Presurgical Brain Mapping: fMRI & DTI

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The aim of Neuro-Oncological Surgery is to preserve patients' functional integrity and to prolong progression free and overall survivals by achieving maximal tumor cytoreduction in the operating theater. In order to achieve this goal it is mandatory not only to preserve eloquent cortex but also to safeguard indispensable white matter pathways. Intraoperative direct cortical and subcortical electrical stimulation mapping (ESM) is the method of choice to map functional sites in the adjacent cortex and in the proximity of the resection cavity. Functional neuro-oncological surgery has allowed to extend the indications to previously considered off-limits brain regions, it has increased the extent of the resection and reduced permanent morbidity. Overall intraoperative function monitoring has significantly improved the survival rate of patients undergoing resection of low-grade gliomas(1).

Modern Neuroradiology is then asked to provide not only morphological and information about the relationship of the tumor with vessels and nerves, or metabolic information about tumor heterogeneity, but to provide also information about the functional status of the relevant networks. In particular to disclose the relationship of active nodes and connections with the mass. Currently, functional MRI (fMRI) and MR diffusion tractography studies evaluating one of the following four functional networks is requested before surgery: sensorimotor (corticospinal), speech (dominant dorsal and ventral language pathways), visual (optic radiations) and attention (non-dominant dorsal and ventral language pathways). The study request depends on the tumor location.

A fMRI study is requested to determine the degree of cortical reorganization the brain has gone through as the result of tumor infiltration and growth. The tumor may have dislocated eloquent cortical sites to perilesional areas. In more severe cases the tumor may have completely destroyed a cortical node and activity may appear at a distant location or in the contralateral hemisphere. It has not been determined yet how reliable fMRI is to measure these pre-operative plasticity changes.

Diffusion MR tractography has recently emerged as a valuable clinical tool for presurgical planning(2-4) and intraoperative imaging-guided navigation in the operating room(5). Diffusion MR tractography has the potential to provide unique information about connectional anatomy and pathology-induced changes. This

information has not been available before and it can be acquired with clinical 1.5 and 3 tesla MR units. Despite several challenges and limitations inherent to current diffusion imaging methods(6), the information provided by tractography is good enough to be used in the clinic. Currently tractography is a user-dependent method. The challenges, limitations and pitfalls(7) must be understood carefully before interpreting the results of tractography for presurgical planning. Useful imperfect and user-dependent tests are used in the clinic everyday all the time.

Challenges of MR tractography for brain surgery

Diffusion MR imaging provides unique insights into both macrostructure and microstructure. Water molecules move preferentially along the bundle of parallel axon and diffusion imaging reveals the dominant orientation of these bundles. In the proximity of a tumor, white matter bundles can be displaced, infiltrated, diluted by vasogenic edema, or destroyed(8). Diffusion anisotropy is typically reduced in areas of tumor infiltration and/or vasogenic edema. Preliminary validation studies of DTI MR tractography with intraoperative ESM have shown that false negative results may be found in the proximity of infiltrating low-grade glioma(9-11).

It is important to remark that tractograms are virtual estimation (streamlines) of the orientation of white matter bundles. The estimate depends on the microstructural properties of the tissue. The degree of uncertainty of the estimate is reduced in anatomical and pathological conditions: in voxels with more than one bundle (such as in the deep fronto-parieto-temporal white matter at the crossroad between the corticospinal tract, corpus callosum and SLF) and in voxels with increased free water content secondary to tumor infiltration or edema leading to apparent reduced anisotropy. The former type of challenge can be overcome with advanced diffusion methods such as high angular resolution diffusion imaging (HARDI)(12) and constrained spherical deconvolution (cSD)(13) which have the ability to extract multiple orientations of fibers in voxels containing more than one bundle. The latter type of challenge can be overcome with advanced imaging methods able to separating diffusion properties of the bundles from surrounding free water. Implementation of new advance methods such as Noddi(14), CHARMED(15), AxCaliber(16) and ActiveX(17) should offer a new class of microstructural tissue parameters, such as mean axonal diameter, that may give a more specific estimation of regional changes than measures derived from DTI. It has been shown that NODDI performs better than DTI in brain gliomas with vasogenic edema(18). In the future implementation of the new methods in the clinics may have the potential to generate more reproducible, less user-defined tract reconstruction in patients with glioma.

Clinical value of MR tractography

Several important issues are the focus of current basic and clinical research: function, importance, vulnerability and indispensability of each pathway in reference to network functionality. Gliomas infiltrating the perisylvian region on the dominant hemisphere offer a unique opportunity to identify gray and white matter structures that are essential for speech production. In a study on 19 right-handed patients it was shown that gliomas growing in the ventrolateral aspect of the left frontal lobe may cause mild to moderate speech deficits. Gliomas growing in the left VPCG were much more likely to cause speech deficits than gliomas infiltrating the IFG, including Broca area. MR DTI tractography was valuable to demonstrate that lesion extension to the AF was a requisite for the appearance of aphasia in brain tumor patients(19). Patients with glioma infiltrating either the IFG or the VPCG without involvement of the AF-direct segment did not show conduction aphasia (Figs. 3-5).

A prominent role for the insula in speech production has been suggested by an MRI study in 25 stroke patients with a deficit in motor planning of articulatory movements(20). All patients with the deficit had lesions that included a discrete region of the dominant precentral gyrus of the insula, but not all had a lesion in pars opercularis. This area was completely spared in other 19 stroke patients without these articulation deficit. fMRI studies have confirmed the important role of the insula for motor planning of speech. However, patients with diffuse LGG infiltrating the insula, the temporal stem and the anterior temporal region have normal scores on language tests despite large tumor size (Bizzi A, manuscript in preparation).

In conclusion, fMRI and DTI provide unique information that has been changing presurgical evaluation of patients with brain gliomas, and in particular when the mass is located nearby eloquent areas. Virtual dissection of the major white matter tracts should be used only as a road map for presurgical planning and as guidance for intraoperative subcortical ESM.

Clinical studies with MR diffusion tractography are showing that lesion extension to the white matter pathways (i.e. AF and IFOF) connecting frontal to parietal and temporal speech regions is an important mechanism for the appearance of aphasia.

More advanced diffusion imaging methods such as Noddi and Spherical Deconvolution are being implemented to meet the challenges of presurgical planning in patients with a brain tumor.

References

1. Duffau H. Lessons from brain mapping in surgery for low-grade glioma: insights into associations between tumour and brain plasticity. Lancet Neurol. 2005;4(8):476-86. Epub 2005/07/22.
2. Clark CA, Barrick TR, Murphy MM, Bell BA. White matter fiber tracking in patients with space-occupying lesions of the brain: a new technique for neurosurgical planning? Neuroimage. 2003;20(3):1601-8.
3. Field AS, Alexander AL, Wu YC, Hasan KM, Witwer B, Badie B. Diffusion tensor eigenvector directional color imaging patterns in the evaluation of cerebral white matter tracts altered by tumor. J Magn Reson Imaging. 2004;20(4):555-62.
4. Mori S, Frederiksen K, van Zijl PC, Stieltjes B, Kraut MA, Solaiyappan M, et al. Brain white matter anatomy of tumor patients evaluated with diffusion tensor imaging. Ann Neurol. 2002;51(3):377-80.
5. Nimsky C, Ganslandt O, Hastreiter P, Wang R, Benner T, Sorensen AG, et al. Intraoperative diffusion-tensor MR imaging: shifting of white matter tracts during neurosurgical procedures--initial experience. Radiology. 2005;234(1):218-25.
6. Jones DK. Studying connections in the living human brain with diffusion MRI. Cortex. 2008;44(8):936-52. Epub 2008/07/19.
7. Jones DK, Cercignani M. Twenty-five pitfalls in the analysis of diffusion MRI data. NMR Biomed. 2010;23(7):803-20. Epub 2010/10/05.
8. Jellison BJ, Field AS, Medow J, Lazar M, Salamat MS, Alexander AL. Diffusion tensor imaging of cerebral white matter: a pictorial review of physics, fiber tract anatomy, and tumor imaging patterns. AJNR Am J Neuroradiol. 2004;25(3):356-69. Epub 2004/03/24.
9. Bello L, Gambini A, Castellano A, Carrabba G, Acerbi F, Fava E, et al. Motor and language DTI Fiber Tracking combined with intraoperative subcortical mapping for surgical removal of gliomas. Neuroimage. 2008;39(1):369-82. Epub 2007/10/04.
10. Leclercq D, Duffau H, Delmaire C, Capelle L, Gatignol P, Ducros M, et al. Comparison of diffusion tensor imaging tractography of language tracts and intraoperative subcortical stimulations. J Neurosurg. 2010;112(3):503-11. Epub 2009/09/15.
11. Spena G, Nava A, Cassini F, Pepoli A, Bruno M, D'Agata F, et al. Preoperative and intraoperative brain mapping for the resection of eloquent-area tumors. A prospective analysis of methodology, correlation, and usefulness based on clinical outcomes. Acta Neurochir (Wien). 2010;152(11):1835-46. Epub 2010/08/24.
12. Berman JI, Chung S, Mukherjee P, Hess CP, Han ET, Henry RG. Probabilistic streamline q-ball tractography using the residual bootstrap. Neuroimage. 2008;39(1):215-22. Epub 2007/10/04.
13. Tournier JD, Calamante F, Connelly A. Robust determination of the fibre orientation distribution in diffusion MRI: non-negativity constrained super-resolved spherical deconvolution. Neuroimage. 2007;35(4):1459-72. Epub 2007/03/24.
14. Zhang H, Schneider T, Wheeler-Kingshott CA, Alexander DC. NODDI: practical in vivo neurite orientation dispersion and density imaging of the human brain. Neuroimage. 2012;61(4):1000-16. Epub 2012/04/10.
15. Assaf Y, Basser PJ. Composite hindered and restricted model of diffusion (CHARMED) MR imaging of the human brain. Neuroimage. 2005;27(1):48-58. Epub 2005/06/28.
16. Assaf Y, Blumenfeld-Katzir T, Yovel Y, Basser PJ. AxCaliber: a method for measuring axon diameter distribution from diffusion MRI. Magn Reson Med. 2008;59(6):1347-54. Epub 2008/05/29.
17. Zhang H, Hubbard PL, Parker GJ, Alexander DC. Axon diameter mapping in the presence of orientation dispersion with diffusion MRI. Neuroimage. 2011;56(3):1301-15. Epub 2011/02/15.
18. Figini MB, G. Riva, M. Bello, L. Zhang, H. Bizzi, A. NODDI performs better than DTI in brain tumors with vasogenic edema. Proceeding ISMRM-ESMRMB Milan 2014. 2014:6857.
19. Bizzi A, Nava S, Ferre F, Castelli G, Aquino D, Ciaraffa F, et al. Aphasia induced by gliomas growing in the ventrolateral frontal region: assessment with diffusion MR tractography, functional MR imaging and neuropsychology. Cortex. 2012;48(2):255-72. Epub 2012/01/13.
20. Dronkers NF. A new brain region for coordinating speech articulation. Nature. 1996;384(6605):159-61. Epub 1996/11/14.