



Original Article

# Acute changes in diffusion tensor-derived metrics and its correlation with the motor outcome in gliomas adjacent to the corticospinal tract

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Received : 02 December 2020

Accepted : 14 January 2021

Published : 10 February 2021

DOI

10.25259/SNI\_862\_2020

Quick Response Code:



## ABSTRACT

**Background:** This study involves analysis of the relationship between variables obtained using diffusion tensor imaging (DTI) and motor outcome in gliomas adjacent to the corticospinal tract (CST).

**Methods:** Histologically confirmed glioma patients who were to undergo surgery between January 2018 and December 2019 were prospectively enrolled. All patients had a preoperative magnetic resonance imaging (MRI) study that included DTI, a tumor 2 cm or less from the CST, and postsurgical control within 48 h. Patients with MRI that was performed at other center, tumors with primary and premotor cortex invasion, postsurgical complications directly affecting motor outcome and tumor progression <6 months were excluded in the study. In pre- and post-surgical MRI, we measured the following DTI-derived metrics: fractional anisotropy (FA), mean diffusivity, axial diffusivity, and radial diffusivity of the entire CST and peritumoral CST regions and in the contralateral hemisphere. The motor outcome was assessed at 1, 3, and 6 months using the Medical Research Council scale.

**Results:** Eleven patients were analyzed, and six corresponded to high-grade gliomas and five to low-grade gliomas. Four patients had previous motor impairment and seven patients had postsurgical motor deficits (four transient and three permanent). An FA ratio of 0.8 between peritumoral CST regions and the contralateral hemisphere was found to be the cutoff, and lower values were obtained in patients with permanent motor deficits.

**Conclusion:** Quantitative analysis of DTI that was performed in the immediate postsurgery period can provide valuable information about the motor prognosis after surgery for gliomas near the CST.

**Keywords:** Corticospinal tract, Diffusion tensor imaging, Fiber tracking, Glioma, Motor outcome

## INTRODUCTION

Gliomas are neoplasms that are characterized by their ability to extend through white matter (WM) tracts compromising structures that are involved in movement, language, and cognition. Gliomas located near the corticospinal tract (CST) are a surgical challenge because of the proximity between the borders of the resection and important structures that may lead to neurosurgical deficits. Surgery on these tumors has reached a high level of technological complexity, using tools such as intraoperative fluorescence, neuronavigation, and neurophysiological monitoring.<sup>[8,33,37]</sup>

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The motor cortex is divided into the primary motor cortex, premotor cortex, cingulate motor area, and supplementary motor area. The CST is the main pathway that is involved in voluntary movement control. Pyramidal neurons of the primary motor cortex form the CST, which also receives fibers from the accessory motor areas, and from the parietal/somatosensory cortex.<sup>[11]</sup>

Diffusion tensor imaging (DTI) is a non-invasive magnetic resonance imaging (MRI) technique that measures the anisotropic diffusion of water molecules. WM tractography, which is also known as fiber tracking, allows a three-dimensional visualization of WM tracts. In addition, the architecture and integrity of WM fascicles can be assessed using a mathematical model that is composed of eigenvalues ( $\lambda$ ) and eigenvectors ( $\epsilon$ ) by which the displacement of the water molecule signal within a voxel is characterized.<sup>[3-5,15,27,28,32]</sup> In addition, quantitative information on DTI can be used to assess the degree of invasion or infiltration of the WM<sup>[16,21]</sup> and the CST.<sup>[20,45]</sup> The quantitative analysis of DTI through its derived metrics may reflect the effects of the tumor on the surrounding WM, allowing, for example, analysis of how gliomas change the microstructural integrity of the main WM tracts. In the WM, water molecules diffuse more rapidly along the fibers and more slowly perpendicular to them, which is called anisotropic diffusion.<sup>[31]</sup> The following four coefficients or scalars can be extracted from the DTI: axial diffusivity (AD), which represents the diffusivity along the direction of dominant diffusion, radial diffusivity (RD), which represents the average diffusivity perpendicular to the first eigenvector, mean diffusivity (MD), which describes the magnitude of the diffusion, and fractional anisotropy (FA), which describes the degree of anisotropy. These metrics provide information about the state of the WM tracts and may also suggest specific types of neuronal damage such as axonal injury, demyelination, inflammation, or necrosis.<sup>[2,10,13,24,30,39]</sup>

Several publications have studied the acute diffusivity changes in WM and selected regions of the CST in patients early after a stroke. A relationship between decreased anisotropic diffusivity and worse motor outcome has been described.<sup>[17,18,35,44]</sup>

For brain tumors, there are few studies that use DTI as a prognostic tool for motor function.<sup>[23,49]</sup> To the best of our knowledge, this is the first study that aims to quantitatively analyze the DTI information that was obtained in the immediate postsurgical period (within 48 h). The objective is to find a correlation with the motor outcome in surgical excised gliomas. The secondary objective is to establish a cutoff point based on the tensor metrics that allow identification of patients who will develop a permanent postsurgical motor deficit.

## MATERIALS AND METHODS

We prospectively enrolled histologically confirmed glioma patients who were to undergo surgery in our department between January 2018 and December 2019. All patients had a preoperative MRI study that included DTI. We included patients in whom the tumor was located 2 cm or less from the CST and who had postsurgical MRI control within 48 h. The surgeries were performed in a standardized manner using microsurgical techniques, neuronavigation, neurophysiological monitoring, and intraoperative ultrasound.

We excluded patients with MRI that was performed at other centers, tumors that invaded the primary motor cortex, supplementary motor area, and premotor cortex, and patients who had postsurgical complications with a direct impact on motor outcome (hematomas or ischemia). Stereotactic biopsies and patients with tumor progression for <6 months that were demonstrated in control MRI studies were also excluded from the study.

The clinical and radiological variables are summarized in [Table 1]. Motor function was assessed using the Medical Research Council (MRC) scale, with scores ranging from 0 to 5.<sup>[6]</sup> Using this scale, the presence or absence of pre- and post-surgical motor deficits was determined. In the postsurgical period, patients were assessed in the 1<sup>st</sup> week, at 1–3 and 6 months. A permanent deficit was defined as a deficit that persisted for 3 months after surgery.

### Image acquisition protocol

All subjects were scanned using a 1.5 T MRI scanner (Signa HDxt; GE Healthcare, Milwaukee, WI, USA). DTI data were acquired using a single shot echo-planar imaging sequence (TE, 96 ms; TR, 13675 ms; field of view, 256 × 256 mm; matrix size, 128 × 128; voxel size, 1.015 × 1.015 × 3 mm). The diffusion-weighting gradient was applied in 25 isotropically distributed directions using a b value of 1000 s/mm<sup>2</sup>. Fifty gapless slices were obtained to cover the whole brain, with a thickness of 3 mm. The total DTI acquisition time was approximately 4 min. The b-table was checked by an automatic quality control routine to ensure its accuracy.<sup>[38]</sup> Conventional MR sequences T1, T2-weighted imaging, fluid attenuated inversion recovery (FLAIR), and specific neuronavigation images were also acquired.

### Imaging analysis and fiber tracking

Fiber tracking was performed with a deterministic algorithm using DSI Studio ([dsi-studio.labsolver.org](http://dsi-studio.labsolver.org)).<sup>[47]</sup> We used a FA threshold of 0.15, angulation threshold of 50°, and minimum fiber length of 50 mm. Diffusion coefficient (FA, MD, AD, and RD) maps were automatically obtained for each patient.

CST was reconstructed using the regions of interest (ROIs) that were located at the midbrain, posterior limb of internal capsule, and primary motor cortex [Figure 1].<sup>[43]</sup> Using manual tools, fibers that were not anatomically related to the tract were removed (contralateral hemisphere, cerebellum,

or thalamus). Volumetric tools (Elements [Brainlab AG, Feldkirchen, Germany]) were used to calculate tumor volume based on preoperative MRI. The minimum distance between the CST and the tumor was measured. In all cases, the contralateral CST was reconstructed after ensuring that there were no alterations in the hemisphere contralateral to the lesion. Using the color map and coregistered T1 and T2-FLAIR images, ROIs (diameter = 8 mm) were drawn in the region of the CST that was closest to the tumor and its mirror image in the healthy hemisphere [Figure 2]. The different metrics derived from the tensor were obtained for the entire CST and the peritumoral regions of the ipsilateral and contralateral tract. We also calculated their ratio, as follows: ipsilateral (affected)/contralateral (healthy).

**Table 1: Patient characteristics.**

Variable	n
Age	49.82±14.34
Sex	
Female	5 (45.5 %)
Male	6 (55.5%)
Preoperative KPS (IQR)	80 (20)
Histopathology	
High-grade gliomas	
Glioblastoma	5 (45.5%)
Anaplastic astrocytoma Grade III	1 (9.1%)
Low-grade gliomas	
Astrocytoma Grade II	1 (9.1%)
Oligodendroglioma Grade II	4 (36.4%)
Tumor location	
Frontal	7 (63.6%)
Parietal	1 (9.1%)
Temporal	1 (9.1%)
Insular	2 (18.2%)
Initial volume (cm <sup>3</sup> )	43.32±33.01
Type of resection	
PR	2 (18.2%)
STR	2 (18.2%)
GTR	7 (63.6%)
CST compromise	
None	4 (36.4%)
Displaced	4 (36.4%)
Infiltrated/Disrupted	3 (27.3%)
Days between preoperative MRI and surgery (IQR)	1 (6)
Preoperative motor score (MCR)	
Upper limb	
3	1 (9.1%)
5	10 (90.9%)
Lower limb	
4	3 (27.3%)
5	8 (72.7%)
Postoperative motor score (MCR) at 6 <sup>th</sup> month	
Upper limb	
3	1 (9.1%)
4	2 (18.2%)
5	8 (72.7%)
Lower limb	
0	1 (9.1%)
3	1 (9.1%)
4	1 (9.1%)
5	8 (9.1%)

Values are expressed as the mean±standard deviation or as the frequency (%). KPS: Karnofsky Performance Score, MRC: Medical Research Council, IQR: Interquartile range, CST: Corticospinal tract, PR: Partial resection, STR: Subtotal resection, GTR: Gross total resection

### Statistical analysis

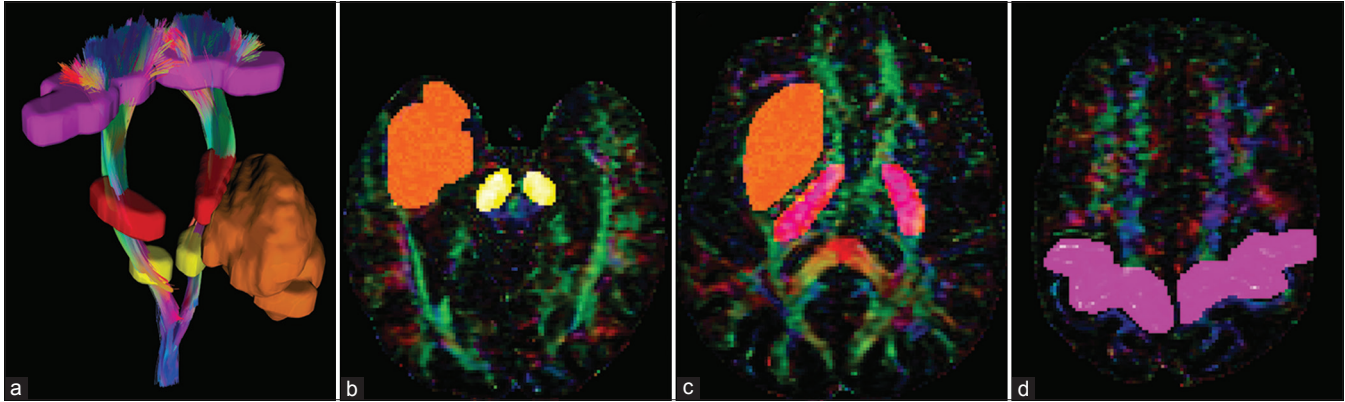
A normality test was applied to the sample using the Shapiro–Wilk test. Variables that were derived from the tensor had a non-normal distribution. The DTI values were compared with the presence of a preoperative deficit using the Wilcoxon–Mann–Whitney test, calculating the *U* statistic and the effect size with the *r* coefficient. The postsurgical motor status that was represented by the categories “no deficit,” “transient deficit,” and “permanent deficit” was compared with the tensor metrics using the Kruskal–Wallis test, using the epsilon squared ( $\epsilon^2$ ) coefficient as a measure of the effect size. A *post hoc* study was also performed using the Holm correction and the Wilcoxon rank-sum test.

The medians of the tensor values were also analyzed according to the presence or absence of motor impairment, comparing the ipsilateral to the contralateral values in both pre- and post-operative MRI. Thus, we used the Wilcoxon signed-rank test. All statistical analyses were performed in R version 3.5.0 (R Foundation for Statistical Computing, Vienna, Austria).

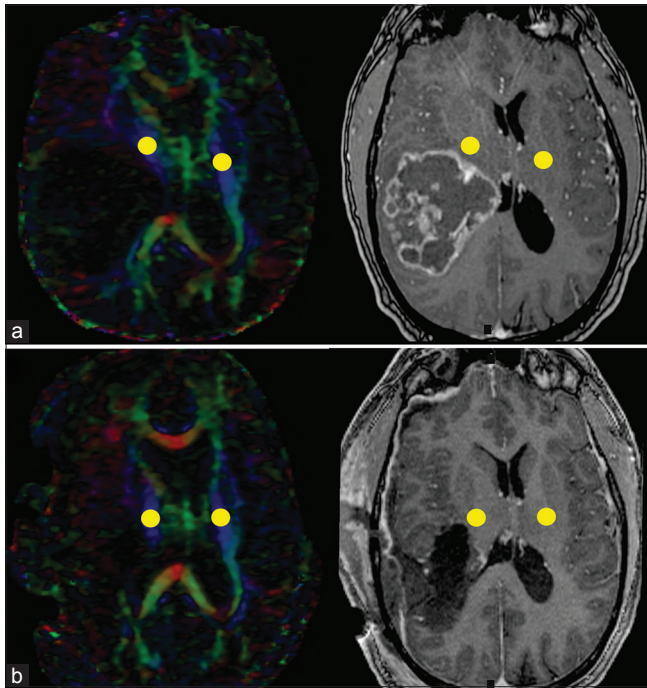
### RESULTS

During the study period, 53 patients with histologically confirmed glioma underwent surgical resection. Fourteen patients met the criteria of proximity to the CST. Three patients were excluded because of motor/premotor cortex invasion, postsurgical primary motor cortex infarction, or DTI performed at another center. Thus, 11 patients met the selection criteria and were included in the analysis.

Six (55.5%) patients were men and five (45.5%) patients were women. The mean age was  $49.82 \pm 14.34$  years, the median presurgical Karnofsky performance scale (KPS) was 80 (20). Six were high-grade and five were low-grade gliomas. The mean initial volume was  $43.32 \pm 33.1$  cm<sup>3</sup>. Four patients presented a presurgical motor deficit and the motor balance is summarized in [Table 1]. Three patients who presented a



**Fig 1:** Example of the methodology used for fiber tracking. (a) Three-dimensional visualization of CST tracts (ipsitumoral and healthy) along with the tumor and regions of interest (ROIs) that were used. Axial slices of diffusion tensor imaging-based color map showing ROI for the midbrain (b), posterior limb of internal capsule (c), and primary motor cortex (d).



**Fig 2:** Illustrative case showing the methodology that was used to determine the peritumoral corticospinal tract (CST) region. (a) Preoperative diffusion tensor imaging (DTI) color map (left) and T1-weighted postcontrast (right) axial images showing a high grade glioma adjacent to CST. ROI is placed over the area corresponding to the CST, as determined by the color fiber direction. A second ROI is placed in the contralateral hemisphere. (b) Postoperative DTI color map (left) and T1-weighted postcontrast (right) axial images. The ipsilateral ROI is placed in the CST region that is adjacent to the postsurgical cavity; a second ROI is placed in the contralateral CST region in the healthy hemisphere.

previous deficit showed worsening of their motor balance postoperatively [Figure 3], and one of the patients with a previous deficit improved after the intervention. In four patients, new postsurgical deficits were observed, and all of

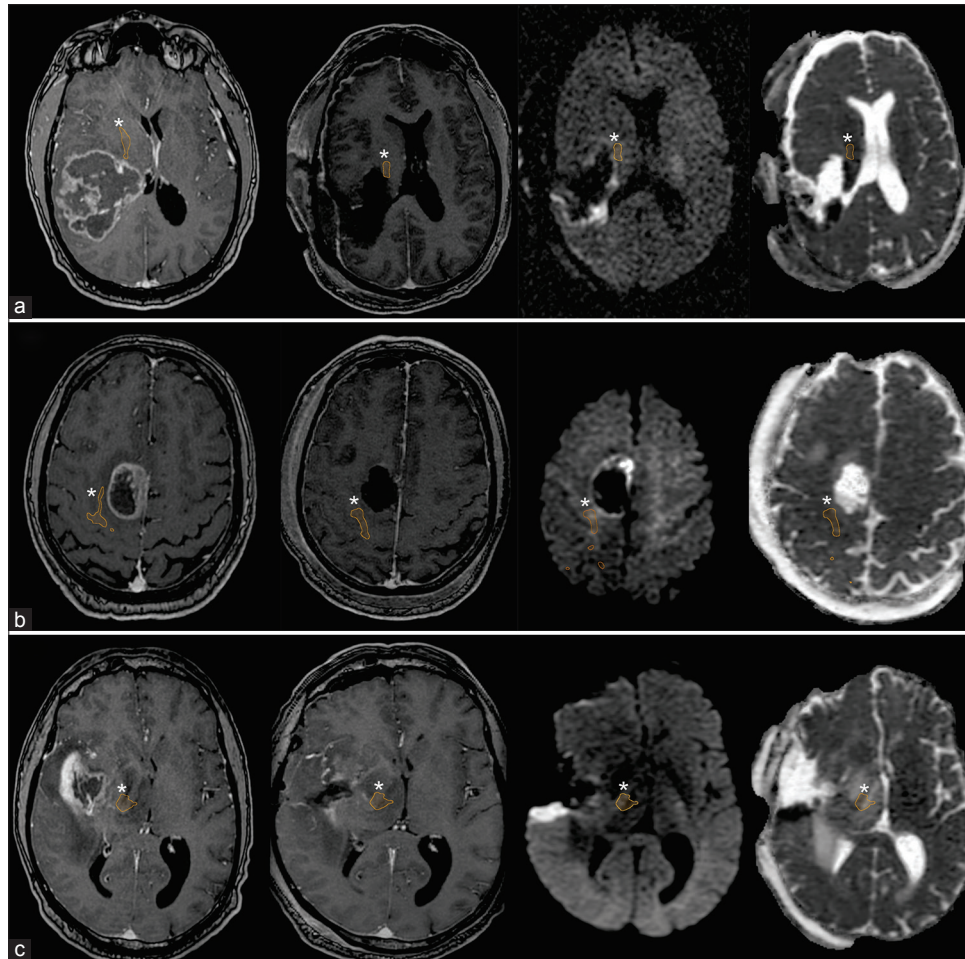
them were transient motor deficits. Significant alterations were observed during intraoperative neurophysiological monitoring in three patients (27.7%), with a reduction in MEP amplitude. Two of these patients had a permanent motor deficit. The third patient with a permanent motor deficit did not register alterations during neurophysiological monitoring, presumably due to a technical failure.

The presence of a permanent motor deficit was not correlated with the clinical or radiological variables including initial tumor volume, extent of resection, and distance to the CST. Although the three patients with a permanent deficit corresponded to high-grade gliomas, this relationship did not reach statistical significance. [Supplementary Table 1] shows descriptive statistics for the pre- and post-operative DTI values in the overall study sample.

Quantitative analysis of the tensor metrics is summarized in [Supplementary Tables 2 and 3]. In patients without motor impairment, there were no differences between the overall CST values on the affected and contralateral sides in the pre- and post-surgical studies. However, in the peritumoral regions, the values of FA, MD, and RD were significantly different in patients who had a motor deficit.

[Supplementary Table 4] shows the relationship between the tensor values and the presence of a preoperative deficit. The peritumoral regions and their ratio exhibited significantly lower FA values in cases of deficit, while the MD and RD values were higher.

The results of the postoperative DTI and motor outcome analyses are shown in [Table 2] and [Figure 4]. There were differences between the MD values of overall CST between the groups ( $H=6.96$ ,  $df=2$ ,  $P=0.031$ ,  $\epsilon^2=0.70$ ), and the difference between the groups with non-deficit and permanent deficit was statistically significant ( $Z=2.42$ ,  $P=0.047$ ,  $r=0.66$ ). In the peritumoral regions, there were differences between the values of FA, MD, and RD. For



**Figure 3:** Illustrative cases of permanent motor deficits. From left to right: preoperative T1-weighted postcontrast and postoperative images: T1-weighted postcontrast, diffusion-weighted imaging (DWI), and apparent diffusion coefficient (ADC) map. The location of the pyramidal tract that was determined by fiber tracking is also shown (white asterisk). (a) A 53-year-old man with a parieto-temporal glioblastoma; (b) a 65-year-old man with a right frontal glioblastoma; and (c) a 54-year-old man with a right temporo-insular glioblastoma.

the ratios, only the rFA showed a significantly different distribution ( $H = 7.48$ ,  $df = 2$ ,  $P = 0.24$ ,  $\epsilon^2 = 0.75$ ), and this difference was statistically significant between the cohorts with and without permanent deficit ( $Z = 2.65$ ,  $P < 0.001$ ,  $r = 0.80$ ). Although the median values for the FA ratio in patients with permanent motor deficits were lower (0.77) compared to patients with transient deficits (0.88), these differences did not reach statistical significance ( $P = 0.331$ ).

A cutoff based on the receiver operating characteristic curves was calculated, establishing a threshold value of 0.8 for the rFA, and thus, lower values are related to the presence of a permanent motor deficit in our series [Supplementary Table 5 and Figure 5].

## DISCUSSION

In the present study, we implemented DTI quantitatively to elucidate the relationship between the clinical outcome

and this radiological-derived information. Among the main findings of this investigation, patients who presented a postsurgical motor deficit had lower FA and higher MD and RD values compared to patients who did not show any deficit.

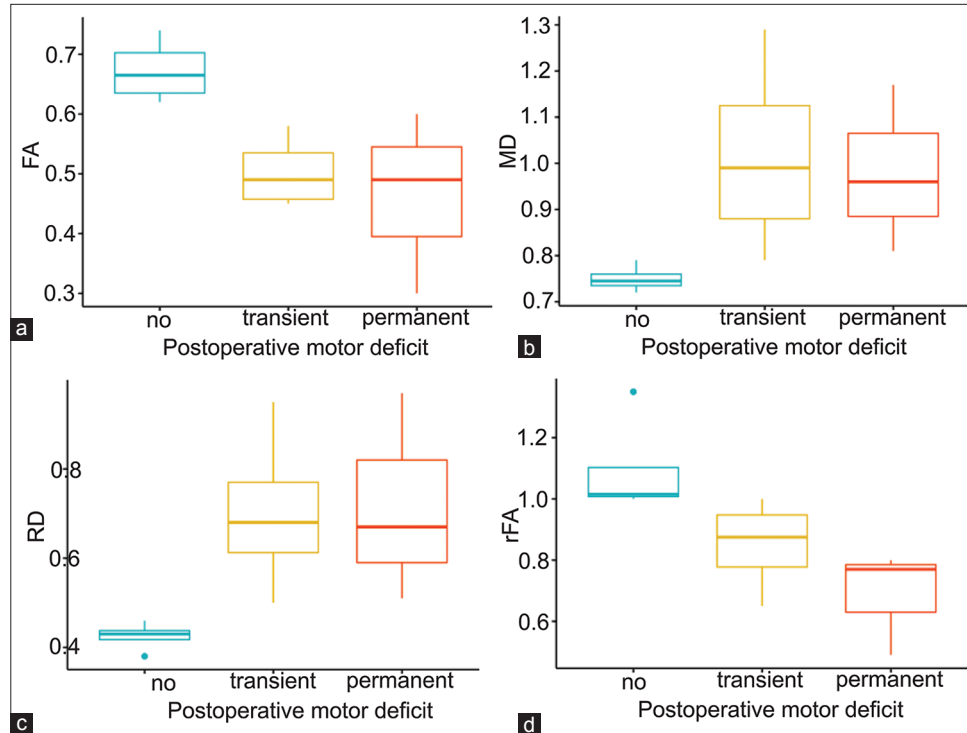
Among the strengths of our study, our results rely on DTI studies that were performed within the first 48 postoperative h. In addition, the analysis and image processing focus on the CST regions that are adjacent to the tumor and surgical cavity, and these areas are susceptible to postsurgical changes. Qualitative representation of the variable of interest (motor outcome) simplifies the analysis and its interpretation.

We established an objective definition of the tumor's proximity to the CST based on previous publications.<sup>[26,34]</sup> We discarded cases that may bias the analysis of the results, such as tumors that had invaded the motor and premotor cortex, because the damage in these areas could lead to motor impairments that do not directly involve the CST.

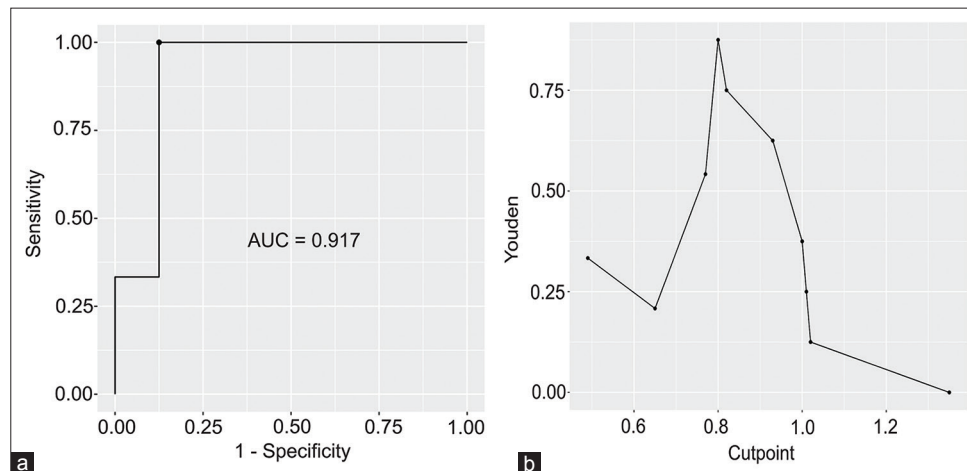
**Table 2:** Univariate analysis between quantitative DTI-derived metrics and postoperative motor deficit.

Variable	DTI metric	Postoperative deficit		Kruskal-Wallis test			Post hoc Dunn test		Wilcoxon rank sum test					
		No (n=4)	Yes	$\chi^2$	P	df	$\epsilon^2$	95% CI	Comparison (type of Motor deficit)	P (Holm)	Z	P	r	
		Transient (n=4)	Permanent (n=3)											
Overall CST	FA	0.60 (0.04)	0.57 (0.06)	0.55 (0.02)	3.55	0.169	-	0.36	0.08-0.85					
	MD	0.84 (0.02)	0.90 (0.03)	0.93 (0.02)	6.96	0.031	2	0.7	0.36-0.92	NO-PERM	0.047	2.42	0.049	0.66
										NO-TRANS	0.080			
Peritumoral CST region	AD	1.45 (0.05)	1.50 (0.05)	1.50 (0.04)	1.19	0.551	-	0.12	0.01-0.78	PERM-TRANS	0.605			
	RD	0.54 (0.03)	0.62 (0.07)	0.64 (0.01)	5.86	0.053	2	0.59	0.25-0.91					
	FA	0.67 (0.07)	0.49 (0.01)	0.49 (0.15)	7	0.030	2	0.70	0.27-0.91	NO-PERM	0.045	2.17	0.047	0.65
										NO-TRANS	0.057			
										PERM-TRANS	1			
MD		0.75 (0.03)	0.99 (0.25)	0.96 (0.18)	6.54	0.038	2	0.65	0.26-0.89	NO-PERM	0.033	2.12	0.047	0.64
										NO-TRANS	0.075			
										PERM-TRANS	0.961			
AD		1.38 (0.09)	1.62 (0.42)	1.54 (0.09)	2.1	0.351	-	0.21	0.02-0.86					
		0.43 (0.02)	0.68 (0.16)	0.67 (0.23)	7.1	0.029	2	0.71	0.30-0.92	NO-PERM	0.063			
										NO-TRANS	0.037	2.24	0.029	0.68
										PERM-TRANS	0.817			
Ratio ipsilateral/contralateral	rFA	0.98 (0.03)	0.92 (0.07)	1.02 (0.05)	5.21	0.070	-	0.53	0.15-0.92					
	rMD	1.05 (0.04)	1.04 (0.07)	1.01 (0.01)	1.53	0.466	-	0.15	0.01-0.86					
	rAD	1.02 (0.03)	0.98 (0.04)	1.03 (0.03)	3.45	0.178	-	0.35	0.04-0.84					
Overall CST	rRD	1.08 (0.07)	1.10 (.13)	0.98 (0.03)	2.27	0.322	-	0.23	0.02-0.9					
		1.02 (.10)	0.88 (0.17)	0.77 (0.16)	7.48	0.024	2	0.75	0.41-0.92	NO-PERM	0.024	2.65	<0.001	0.80
										NO-TRANS	0.139			
										PERM-TRANS	0.331			
Ratio Ipsilateral/Contralateral Peritumoral CST region	rMD	0.99 (0.14)	1.28 (0.26)	1.19 (0.23)	3.3	0.192	-	0.33	0.02-0.86					
	rAD	0.99 (0.15)	1.21 (0.20)	1.05 (0.15)	3.61	0.165	-	0.36	0.05-0.86					
	rRD	1 (0.15)	1.38 (0.34)	1.59 (0.25)	5.63	0.060	-	0.56	0.18-0.91					

Values are expressed as the median and IQR (interquartile range). CST: Corticospinal tract, PERM: Permanent, TRANS: Transient. DTI values are expressed in  $10^{-3}$  mm<sup>2</sup>/s



**Figure 4:** Box plots showing differences in the peritumoral diffusion imaging-derived metrics according to the type of postoperative motor deficit. (a) Peritumoral fractional anisotropy (FA); (b) peritumoral mean diffusivity; (c) peritumoral radial diffusivity; and (d) FA ratio (rFA; affected/unaffected).



**Figure 5:** Graphic output of cutoff determination using the Youden index. (a) Metric values by the optimal criterion. (b) Cutoff point for peritumoral FA ratio (rFA; affected/unaffected). AUC: Area under the curve.

We emphasize the importance of standardizing MRI acquisition and postprocessing imaging, especially the time at which the postoperative control study is performed. Other studies that correlated MRI data with the motor outcome are based on preoperative studies<sup>[9,14,19,40]</sup> that provide limited prognostic information. In our series, we also distinguished patients with transient postoperative motor deficits from those with permanent deficits.

The robustness of our methodology relies on the addition of a quantitative, comparative analysis based on data that were derived from pre and postoperative DTI. Most of previous studies had methodologies that often disregarded this important information. In a study by Laundre *et al.*,<sup>[23]</sup> in which qualitative analysis of DTI was performed using late postsurgical images, the author found an association between normalization of the position and anisotropy of the CST with

a clinical improvement of postoperative motor function. In a study by Yuanzheng's *et al.*,<sup>[49]</sup> intraoperative tractography was used, establishing the distance from the postsurgical cavity to the CST as a risk factor for the appearance of postoperative deficits, and the author did not use any quantitative parameters. Roberts *et al.*<sup>[36]</sup> used the fiber density index as a measure of the number of fibers (NFs) that are measured in a transverse ROI of the tract, which provides a semi-quantitative study parameter, although it is not an absolute measure. Similarly, Ius *et al.*<sup>[19]</sup> assessed the NF index, and they found significant differences between the ipsilesional and contralateral NF. In that series, a NF value  $<0.22$  in the preoperative DTI study was correlated with a low probability of developing a transient postsurgical deficit. Yao *et al.*<sup>[46]</sup> sought to determine the prognostic value of DTI in brainstem surgery using FA and ADC values and a laterality index. The consistency of those study methods can be improved because only seven of 14 patients had a postsurgical DTI, and none of them presented deficits postoperatively. Similarly, Abhinav *et al.*<sup>[1]</sup> studied the relationship between the degree of muscular strength and the presurgical DTI metrics, and in his series of deep intracranial cavernous malformations, only nine of 18 patients underwent postoperative study.

In a study by Gao *et al.*,<sup>[14]</sup> based on the preoperative DTI, the author performed his measurement on the posterior limb of the internal capsule, he used the absolute value of FA and the tumoral-to-healthy FA ratio, as well as the FDI and the rFDI ratios. In this study, the authors found a positive correlation between muscular strength and rFA and between FDI and rFDI. However, it seems that the most important differences occur in the regions of the tract near the tumor. As shown by D'Souza *et al.*<sup>[9]</sup> and Stadlbauer *et al.*,<sup>[40-42]</sup> these changes mainly consist of a decrease in FA and an increase in MD with respect to the contralateral hemisphere. Other research in the field of stroke corroborates these trends.<sup>[17,22,29,35]</sup>

In our series, the tensor metrics of the preoperative studies in which the entire CST is measured are similar for both the ipsilesional and contralateral healthy hemisphere. The values are similar to the series described by Cosottini *et al.*,<sup>[7]</sup> Roberts *et al.*,<sup>[36]</sup> and Stadlbauer *et al.*<sup>[40]</sup> For the postoperative study, the only value of the entire CST that is significantly different between patients who do not have postoperative deficits and those with permanent deficits was the increase in MD ( $0.84$  vs.  $0.93 \times 10^{-3} \text{ mm}^2/\text{s}$ ,  $P = 0.047$ ,  $Z = 2.42$ ,  $r = 0.66$ ).

The most important differences have been found when studying the CST regions that are adjacent to the tumor and the postsurgical cavity. We showed that in these areas, patients who presented with a postsurgical motor deficit had lower FA and higher values of MD and RD compared to patients who did not show any deficit. Doughty *et al.*<sup>[12]</sup> showed that reduced FA is found in the first 3–4 days after a stroke only when the ROI was very close to the ischemic lesion, but not

when the ROI was further away, and because of Wallerian degeneration, it took time to become established.<sup>[12]</sup>

For the ratio between peritumoral CST areas and the contralateral hemisphere, rFA was significantly lower in patients with permanent deficits. Through ROC curve analysis, the threshold we set in our series of 0.8 was related to a permanent postoperative motor deficit, and this threshold value was similar to that described in papers that assessed motor outcome in patients after a stroke,<sup>[22,25,48]</sup> although the pathophysiological mechanisms could be different.

These regional variations of the CST can represent irreversible damage to the tract, which is also found in patients with transient deficits but with a different magnitude. Among the three patients with a permanent deficit in our series, all had a preoperative motor deficit, while the four patients with a new postoperative deficit presented peritumoral CST alterations. However, these values did not become significant for the group that did not present deficits. This suggests that alterations of the tensor metrics in this group may be related to surgical manipulation and displacement or decompression of the CST instead of structural damage, as would occur in patients with an irreversible deficit.

The study of early postsurgical DTI suggests that the presence of artifacts in the acquisition, the presence of blood, small areas of ischemia, or patient movements can make it difficult to reconstruct the pyramidal tract as well as the values that are derived from its analysis.

Our study has some limitations. These include a small study sample size; images acquired using a 1.5 T scanner, and the absence of long-term DTI controls that would allow us a longitudinal analysis of the tensor values and the motor outcomes.

Future studies should focus on validation of the present methodology and results with a larger prospective series. We believe that DTI can provide valuable prognostic information in glioma surgery near eloquent areas. Efforts should be directed toward the creation of predictive models based on DTI and clinical variables that allow identification of patients who have a high risk of permanent motor sequelae. However, if we can differentiate postsurgical alterations based on CST metrics, we can provide patients with transient deficits valuable information about its functional prognosis, potential recovery, and rehabilitation strategies. These image processing tools should evolve into user friendly software, and improvements in spatial resolution and tensor reconstruction techniques should help to overcome the current technical difficulties.

## CONCLUSION

Quantitative DTI analysis that was performed in the immediate postsurgical period revealed changes in the CST area values near the tumor, which were consistently related



to the motor outcome in our series. Our results showed that the peritumor-to-healthy FA ratio in the CST allows discrimination between patients who will and will not develop a permanent postoperative deficit.

### Acknowledgments

We thank all the members of the Radiology Department of our center for their support in carrying out this work.

### Declaration of patient consent

Institutional Review Board permission obtained for the study.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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**How to cite this article:** Cepeda S, García-García S, Arrese I, Velasco-Casares M, Sarabia R. Acute changes in diffusion tensor-derived metrics and its correlation with the motor outcome in gliomas adjacent to the corticospinal tract. *Surg Neurol Int* 2021;12:51.

## SUPPLEMENTARY TABLES

**Supplementary Table 1:** Descriptive statistics of quantitative DTI-derived metrics.

Variable	DTI metric	Preoperative			Postoperative		
		Median	IQR	CI 95%	Median	IQR	CI 95%
Overall CST Ipsilateral	FA	0.56	0.04	0.53–0.58	0.57	0.04	0.54–0.6
	MD	0.88	0.12	0.82–0.96	0.9	0.06	0.84–0.93
	AD	1.47	0.14	1.39–1.58	1.49	0.07	1.44–1.52
	RD	0.6	0.11	0.54–0.65	0.59	0.09	0.54–0.64
Overall CST contralateral	FA	0.56	0.03	0.55–0.58	0.58	0.07	0.55–0.63
	MD	0.88	0.07	0.85–0.92	0.87	0.08	0.83–0.93
	AD	1.47	0.09	1.43–1.54	1.48	0.1	1.41–1.51
	RD	0.59	0.09	0.58–0.64	0.58	0.1	0.51–0.62
Peritumoral	FA	0.44	0.28	0.33–0.65	0.58	0.16	0.46–0.64
	MD	0.95	0.37	0.68–1.16	0.81	0.25	0.75–1.07
	AD	1.47	0.24	1.33–1.71	1.44	0.22	1.37–1.61
	RD	0.73	0.44	0.39–0.87	0.51	0.25	0.43–0.71
Healthy CST region	FA	0.64	0.20	0.51–0.74	0.61	0.12	0.56–0.69
	MD	0.72	0.06	0.70–0.76	0.77	0.05	0.74–0.80
	AD	1.31	0.29	1.11–1.46	1.39	0.13	1.31–1.46
	RD	0.44	0.17	0.34–0.53	0.44	0.08	0.41–0.51
Ratio ipsilateral/contralateral	rFA	0.97	0.06	0.95–1.04	0.98	0.07	0.94–1.02
Overall CST	rMD	1.01	0.05	0.95–1.02	1.03	0.05	1–1.05
	rAD	1	0.02	0.99–1.01	1.01	0.05	0.97–1.03
	rRD	1.02	0.09	0.9–1.03	1.08	0.12	0.97–1.09
Ratio	rFA	0.92	0.27	0.71–0.99	0.93	0.22	0.77–1.01
Ipsilateral/Contralateral	rMD	1.34	0.51	1–1.59	1.19	0.29	1.01–1.34
Peritumoral CST region	rAD	1.12	0.29	0.96–1.34	1.05	0.02	0.94–1.24
	rRD	1.45	0.64	1.08–1.78	1.37	0.58	0.98–1.59

IQR: Interquartile range, CST: Corticospinal tract. DTI values are expressed in  $10^{-3}$  mm<sup>2</sup>/s

**Supplementary Table 2:** Quantitative analysis of preoperative DTI.

Variable	DTI metric	Whole sample (n=11)						Motor deficit							
		Ipsilateral			Contralateral			No (n=7)			Yes (n=4)				
		W	P	Ipsilateral	W	P	Contralateral	W	P	Ipsilateral	W	P	Contralateral	W	P
Overall CST	FA	0.56 (0.04)	0.56 (0.03)	0.56 (0.03)	43	0.259	0.56 (0.03)	0.57 (0.03)	0.53 (0.01)	21.5	0.747	0.53 (0.01)	0.56 (0.02)	3	0.180
	MD	0.88 (0.12)	0.88 (0.07)	0.92 (0.11)	64	0.843	0.92 (0.11)	0.92 (0.05)	0.88 (0.05)	22.5	0.847	0.88 (0.05)	0.86 (0.03)	12.5	0.240
	AD	1.47 (0.14)	1.47 (0.09)	1.48 (0.12)	58.5	0.921	1.48 (0.12)	1.49 (0.07)	1.43 (0.07)	20.5	.654	1.43 (0.07)	1.43 (0.02)	8	1
Peritumoral CST region	RD	0.6 (0.11)	0.59 (0.09)	0.64 (0.11)	66	0.742	0.64 (0.11)	0.62 (0.06)	0.6 (0.04)	23	0.898	0.6 (0.04)	0.58 (0.03)	13	0.189
	FA	0.44 (0.28)	0.64 (0.20)	0.64 (0.25)	32	0.066	0.64 (0.25)	0.64 (0.22)	0.34 (0.11)	20	0.609	0.34 (0.11)	0.63 (0.12)	0	0.029
	MD	0.95 (0.37)	0.72 (0.06)	0.81 (0.27)	89	0.065	0.81 (0.27)	0.72 (0.04)	1.18 (0.23)	29	0.607	1.18 (0.23)	0.73 (0.06)	16	0.027
AD	1.47 (0.24)	1.31 (0.29)	1.43 (0.18)	93	0.034	1.43 (0.18)	1.31 (0.22)	1.62 (0.2)	34	0.249	1.62 (0.2)	1.34 (0.3)	14	0.114	
	0.73 (0.44)	0.44 (0.17)	0.46 (0.36)	92	0.042	0.46 (0.36)	0.44 (0.19)	0.96 (0.42)	26.5	0.443	0.96 (0.42)	0.43 (0.06)	16	0.023	

Values are expressed as the median and IQR (interquartile range). CST: Corticospinal tract. DTI values are expressed in 10<sup>-3</sup> mm<sup>2</sup>/s

**Supplementary Table 3:** Quantitative analysis of postoperative DTI.

Variable	DTI metric	Whole sample (n=11)						Motor deficit							
		Ipsilateral			Contralateral			No (n=4)			Yes (n=7)				
		W	P	Ipsilateral	W	P	Contralateral	W	P	Ipsilateral	W	P	Contralateral	W	P
Overall CST	FA	0.57 (0.05)	0.58 (0.07)	0.60 (0.04)	51.5	0.575	0.60 (0.04)	0.61 (0.07)	0.55 (0.05)	7	0.884	0.55 (0.05)	0.56 (0.07)	19	0.522
	MD	0.90 (0.06)	0.87 (0.08)	0.84 (0.02)	72	0.468	0.84 (0.02)	0.82 (0.05)	0.9 (0.04)	11	0.465	0.9 (0.04)	0.88 (0.07)	33.5	0.272
	AD	1.49 (0.07)	1.48 (0.10)	1.45 (0.05)	63	0.895	1.45 (0.05)	1.44 (0.08)	1.5 (0.04)	8.5	1	1.5 (0.04)	1.51 (0.09)	22	0.797
Peritumoral CST region	RD	0.59 (0.09)	0.58 (0.10)	0.54 (0.03)	72.5	0.448	0.54 (0.03)	0.52 (0.07)	0.64 (0.03)	9	0.884	0.64 (0.03)	0.62 (0.08)	32	0.368
	FA	0.58 (0.16)	0.61 (0.12)	0.67 (0.07)	41	0.211	0.67 (0.07)	0.66 (0.11)	0.49 (0.10)	9.5	0.772	0.49 (0.10)	0.61 (0.08)	5.5	0.018
	MD	0.81 (0.25)	0.77 (0.05)	0.75 (0.03)	87	0.087	0.75 (0.03)	0.76 (0.08)	0.96 (0.26)	7.5	1	0.96 (0.26)	0.78 (0.03)	46.5	0.008
AD	1.44 (0.22)	1.39 (0.13)	1.38 (0.09)	78	0.264	1.38 (0.09)	1.36 (0.08)	1.54 (0.27)	1.4 (0.10)	8	1	1.54 (0.27)	1.4 (0.10)	36	0.159
	0.51 (0.25)	0.44 (0.08)	0.43 (0.02)	88.5	0.070	0.43 (0.02)	0.43 (0.09)	0.67 (0.25)	45.5	0.006	0.67 (0.25)	0.47 (0.07)	45.5	0.006	

Values are expressed as the median and IQR (interquartile range). CST: Corticospinal tract. DTI values are expressed in 10<sup>-3</sup> mm<sup>2</sup>/s

**Supplementary Table 4:** Univariate analysis between quantitative DTI-derived metrics and preoperative motor deficit.

Variable	DTI metric	Preoperative deficit		Wilcoxon-Mann-Whitney Test			
		No ( <i>n</i> =7)	Yes ( <i>n</i> =4)	<i>U</i>	<i>Z</i>	<i>P</i>	<i>r</i>
Overall CST	FA	0.56 (0.03)	0.53 (0.01)	5	1.36	0.212	0.41
	MD	0.92 (0.11)	0.88 (0.05)	13	0.29	0.833	0.09
	AD	1.48 (0.12)	1.43 (0.07)	11	0.57	0.618	0.17
	RD	0.64 (0.11)	0.6 (0.04)	12	0.29	0.830	0.09
Peritumoral CST region	FA	0.64 (0.25)	0.34 (0.11)	3	2.08	0.042	0.63
	MD	0.81 (0.27)	1.18 (0.23)	26	2.28	0.018	0.69
	AD	1.43 (0.18)	1.62 (0.2)	23	1.7	0.109	0.51
	RD	0.46 (0.36)	0.96 (0.42)	26	2.27	0.02	0.68
Ratio Ipsilateral/Contralateral	rFA	0.98 (0.04)	0.95 (0.06)	6	1.43	0.179	0.43
Overall CST	rMD	1 (0.04)	1.02 (0.09)	21	1.34	0.215	0.4
	rAD	1 (0.03)	1 (0.04)	16	0.48	0.673	0.15
	rRD	1 (0.09)	1.03 (0.15)	19	0.97	0.364	0.29
	rFA	0.97 (0.07)	0.56 (0.33)	1	2.46	0.012	0.74
Peritumoral CST region	rMD	1.08 (0.03)	1.6 (0.26)	26	2.27	0.024	0.68
	rAD	1.06 (0.3)	1.21 (0.12)	19	0.95	0.412	0.28
	rRD	1.16 (0.31)	2.44 (1.61)	28	2.65	0.006	0.8

Values are expressed as the median and IQR (interquartile range). CST: Corticospinal tract. DTI values are expressed in  $10^{-3}$  mm<sup>2</sup>/s

**Supplementary Table 5:** Optimal cut-off based on DTI for permanent motor deficit.

Variable	Cut-off	Sensitivity	Specificity	Optimal criterion	AUC
rFA Ipsilateral/Contralateral Peritumoral CST region	0.8	1	0.875	0.875	0.917

rFA: Fractional anisotropy ratio, AUC: Area under the curve