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Editorial

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# The Pre-Surgical Planning of Brain Neoplasms: From Diffusion Tensor Imaging to More Advanced Approaches

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**KEYWORDS:** Brain neoplasm; Tractography; Pre-surgical planning; DTI; CSD.

The pre-surgical planning of brain neoplasms is strongly contributing to change the prognosis of neoplastic patients. Indeed, it supplies more and more detailed and reliable functional and morphological information before as well as during surgery. Both invasive and non-invasive approaches are available to achieve this goal. A powerful technique for the pre-surgical planning of brain neoplasms is Diffusion Weighted Imaging (DWI) based tractography. Differently from other approaches, tractography is able to provide, non-invasively, morphological information regarding brain pathways relationship with the neoplasm, by analyzing water diffusion within white matter. This is important especially for eloquent bundles, such as Cortico-Spinal Tract (CST) and Arcuate Fasciculus (AF), whose damages have a bad impact on the patient's Quality of Life (QoL). Tractography can be performed through several diffusion signal modeling techniques, among which Diffusion Tensor Imaging (DTI) is the most known. DTI has been widely used for neurosurgery both in pre-operative and intra-operative contexts, also in combination with other functional approaches such as functional MRI (fMRI) and cortical stimulation.[1-8] This useful technique was able to reduce post-surgical deficits as well as to improve the survival of neoplastic patients, through a better delineation of maximal safe resection.[9] Moreover, its use provided great benefits in patients with high-grade gliomas in terms of risk of death.[9] Several studies have demonstrated that DTI suffers from many limitations regarding its reliability to correctly model diffusion signal in different conditions.[10,11] Furthermore, tensorial models are not able to resolve different fibers geometries (i.e. crossing fibers) within the same voxel; these complex configurations have been demonstrated to characterize more than 90% of white matter voxels,[12] thus making DTI an unreliable diffusion modeling technique. In order to overcome these limitations, several other approaches were developed; in particular, High Angular Resolution Diffusion-weighted Imaging (HARDI),[13] Q-Ball Imaging (QBI)[14] and Diffusion Spectrum Imaging (DSI)[15] were found to be promising techniques for resolving voxels with multiple fibers orientations. Nevertheless, tractography was further improved by an HARDI modified approach called Constrained Spherical Deconvolution (CSD); this technique does not require very long acquisition time with respect to DSI[16] and it is able to improve angular resolution if compared to QBI.[17] CSD-based tractography was widely used in physiological contexts as well as in pathological ones, showing high sensitivity for the detection of white matter pathways.[18-22] Although tensorial approaches were proved to be inadequate for reliably reconstructing brain pathways[23] and histological validation of CSD-based tractography has been recently provided,[24] more advanced diffusion techniques are still considered not usable in clinical settings due to their too high technical requirements.[25] For these reasons, DTI remains, to date, the most used technique for investigating white matter bundles, also for the pre-surgical planning of brain neoplasms.[26-28] In reality, as recently highlighted by Mormina and colleagues,[29] CSD-based tractography is feasible in clinical settings and it is able to provide very useful information during the pre-surgical evaluation of eloquent bundles in patients with high-grade gliomas. It was shown that DTI-based reconstructions can be affected also by neoplasm's effects on white matter bundles. Indeed, brain pathways might result dislocated, disrupted and/or infiltrated by neoplasm,[30] with simultaneous Fractional Anisotropy (FA) dec-

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rements; tensorial models are not able to distinguish among these different conditions, thus causing partial reconstructions or null detection of bundles involved. Moreover, peritumoral edema surrounding high-grade gliomas is able to reduce FA values,[31] causing, also in this case, misleading fiber tracking. Mormina, et al.[29] showed how CSD-based tractography is able to clearly define fiber bundles involved by high-grade gliomas. Comparative qualitative analysis between CSD-based tractography and DTI-based one in patients with high-grade gliomas is shown in Figures 1 and 2.

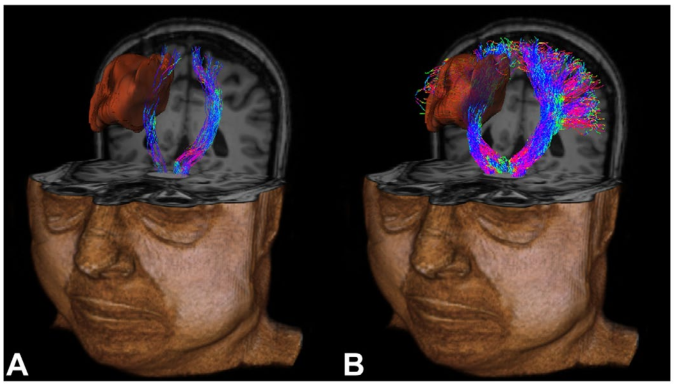


**Figure 1:** Comparative qualitative analysis of bilateral CST reconstructions in a patient with right high-grade glioma (brown volume). DTI-based tractography (A) shows a good detection of the medial CST portion in the healthy side, whereas it is less represented in the affected side. Lateral CST portions are bilaterally missing. CSD-based tractography (B) shows robust detection of the entire CST in the healthy side. The medial CST portion results poorly involved in the affected side; moreover, the lateral CST portion is still detected, although it seems to be more involved by neoplasm. While the lack of DTI detection of lateral CST might be due to DTI intrinsic limitations, different representations of medial CST in the affected side might be caused by peritumoral edema affecting DTI-based reconstruction.

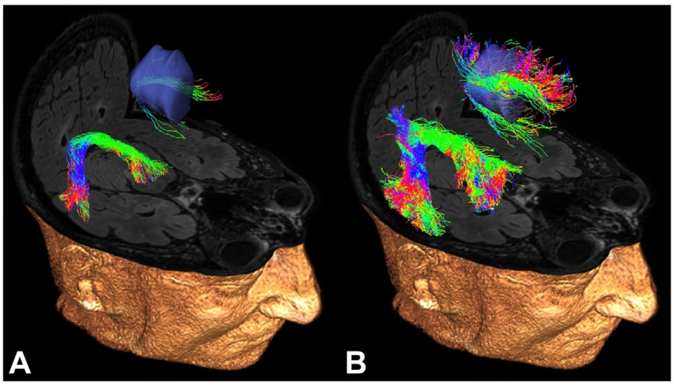


**Figure 2:** Comparative qualitative analysis of bilateral AF reconstructions in a patient with left high-grade glioma (blue volume). DTI-based tractography (A) shows a good AF detection in the healthy side, although several portions are poorly represented, such as the anterior one. AF seems to be widely damaged by neoplasmin the affected side. CSD-based tractography (B) shows a better detection of all AF portions in the healthy side, if compared to DTI-based one. Moreover, it shows a good AF representation in the affected side; this suggests that AF is involved by neoplasm although it is not strongly damaged. Also in this case, both DTI limitations and peritumoral edema might cause differences regarding AF representations in the affected side, if compared to CSD-based one.

Mormina and colleagues[29] showed also how this technique allowed are liable analysis of diffusion-based parameters of reconstructed pathways in neoplastic patients. The quantitative evaluation of white matter streamlines based on diffusion tensor parameters, such as FA and Mean Diffusivity (MD), is considered another important measurement for detecting structural alterations of white matter caused by a loss of axonal integrity. Since DTI-based tractography does not consider voxels with low FA values, the quantitative analysis might provide the erroneous information of not significant white matter alterations; the latter, together with a partial qualitative analysis of affected pathways, might thus suggest false safe resection margins around the neoplasm. Moreover, it is worthy to note that a pre-surgical planning performed by means of DTI-based tractography cannot provide any qualitative and quantitative information regarding well-known undetected white matter bundles, such as the lateral portion of CST as well as the anterior portion of AF.[29,32] All these limitations might be avoided by using CSD-based approach. Its sensitivity for reconstructing white matter bundles has been also recently highlighted by a comparative analysis of different tractographic approaches; in detail, CSD-based tractography was able to better detect brain pathways involved by neoplasm if compared to DTI-based one.[33]

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This brief description showed how the use of more advanced DWI-based approaches can provide useful information before surgical treatment of patients with brain neoplasms. It was demonstrated that these techniques are able to improve effectiveness of surgical treatments as well as their outcome by allowing a better delineation of resection margins. Moreover, they may have a good impact on the quality of life of neoplastic patients by helping to preserve eloquent fiber bundles and consequently by reducing post-surgical deficits. Several authors demonstrated that advanced diffusion signal modeling algorithms, such as CSD one, can be compatible with clinical settings and they should be more largely used for pre-surgical planning of brain neoplasms.

Interesting future perspectives for brain neoplasms treatment will regard the combined use of CSD-based tractography with functional approaches, such as neuronavigated Transcranial Magnetic Stimulation (nTMS), in order to further improve detection of eloquent bundles. Indeed, a recent study has adopted nTMS for subject-specific localization of the motor area and then DTI-based tractography for CST tracking; this approach allowed a good detection of CST, although tractographic reconstructions were found affected by above described DTI limitations, such as the peritumoral edema.[34] The use of CSD-based tractography in a similar study protocol might provide a better subject-specific detection of CST. Finally it will be important to assess potential improvements and advantages for neurosurgeons provided by the integration of these techniques into intraoperative navigation systems.

## CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

## CONSENT

Patients has provided written consent for submission of this manuscript for publication.

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