

Diffusion tensor tractography can affect treatment strategy to remove brain occupying mass lesions

Zahra Farshidfar¹, Fariborz Faeghi^{2*}, Mostafa Mohseni³, Afsoun Seddighi⁴, Homayoun Hadizadeh Kharrazi⁵, Jamil Abdolmohammadi¹

¹Students' Research committee, Shahid Beheshti University of Medical Sciences, Tehran, Iran

²Radiology Technology Department, School of Paramedicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

³Neurosurgery Department, Shohada-E Tajrish hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁴Functional Neurosurgery Research center of Shohada Tajrish hospital, Tehran, Iran

⁵Radiology Department, Rasule Akram hospital, Tehran University of Medical Sciences, Tehran, Iran

* Corresponding author: e-mail address: f_faeghi@sbmu.ac.ir (F.Faeghi)

ABSTRACT

Radical resection of a pathological lesion along with the preservation of eloquent cerebral tissue is the principle goal of neurosurgery. Brain lesions are usually diagnosed by conventional magnetic resonance imaging (MRI), but this method is unable to describe the relationship between lesions and neighboring specific white matter (WM) tracts. Diffusion tensor tractography (DTT) is a new sophisticated imaging modality to reveal the neural fibers and their relationships with lesions. In the current study we assess that how diffusion tensor tractography can affect on treatment planning in patients afflicted by different types of brain lesions. In this prospective observational study, eight patients with brain mass lesion underwent conventional brain MRI pulse sequences and DTT imaging with 1.5 Tesla system using 64 independent diffusion encoding directions between December 2011 to January 2013. Acquired images were assessed by the neuroradiologist and neurosurgeon. Finally, the treatment strategies were compared using data before and after the tractography. The treatment strategy in six patients changed from radiotherapy into the craniotomy by using tractography data, in one patient changed from radio surgery to craniotomy and in one patient, neurosurgeon preferred to avoid operation. As we can infer from this study, based on the tractography results, the treatment technique may be changed, and the treatment plan could be devised with more accuracy and in case of surgery, may lead to less post-operative neurological deficits and better outcome results.

Key words: diffusion tensor tractography; brain mass lesion; treatment strategy

INTRODUCTION

Even though increase the extent of the tumor resection is the best option in the surgical neurooncology, but keeping the vital cerebral tissue safe is the critical point which should be considered [1]. According to this, in addition to minimizing post-operative neurological deficits, patient enjoy better prognosis by maximizing the tumor resection. Although, routine structural MR images can accurately demonstrate brain tumors, they do not give precise information about the involvement and integrity of the white matter tracts in the immediate region surrounding tumor[1, 2]. Diffusion tensor imaging (DTI) can be used to show white matter fiber orientations, and consequently construct paths that connect different brain regions. This technique is called

tractography and is currently the only non-invasive, in-vivo method that can provide estimates of brain structural connectivity. Tractography is gradually becoming an important tool for clinical applications such as pre-surgical planning. More specifically, fiber tracking has been used to map the cortico-spinal tract, subcortical pathways serving language sites and superior longitudinal fasciculus in patients with brain tumors or other space occupying lesions located in the vicinity of these fiber tracts. In all cases, knowledge of exact location of the lesion with respect to eloquent white matter pathways was of great value to the neurosurgeons in planning the appropriate surgical strategy[3]. Numerous studies have confirmed that the anatomical accuracy of DTT in tumors, vascular lesions, intra-cerebral hemorrhage and even surgery for

epilepsy is comparable to intraoperative direct subcortical stimulation[4]. Diffusion tensor imaging measures the diffusion displacement properties of water molecule in a three-dimensional space. Water diffusion parallel to the white matter tracts is less restricted than water diffusion perpendicular to them; consequently the measured image signals are higher for diffusion-gradient encoding perpendicular to the white matter tracts rather than parallel. This directional variation in the signal intensity is termed "diffusion anisotropy". By acquiring DW images with at least six independent gradient-encoding directions, it is possible to estimate the diffusion tensor (DT). The principle eigenvector represents the direction of greatest diffusion which also corresponds to the fiber tract axis. With this directional information, the white matter tract organization may be represented using directionally color-coded schematic maps of major eigenvector orientation [1,2 , 5-9]. We usually categorize the neural fiber involvement based on FA and color-coded FA maps and T2 weighted images into four groups: edema, infiltration, deviation or displacement and disruption or destruction [2, 10]. It is crucial to reveal fiber tracts and lesion synchronously[11]. The aim of the current study is to assess that how diffusion tensor tractography can affect treatment planning in patients afflicted by different types of brain lesions.

MATERIALS AND METHODS

Eight patients (mean age: 45, ranging from 25 to 60 years old) between December 2011 and January 2013 were participated in this prospective observational study. They had been diagnosed with brain mass lesion verified through conventional MRI. Seven patients had been decided to undergo radiotherapy or radiosurgery following stereotactic biopsy for treatment during a week after MRI examination; and one patient who underwent stereotactic biopsy four months earlier had been decided to do craniotomy. All patients provide routine informed consent prior to the investigations.

Data Acquisition

All patients underwent MRI examination by 1.5 Tesla, Siemens, Espree scanner with 8 channel head coil. First anatomical T1-weighted images (3-D fast spoiled gradient recalled echo sequences) acquired in order to overlay the selected fiber on them; also T2-weighted

images may be acquired before fiber tracking in case of better evaluation of tumor margins if necessary. After that, diffusion weighted images have been taken in the corresponding time period, covering the entire brain volume with the following parameters: single shot echo planar imaging sequences; TR: 9000 ms; TE:106.2 s; slice thickness: 2.3mm; Matrix size: 96×96; FOV:180×180mm; NEX:2; the number of diffusion encoding directions for each slice was 64 with two b-values:0 and 1000 s/mm²; usually 60 axial slices needed for complete coverage of the brain.

DTI Data Processing

All acquired data have been transferred into our image processing lab and were processed with DTI Studio software (Johns Hopkins University, USA). Fractional anisotropy (FA), apparent diffusion coefficient (ADC) maps were generated with noise removal level 50; and tensor also calculated. Then we did fiber tracking by drawing ROI on the selected fibers using color-FA images (which in most patients, it was corticospinal tract). The last step in DTI data processing was overlaying the selected fibers on T1 or T2 weighted anatomical images.

Evaluation

All acquired images (FA, ADC maps, color-FA and 3-D reconstructed fibers) were evaluated by an expert radiologist in order to report which neuronal fibers and how afflicted by the lesions. Then, overlaid images were shown to the neurosurgeons; the treatment strategy or the best way to approach to the lesion in case of craniotomy which has chosen after fiber tracking was noted. Finally, these results were compared with the treatment techniques to the lesion based on the conventional MR images.

RESULTS

Eight patients who diagnosed with cerebral lesions referred to imaging center. Six patients diagnosed with different types of glioma (intra-axial tumor) and two patients had extra-axial lesions (meningioma and arteriovenous malformation: AVM). Diffusion tensor imaging has done for them. In first step, FA, ADC and directional maps (color-coded FA map) have been calculated; then fiber tracking was performed (fig.1 and 2). The calculated maps and images reported by an expert neuroradiologist who is expert in reporting tractography results images.

Table1. Information of patients and treatment strategy before and after diffusion tensor tractography

Pt. NO.	Age/Sex	Pathology	Tumor location	WM involvement	treatment technique before DTT	treatment technique after DTT	Post op. deficit
1	M-36	Oligodendrioma, grade II	Lt paritofrontal	Deviation and edema involvement of WM tracts	radiotherapy	craniotomy	Temporary hemiplegia
2	M-60	Glioblastoma	Lt frontal	Displacement of frontal CC*, destruction and distortion of SFC* fibers	radiotherapy	Craniotomy	none
3	M-51	Gliosarcoma(GBM), grade IV	Lt parietal	Destruction of WM tracts near tumor	radiotherapy	craniotomy	none
4	M-48	Astrocytoma, grade II	lt frontal	Infiltration and destruction of WM tracts near tumor	radiotherapy	craniotomy	none
5	F-60	Oligodendrioma, grade I	Lt temporo-occipital	Deviation of Lt. internal capsule, posterior CST*, splenium of CC	radiotherapy	craniotomy	none
6	M- 25	Meningioma, grade I	Rt temporo-occipital	Deviation of Rt. internal capsule, posterior CST, splenium of CC	Radiotherapy	craniotomy	none
7	M- 40	AVM	Lt. parietal	Distortion of retrolenticular part of internal capsule, involvement of angular gyrus	Radiosurgery	craniotomy	none
8	M-39	Oligodendrioma, grade II	Rt frontal	Infiltration and destruction of WM tracts near tumor	Craniotomy	No operation	-

*CC: corpus callosum, SFC: superior frontal connecting fibers, CST: corticospinal tract.

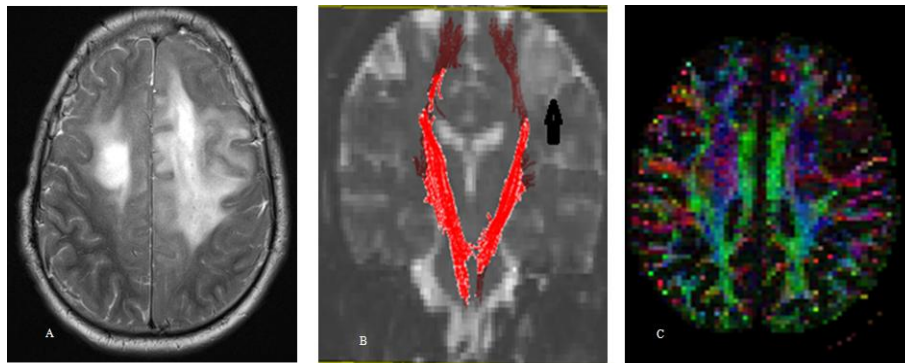


Figure.1. Diffusion tensor tractography in patient with left parieto-frontal oligodendrioma grade II. The tumor can visualize in axial T2-w spin echo (A). The corticospinal tract overlaid on coronal b0 image (B). color - coded FA has been shown on picture C. Corticospinal tract remains intact with slightly deviated medially due to lesion pressure. In this patient treatment strategy changed from radiotherapy to craniotomy.

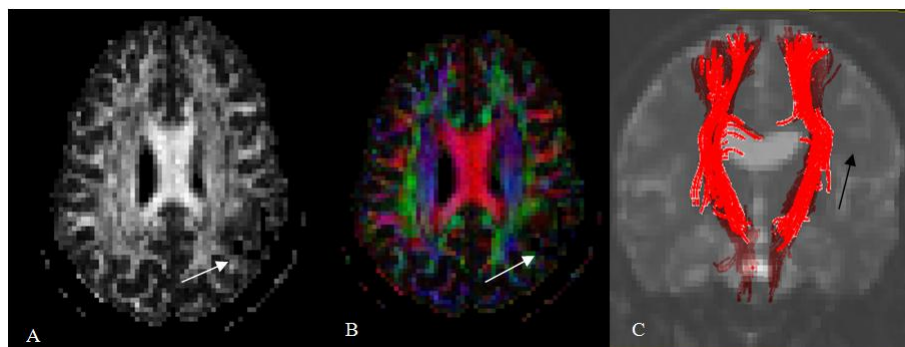


Figure.2. Diffusion tensor tractography in patient with left deep parietal arterio- venous malformation (AVM). The site of lesion has been represented by white and black arrows in FA map (A), color- coded FA (B) and tractography result (C). As you can see in C, corticospinal tract is not deviated and there is not any pressure on it; so, in this patient treatment strategy changed from radiosurgery to craniotomy

Then, these reports with fiber tracking images were shown to the neurosurgeons and the treatment procedures before and after fiber tracking were recorded (table 1). As it can be seen in table 1, in six patients (number 1-6) the treatment strategy changed from radiotherapy to craniotomy; radiosurgery was replaced by craniotomy in one patient which is more effective to make better prognosis for patients, and in one patient, physicians preferred to avoid operation because of many connections between tumor and adjacent WM tracts. The operation strategy before tractography in this patient was craniotomy. According to DTT results, treatment technique changed in all patients. No significant additional neurological deficits occurred after surgery except in patient number one which was temporary hemiplegia during one week after surgery.

DISCUSSION

Brain occupying mass lesions may invade both functional cortical gray and white matter tracts[1]. In the surgery of patients with brain lesions preservation of vital cerebral functions is as important as maximizing tumor resection. The associated morbidity of aggressive resection can be significantly reduced by carefully preservation of vital cerebral function and the quality of life will be largely improved. Simultaneously maximizing tumor resection can reduce the chance of recurrence of tumors and improve longer patient survival and long- term functional status[12, 13]. So a comprehensive assessment of the extent of the lesion is vital to all neurological and surgical therapies. The development of accurate, noninvasive and in vivo methods like tractography to map WM fiber tracts is of critical importance[2, 3, 14]. Applying DTT to depict WM neural fibers initiated since 2002 and many studies have been done till now. The majority of these studies have proved the effectiveness of diffusion tensor tractography in presurgical and also intra-operative assessments of intra- axial brain tumors. They have shown that it's possible for anatomically intact neural fibers located in abnormal areas in the brain [15], and removing these tracts might have neurological deficits. Researchers showed that DTT could be a trustable device for neurosurgeons to specify major neural pathways, and show them beside the high resolution anatomical data during

surgery, and eventually provide the information about the way of access to the tumor in order to maximum safe resection [16]. Other studies also showed the consistency of DTT results with histopathological information. Pay attention that there are informative and technical shortages regarded to small and complicated neural fibers and the reliability of this imaging modality [17, 18]; so it is so clear that we need many studies research on these issues. In spite of these researches, some studies could not show the efficiency of tractography in treatment planning in case of tumors; nevertheless, they recommended performing DTT in presurgical assessment of tumors because of potential usefulness effects of this imaging modality.

However, we are aware of the utility and important role of new imaging modality based on MRI such as fMRI and DTI in neuroimaging to help neurosurgeons to choose treatment plan with more accuracy in order to reduce post-operative neurological deficits, these imaging techniques are not routine and they are performed in very limited imaging centers in Iran; so approximately all neurosurgery department operate patients with brain lesions completely blind and without any information about eloquent cortex and WM tracts or preferred to choose another treatment method rather than open surgery such as radiotherapy or radiosurgery which have some problems[19]. In Shohada neurosurgery department that co-operated us in this study, the treatment strategy in patients with intra-axial brain tumor which is located in or near motor or language areas is radiotherapy or radiosurgery following stereotactic biopsy and the treatment strategy in case of extra- axial brain lesions is similar to intrinsic lesions mentioned earlier. Based on the opinion of our neurosurgeons team, if the distance between the tumor and neural fibers is at least one gyrus, they can do craniotomy with a little concern about post- operative neurological deficit; and in case of extra-axial lesions such as meningioma they believe that if there is no pressure on neural fibers or in the other words, if fibers are not deviated in tractography images, craniotomy can be substituted other treatment strategies. As I mentioned before, maximum resection of the tumor is valuable treatment in patients with brain occupying mass lesions which make

patients enjoy better prognosis and reduce the chance of tumor recurrence.

In the current study we compared the treatment strategy before and after fiber tracking in eight patients with different types of brain lesions. The strategy changed after tractography in all patients. No neurological deficits were shown two months after surgery in all seven patients underwent craniotomy except in one patient which is temporary. Finally, we consider that tractography may have a lot of advantages for the patients.

CONCLUSION

We should consider that diffusion tensor tractography is a new method to extract specific white matter tracts noninvasively. Although this

modality is so complicated, and more studies should be done on it to optimize and simplify fiber tracking, but its potential possibilities to help neurosurgeons to access brain lesions with minimal post-operative deficits is important issue that could not be ignored.

ACKNOWLEDGEMENT

We would like to thank Day and Babak imaging centers; and we really wish to appreciate Dr. Susumu Mori and DTIstudio experts from Johns Hopkins University for helping us to solve DTI processing problems. Finally, we would like to thank the neurosurgery department at Shohada Tajrish hospital especially Dr. Amir S. Seddighi for his helpful advices.

REFERENCES

1. Witwer B, Moftakhar R, Hasan K, Deshmukh P, Haughton V, Field A, et al. Diffusion-tensor imaging of white matter tracts in patients with cerebral neoplasm. *J Neurosurg* 2002;97:568-575.
2. Stadlbauer A, Nimsky C, Buslei R, Salomonowitz E, Hammen T, Buchfelder M, et al. Diffusion tensor imaging and optimized fiber tracking in glioma patients: Histopathologic evaluation of tumor-invaded white matter structures. *NeuroImage* 2007;34:949-956.
3. Gui M, Peng H, Carew JD, Lesniak MS, Arfanakis K. A tractography comparison between turboprop and spin-echo echo-planar diffusion tensor imaging. *NeuroImage* 2008;42:1451-1462.
4. Bagadia A, Purandare H, Misra B, Gupta S. Application of magnetic resonance tractography in the perioperative planning of patients with eloquent region intra-axial brain lesions. *Journal of Clinical Neuroscience* 2011;18:633-639.
5. Ferda J, Kastner J, MukenSnabl P, Kreuzberg B, Choc M, HoremuZova J, et al. Diffusion tensor magnetic resonance imaging of glial brain tumors. *European Journal of Radiology*. 2010;74:428-436.
6. Jellison B, Field A, Medow J, Lazar M, Salamat M, Alexander A. Diffusion Tensor Imaging of Cerebral White Matter: A Pictorial Review of Physics, Fiber Tract Anatomy, and Tumor Imaging Patterns. *AJNR Am J Neuroradiol* 2004;25:356-369.
7. Mori S. Introduction to Diffusion Tensor Imaging 2007.
8. Mori S, Zhang J. Principles of Diffusion Tensor Imaging and Its Applications to Basic Neuroscience Research. *Neuron* 2006;51:527-539.
9. Reiser MF, Semmler W, Hricak H. magnetic resonance tomography 2008, 130-152.
10. Yen p, Teo B, Chiu C, Chen S, Chiu T, Fa Su C. White matter tract involvement in brain tumors: a diffusion tensor imaging analysis. *Surgical Neurology*. 2009;72:464-9.
11. Qiu T, Zhang Y, Wu J, Tang W, Zhao Y, Pan Z, et al. Virtual reality presurgical planning for cerebral gliomas adjacent to motor pathways in an integrated 3-D stereoscopic visualization of structural MRI and DTI tractography. *Acta Neurochir* 2010;152:1847-1857.
12. Kovanlikaya I, Firat Z, Kovanlikay A, Uluga A, Cihangiroglub MM, Johnd M, et al. Assessment of the corticospinal tract alterations before and after resection of brainstem lesions using Diffusion Tensor Imaging (DTI) and tractography at 3 T. *European Journal of Radiology* 2011;77:383-391.
13. Yu C, Li K, Xuan Y, Ji X, Qin W. Diffusion tensor tractography in patients with cerebral tumors: A helpful technique for neurosurgical planning and postoperative assessment. *European Journal of Radiology* 2005;56:197-204.
14. Winston GP, Mancini L, Stretton J, Ashmore J, Duncan MR, Yousry TA. Diffusion tensor imaging tractography of the optic radiation for epilepsy surgical planning:

Acomparison of two methods. *Epilepsy Research*. 2011;97:124-32.

15. Buchmann N, Gempt J, Stoffel M, Foerschler A, Meyer B, Ringel F. Utility of diffusion tensor-imaged (DTI) motor fiber tracking for the resection of intracranial tumors near the corticospinal tract. *Acta Neurochir* 2011;153:68-74.

16. Nimsky C, Ganslandta O, Enders F, Merhof D, Fahlbusch R. Visualization strategies for major white matter tracts identified by diffusion tensor imaging for intraoperative use. *International Congress Series* 2005;1281:793-7.

17. Winston G, Mancini L, Stretton J, Ashmore J, Symms M, Duncan J, et al. Diffusion tensor imaging tractography of the

optic radiation for epilepsy surgical planning: A comparison of two methods. *Epilepsy Research* 2011;97: 124-132.

18) Qazi A, Radmanesh A, O'Donnell L, Kindlmann G, Whalen S, Westin C, et al. Resolving crossings in the corticospinal tract by two-tensor streamline tractography: Method and clinical assessment using fMRI. *NeuroImage* 2009; 47:98-106.

19. Maruyama K, Kamada K, Ota T, Koga T, Itoh D, Tago M, Ino K, et al. Tolerance of pyramidal tract to gamma knife radiosurgery based on diffusion-tensor tractography. *Int. J. Radiation Oncology Biol. Phys.*2008; 70: 1330–1335.