Clinical Neurology and Neurosurgery 124 (2014) 51–58

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

The role of diffusion tensor imaging in brain tumor surgery: A review of the literature

Adriaan R.E. Potgieser [a,*], Michiel Wagemakers [a], Arjen L.J. van Hulzen [a], Bauke M. de Jong [b], Eelco W. Hoving [a], Rob J.M. Groen [a]

[a] Department of Neurosurgery, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
[b] Department of Neurology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

ARTICLE INFO

Article history:
Received 25 February 2014
Received in revised form 27 May 2014
Accepted 8 June 2014
Available online 17 June 2014

Keywords:
Diffusion tensor imaging
Tractography
Glioma
Neuronavigation

ABSTRACT

Diffusion tensor imaging (DTI) is a recent technique that utilizes diffusion of water molecules to make assumptions about white matter tract architecture of the brain. Early on, neurosurgeons recognized its potential value in neurosurgical planning, as it is the only technique that offers the possibility for in vivo visualization of white matter tracts. In this review we give an overview of the current advances made with this technique in neurosurgical practice. The effect of brain shift and the limitations of the technique are highlighted, followed by a comprehensive discussion on its objective value. Although there are many limitations and pitfalls associated with this technique, DTI can provide valuable additional diagnostic information to the neurosurgeon. We conclude that current evidence supports a role for DTI in the multimodal navigation during tumor surgery.

Contents

1. Introduction ... 51
   1.1. Principles of DTI ... 52
   1.2. Technical limitations of the technique ... 52
   1.3. Method of tracking ... 52
   1.4. User-dependent factors influencing the technique ... 53
   1.5. Effect of brain shift ... 53
   1.6. White matter tract organization ... 53
2. Discussion ... 55
3. Conclusion ... 55
   Financial disclosure ... 56
   References ... 56

1. Introduction

The consequence of the extent of glioma resection regarding life expectancy is still debated due to lack of class I evidence, although current results seem to favor a more radical resection for both low grade and high grade gliomas [1]. The ultimate goal and major challenge in glioma surgery is to obtain maximal resection while minimizing loss of neurological function. Diffusion tensor imaging (DTI) is a tool that contributes to achieve this goal by visualizing white matter tracts. From the early introduction of the fiber tracking technique neurosurgeons saw potential for non-invasive mapping of white matter tracts, especially in planning the optimal approach to a lesion. The first practical implementation was the integration of the pyramidal tracts, estimated with diffusion weighted imaging, in a neuronavigation system [2]. Meanwhile, a large number of studies investigated the value of diffusion tensor

* Corresponding author at: Department of Neurosurgery, University Medical Center Groningen, Hanzeplein 1, P.O. Box 30001, 9700 RB Groningen, The Netherlands. Tel.: +31 50 361 2400; fax: +31 50 361 1707.
E-mail address: a.r.e.potgieser@umcg.nl (A.R.E. Potgieser).

http://dx.doi.org/10.1016/j.clineuro.2014.06.009

tractography for neurosurgical planning, focusing mainly on the major white matter tracts as they are most easily visualized. Most studies involved benign or malignant lesions involving the corticospinal tract [3–35], optic tract [3,17,19,23,29,36–43], superior longitudinal fasciculus [5,26,27,44] and arcuate fasciculus [3,19,29,45,46]. Nearly all authors report a positive experience with this relatively new technique. However, the beneficial effect is hard to quantify. Many authors describe the use of tractography as 'helpful', 'of great help' or 'beneficial', without exactly determining what the value was. It may have influenced the choice of approach and intra-operative decision making, but whether it has affected the quality and quantity of the resection remains difficult to ascertain. Few authors described in detail how tractography changed their surgical strategy, e.g. Chen et al. or Nimsky et al. [22,34]. Until now, there are no controlled studies that relate clinical outcome to the integration of DTI in a neuronavigation system.

Following a general introduction to the method, we want to outline the pitfalls and potential benefits of DTI as a tool for pre- and intra-operative neurosurgical planning in tumor resection in this review.

1.1. Principles of DTI

In vivo quantification of diffusion of water molecules using magnetic resonance imaging (MRI) was first described in 1986 [47]. Diffusion can be described as random thermic motion, or Brownian motion [48]. The technique utilizes the fact that in tissue diffusion is not necessarily random due to barriers that limit diffusion in one or more directions (see Le Bihan and Johansen-Berg for an excellent introduction) [49]. Unhindered diffusion of water molecules is referred to as isotropic diffusion. Restriction of movement along only one axis is called anisotropic diffusion. Among others, the measured diffusion process depends on the applied magnetic gradients and the axis of myelinated white matter tracts [50–53]. The mechanism of this anisotropy along white matter tracts is not exactly known. From studies in developing brains it has become clear that the degree of myelinisation has a role, with more myelinisation causing more anisotropy [54–57]. However, this is only a partial explanation, because anisotropy is also apparent before the white matter is myelinated [58]. With DTI it is possible to use anisotropy to analyze axonal organization of brain. This is based on the concept of a diffusion tensor, which is a mathematical model that describes the three-dimensional process of diffusion in different axes [59]. In theory, it is already possible to get an impression of the diffusion process if scanning is performed in six directions [60,61], but generally many more directions are scanned to obtain a better recording. There are various ways to perform tractography based on the diffusion tensor. Fiber assignment by a continuous tracking (FACT) algorithm is frequently used [62]. This is a deterministic approach that uses the average axonal orientation within a voxel to estimate axonal projections, based on user-defined variables such as the fractional anisotropy (FA) and the maximum tract angle. Later on, a probabilistic approach was introduced to be able to trace tracts up to and within the gray matter without relying on the arbitrary anisotropy threshold [63]. This method is also more resistant to noise, because it is less vulnerable to halts in the tractography due to individual voxels with an ambiguous fiber direction.

Several research groups used DTI to create white matter tracts atlases [64–68]. These atlases show good correspondence with atlases created with real-tissue dissections.

1.2. Technical limitations of the technique

Numerous technical considerations should be addressed in order to create a realistic concept of DTI when using this technique for neurosurgical planning. Current DTI techniques fall short on spatial resolution, signal to noise ratio (SNR) and susceptibility to a heterogenic magnetic field [69]. A first remark should be made about the resolution of diffusion-weighted imaging, which is in the range of millimeters. The diffusion process that is the source for computational modeling of white matter tracts takes place at molecular level [49]. Thus, DTI does not depict the actual diffusion process and derived actual tracts. For the intraoperative tractography the air-tissue boundary introduces additional susceptibility artifacts. Another issue is the user-dependedness of the technique, which starts at the acquisition of the data. Differences may be introduced in for example the amount of scanning directions, diffusion-weighting [70] and in magnetic field strength. It has been shown that the SNR increases when using a higher field strength [71–74]. This leads to enhanced visualization of fiber tracts. The SNR is a quantitative measure to compare the strength of the MRI signal with the noise. There are many different methods to calculate the SNR [75]. For example, the easiest method to get an impression of the SNR is to define the signal (S) as the mean signal intensity in a 2D region of interest of ten by ten voxels with maximum uniform signal intensity in every slice of the DTI scan. The noise (σ) is the standard deviation of the signal intensity in this region of interest. SNR is then calculated according to the following formula [75]: $\text{SNR} = S/\sigma$.

Recently it has been stated that for analysis of major white matter tracts (such as the corpus callosum with an FA of 0.8) an SNR of 20 is a minimum requirement, being 40 for tracts with lower FA values (0.45) [76]. The optimal FA threshold for integration of tractography in the neuronavigational device was suggested to be in the range of 0.15–0.2 [77], which needs an even higher SNR.

At lower SNR values the accuracy, precision and reproducibility of measured FA values is negatively influenced [78]. More noise has the effect that it converts diffusion isotropy to anisotropy and it augments anisotropy by an underestimation of the smallest eigenvalue (λ_3) and an overestimation of the largest eigenvalue (λ_1) [79,80]. Clearly, this has an effect on the tractography results. SNR appears to be underreported in the studies that investigated the value of DTI in neurosurgical planning. Several methods can be used to increase the SNR, such as scanning with a higher magnetic field, increase the number of repetitions, scan a b_0 image for every eight diffusion weighted images and cardiac gating [81–85].

1.3. Method of tracking

An important choice to be made is the method of tracking. Currently most studies perform tracking using a deterministic or probabilistic approach (for an example see Fig. 1). Most studies evaluating the use of DTI in neurosurgical planning use a deterministic approach, and only a few, such as in studies involving Meyer's loop of the optic tract, use a probabilistic approach [36,40,41,43]. The deterministic method is based on the assumption that the orientation of fibers can be described by a single orientation. Clearly, this is an oversimplification as the millimeter-sized voxels contain thousands of axons, which can have different orientations. The probabilistic method can proceed in areas where the fiber direction is of lower certainty [86]. Due to the fact that this is a very time-consuming method it is currently not possible to intraoperatively integrate this method in the neuronavigation. Furthermore, this method creates a 3D map of possible connectivity, which is not necessarily based on actual anatomy. Newer methods that account for crossing or kissing fibers are being developed [37,87]. These methods take all the eigenvectors of a voxel into account and include high angular resolution diffusion imaging and diffusion spectrum imaging [88–91].