Diffusion Tensor and Kurtosis metrics along the corticospinal tract in patients with intracranial tumors show complex WM involvement

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Introduction Diffusion Tensor Imaging (DTI) metrics, mainly mean diffusivity (MD) and fractional anisotropy (FA), are widely used to assess white matter (WM) involvement in patients with intracranial tumors [1]. Diffusional kurtosis imaging (DKI) is an extension of DTI that characterizes the non-Gaussian motion of water molecules [2]. DKI metrics such as mean kurtosis (MK) and radial kurtosis (RK) are sensitive to tissue complexity; for example, MK may distinguish grade II from grade III gliomas [2-4]. Routinely FA- and MD-maps, as well as WM tracts provided by tractography, are visually assessed for signs of WM involvement [5]. Quantitative analysis of tractography data, if performed, is commonly reported as mean value per tract. However, analysis providing estimates along the entire length of the tract is more sensitive to pathology [6, 7]. The aim of the present work was to evaluate whether DTI- and DKI-metrics along a tract, in this case the arbitrarily chosen corticospinal tract (CST), would provide specific information on WM involvement in individual patients. For this purpose, estimates of DTI- and DKI-metrics along the CST in patients with intracranial tumors and various degree of CST involvement were compared to estimates in healthy controls. In addition, results were compared to the categories of WM involvement, edema, displacement, and infiltration obtained from visual assessment [5].

Material and Methods Eleven patients (mean age 52.8 years, 5 male, 6 female) with intracranial tumors (4 low grade gliomas (LGG), 3 glioblastomas (GBM), 2 meningiomas (MEN) and 1 metastasis (MET)) and ten self-reportedly healthy adults (mean age 27.6 years, 3 male, 7 female) were imaged at a 3T Philips Achieva system. A single-shot EPI pulse sequence was used with 15 diffusion encoding directions, $b = 0$, 0.5, 1.0, 2.5 and 2.75 ms/μm^2, TE/TR = 76/5400 ms/ms, resolution = 2×2×2mm^3, covering a 7 cm thick slab that in patients was centered on the tumor. The diffusion kurtosis tensor was nonlinearly fitted to the data, followed by calculation of MK and RK according to [3]. Fractional anisotropy (FA) and mean diffusivity (MD) were calculated from $b = 0$, 0.5, 1.0 ms/μm^2 [8]. Tractography of the CST was performed using TrackVis [9]; ROIs were placed in (1) the pons at the level of the superior cerebellar peduncle (SCP), (2) the cerebral peduncle (PED), (3) the posterior limb of the internal capsule (PLIC), (4) the corona radiata just below the corpus callosum (COR), (5) the centrum semiovale at the level of the cingulum (CSO) and (6) the precentral gyrus at the level of the motor handarea (MHA) (Fig 2). Normal average values ± two standard deviations were determined from controls for each metric and segment of the CST (1-2, 2-3, etc); metrics were also estimated along available segments in each patient separately (Fig 1). Next, average estimates for each segment of the CST ipsilateral to the tumor were determined in each patient and compared to corresponding values from controls using a two-sided *t*-test with significance level $P < 0.05$. Lastly maps of FA, MD, and directionally color-coded (DCC) FA were used for visual assessment of WM involvement. Patients were assigned one of four categories regarding the CST: 'normal', 'displaced' (normal FA, abnormal location or orientation), 'edema' (normal FA and DCC-FA, T2-signal changes), or 'infiltrated' (FA reduced, tracts identifiable on DCC-FA) [5].

Results The CST was visualized in all patients and estimates along the tract were calculated in available segments (Fig 1, 2). In summary, MD was most sensitive to WM involvement, but unspecific, as was RK. MK was strongly affected only when the CST was 'infiltrated'; notably, patient 9 where the CST was classified as 'infiltrated', suffered from a metastasis at a distance to the CST, thus pure edema without tumor infiltration. FA was affected in opposite ways by 'displacement; also, FA may be affected in opposite ways along the CST as for example in patient 6 where FA was decreased in segment 1-2, approximately normal in segments 2-4 and strongly increased in segment 4-5 (Fig 3).

Discussion and conclusions DTI- and DKI-metrics along the CST were significantly affected by WM involvement in the vicinity of intracranial tumor in individual patients as compared to controls. In this small material, our findings were complex indicating that the definitions of the types of WM involvement used for visual assessment [5], may be an oversimplification, as for example in 'displacement' where FA has been assumed to be normal. Moreover, the definitions do not include the occurrence of multiple types of changes (increase and decrease) along a single tract. In conclusion, the DTI- and DKI-metrics may add to assessment of WM involvement, although a larger material is required to assess their sensitivity and possibly redefine the criteria for each type of WM involvement; patterns described for visual assessment did not fully account for WM involvement.

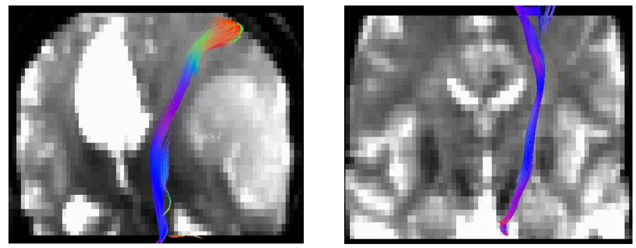

Fig 1. CST superimposed on b0-image in patient 6 (left panel) and in a control (right panel). Considerable displacement of the CST due a large meningioma is seen in the patient.

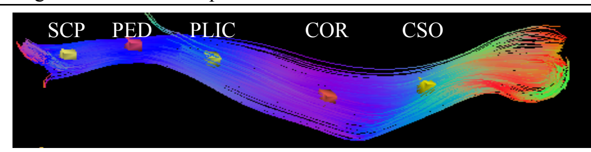

Fig 2. CST from patient 6, with markings denoting start and end of segments 1-5.

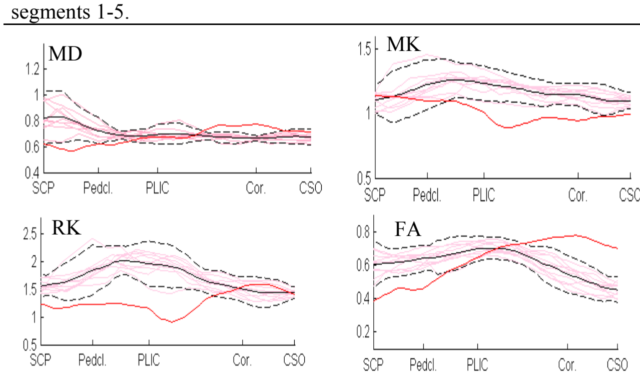

Fig 3. Estimates of DTI- and DKI-metrics along the CST in patient 6.

Table 1. Estimates in patients compared to average in controls: diagnosis, side (R=right, L= left); CST-segment; deviation from normal (↑ denoting 0-30 % difference, ↑↑ denoting > 30 % difference, P<0.05); result from visual inspection.

Pat	Diagn.	Seg.	MD	MK	RK	FA	Visual
1	LGG R	1-3	-	-	-	-	Normal
2	LGG R	4-6	-	-	-	-	Normal
3	LGG L	1-4	-	-	-	-	Normal
4	LGG L	4-5	↑	↓	-	↓	Displaced
5	MEN R	1-2	↑	-	-	↓	Displaced
6	MEN L	3-5	↑	↓	↓↓	↑↑	Displaced
7	GBM R	3-5	↑	↓	↓	↓	Edema
8	GBM R	3-4	↑↑	-	-	-	Edema
9	GBM L	3-6	↑↑	↓	↓↓	↓↓	Edema
10	GBM L	4-6	↑↑	↓↓	↓↓	↓↓	Infiltrated
11	MET L	1-3	↑	↓	↓↓	↓	Infiltrated

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