/mm^2) and 10 averages. FLAIR-sequence: TR/TE/TI 9000/114/2500, field of view 240 mm, data matrix 256x256, 23 slices, thickness 5 mm and 1.5 mm gap. Using the aforementioned method for fiber quantification, we measured the FA at five different positions of the CC. All measurements were performed by two independent readers blinded to the patient group as well as to results of the other reader. Intra- and intrerreader variability was evaluated by Intra Class Correlations (ICC) between these measurements using Stata 9.0 (Stata Statistical Software: Release 9. College Station, TX: StataCorp LP.). Mean FA Values of the five positions of the different groups were compared to age-matched controls with analysis of variance. A p-value of <0.05 was chosen as significance level.

Results

For all subjects, all five measurement points were compared within and between readers. Comparison of the first and second measurement of reader 1 and 2 yielded an ICC-value of 0.998 and 0.995 respectively indicating good intra-reader agreement. Comparison of all four measurements (two measurements of reader 1 and two measurements of reader 2) yielded four ICC-values ranging between 0.996 and 0.999, indicating good inter-reader agreement. CC infiltration could be detected on DTI data as demonstrated in the combined visualization of anatomical and DTI data (Fig. 1). Profiles of FA of patients with suspect lesions contralateral all had a significant, clearly delineated FA decrease whereas patients with no contralateral lesions showed similar profiles when compared to healthy volunteers (Fig 2). DTI yielded additional information concerning tumor extend and delineation when compared to conventional imaging. Figure 3 shows a group comparison of mean FA over all 5 positions in all patient groups and healthy controls. There is no significant difference between group 1 (CLL-/CCI-) and healthy controls ($F(1,16)<.001$, $p>.999$). Furthermore, there is a significantly lower FA in group 3 (CLL+/CCI+) when compared to healthy controls ($F(1,16)=25.22$, $p=.0004$). Moreover, group 2 (CLL+/CCI-) has a significantly lower FA than controls and was not significantly different from patients with visible infiltration ($F(1,16)=17.85$, $p=.0019$).

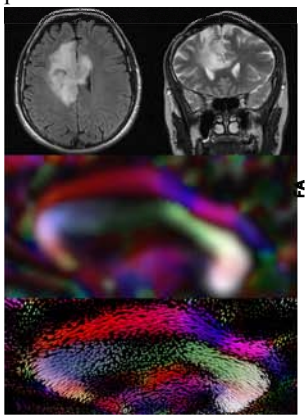

Fig. 1:. Depiction of CC infiltration using FLAIR, colormaps and elipsoid representation (top to bottom)

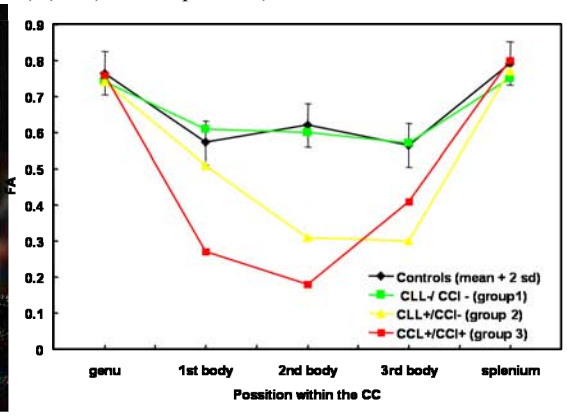

Fig. 3: Profiles of FA in the CC of healthy controls (black line) and example patients of all three patient groups. Note the strong deviations in patients with contralateral lesions, regardless of the status of the CC evaluated using FLAIR imaging.

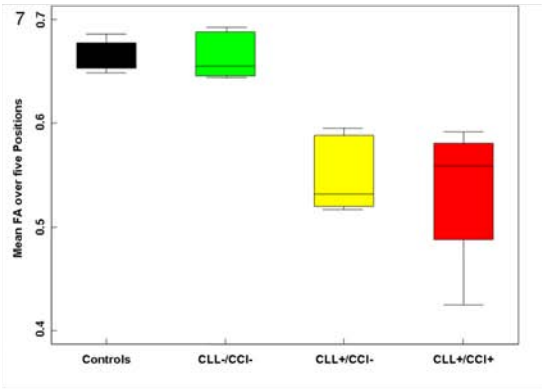

Fig. 2:. Comparison of the different patient groups using the mean FA over the five measured positions within the CC. There is no difference between controls and CLL-/CCI- and significant reduction of FA in the two other groups.

Discussion

The presented method for FA quantification proved to be robust, allowed for detailed assessment of CC infiltration and provides additional information on contralateral involvement in patients with gliomas when compared to FLAIR imaging. An overall measurement variance of 5 % indicates that this method of quantification is reproducible. Some of the variance found can be attributed to the imaging protocol. In a next step we will evaluate the effect these settings on overall measurement reproduciblity. In conclusion we present a method that may lead to a better delineation of the extent of primary brain tumors. This information is critical in pre-surgical evaluation of these patients and may also improve the effectiveness of radiotherapy.

References

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