Role of Diffusion Tensor MR Imaging (DTI) and Fiber Tractography in Predicting Neurological Sequealae in Patients with Head Trauma

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Abstract

Background: Brain imaging by CT and standard MRI is invaluable for defining post-traumatic sequallae that require immediate neurosurgical intervention. However, these tools currently lack the specificity to allow judgment on long-term functional outcome in most cases. This may in part be due to their insensitivity to detect more subtle white matter injuries.

Diffusion tensor imaging (DTI) is a new modality of MRI scanning that can reconstruct the white matter tracts and can assess the structural connectivity in-vivo that could potentially serve as a tool for prognostic assessment and for studying microstructural changes during recovery from head injuries.

This is a prospective study carried out in Radio-diagnosis department, Faculty of Medicine, Cairo University between August 2014 and February 2016 for patients who were subjected to head trauma. The aim of this study is to study the pattern of involvement of the white matter tracts and their integrity following head trauma and correlate this with the clinical outcome.

A total number of 40 patients (30 male and 10 female) with age range 14-67 (mean 34.7). The time of imaging varied from under one week up to 3 weeks following the traumatic insult.

The MRI sequences obtained were axial T1W, T2W, FLAIR, T2* and 3D T1, Diffusion Tensor. Images were post-processed using the Philips software for tractography. The maps obtained were (1) FA maps. (2) Directionally-encoded color FA maps. (3) 3D fiber tractography. The FA values were measured at the region of abnormality and were compared with the normal values on the unaffected contralateral side. Color-coded DTI maps were analyzed, followed by tractography of individual tracts. DTI data and MR tractography of the involved white matter tracts were compared with the corresponding tracts of the contralateral normal hemisphere. The tracts were visually inspected for changes in size and orientation, and compared to those in the contralateral hemisphere. The tracts were characterized as either displaced or disrupted.

Results: Our study included 40 patients who were subjected to head trauma. We found good association between tractography findings and Glasgow outcome scale. Most of the patients with disruption of white matter tracts had residual deficits on clinical follow-up, whereas the patients with displaced and preserved tracts had near complete neurological recovery.

We did not find significant association between the FA at the site of the lesion and the clinical score at admission or the clinical outcome after 6 months and we didn’t find significant statistical association between fractional anisotropy (FA) at lesion and fiber tract morphology changes.

Conclusion: DTI can visualize and quantify the changes in the integrity and orientation of the white matter tracts that are transected by focal brain contusions, which are otherwise not shown on conventional MR imaging. MR tractography offers a potential tool for clinical-imaging correlation of the involved white matter tracts and patient’s clinical recovery.

Key Words: DTI – FA – Head trauma – Tractography – Sequealae.

Introduction

BRAIN imaging by CT and standard MRI (Magnetic resonance imaging) is invaluable for defining post-traumatic sequallae that require immediate neurosurgical intervention. However, while CT evidence of cisternal compression, subarachnoid blood and midline shift and MRI evidence of deep injury (in the pons, medulla, or midbrain) are associated with a poor outcome, these tools currently lack the specificity to allow judgment on long-term functional outcome in most cases. This may in part be due to their insensitivity to detect more subtle white matter injuries [1].

Diffusion tensor imaging (DTI) is a new modality of MRI scanning that can reconstruct the white matter tracts and can assess the structural connectivity in-vivo that could potentially serve as a tool for prognostic assessment and for studying microstructural changes during recovery from head injuries. It also has the potential to detect abnormalities in the brain, even in cases where routine MRI may be normal. It is a sophisticated technique
that examines both the directionality and magnitude of diffusion of water molecules in structures in the brain [1]. It provides unique quantitative information regarding the structural features of the central nervous system and allows calculation of many parameters including mean diffusivity (MD) which represent overall restrictions to water diffusion, and fractional anisotropy (FA) which represents a ratio of 0-1 that reflects the degree of alignment of the underlying fibers in a voxel [2]. Changed FA in association with ADC changes could differentiate the type of edema: Decreased FA in association with increased ADC means vasogenic edema, whereas increased FA in association with decreased ADC in acute stage means cytotoxic edema. Decreased FA in association with decreased longitudinal water diffusivity could mean an impaired axonal transportation. Biomechanical forces such as stretch and shear force exceeding the elastic limit for an axon will result in a change in the morphology of the axon over hours to months, and characterized by swelling and shortening of fibers and eventual fiber loss (Wallerian degeneration). It should be noted that, microscopically, one typically observes damaged, distorted fibers interspersed among normal appearing fibers; this intermixing of normal and abnormal axons would also be represented in a single voxel. Thus, the greater the proportion of damaged distorted axons in a voxel, the lower the FA for the voxel. In the more chronic stage, fiber disruption occurs resulting in lower fiber density (causing decreased FA) and atrophy of WM structures on anatomical imaging [3].

Tractography is a 3D modeling technique used to visually represent neural tracts using data collected by diffusion tensor imaging (DTI). It uses special techniques of magnetic resonance imaging (MRI), and computer-based image analysis. The results are presented in two- and three-dimensional images [4]. The visualization of an entire white matter tract in 3D has clinical and scientific value for detecting gross changes to the anatomic course and the microstructural integrity of specific pathways [5].

Aim of the work: The aim of this study is to study the pattern of involvement of the white matter tracts and their integrity following head trauma and correlate this with the clinical outcome.

Patients and Methods

This is a prospective study carried out in Radiodiagnosis department, Faculty of Medicine, Cairo University between August 2014 and February 2016 for patients who were subjected to head trauma.

A total number of 40 patients (30 male and 10 female) with age range 14-67 (mean 34.7), The time of imaging varied from under one week up to 3 weeks following the traumatic insult.

These patients were subjected to general examination, neurological examination, revision of previous imaging if any, exclusion of contraindicators, clinical neurological deficits were evaluated using the Glasgow Coma scale at the time of imaging and after 6 months they were re-assessed by Glasgow outcome Scale through patient and family interviews.

Inclusion criteria:
• Patients with early neurological deficits related to previous traumatic insult.
• Patients with subtle post-traumatic CT/MRI findings.

Exclusion criteria:
• Patients underwent surgical interventions.
• Patients with pacemaker.

Methods:
Protocol of MRI/DTI:
A- Acquisition:
• Imaging was performed using a standard 1.5 Tesla unit (Intera and Achieva, Philips).
  - A standard head coil was used.
  - The sequences obtained were axial T1W, T2W, FLAIR, T2* and 3D T1, Diffusion Tensor.

B- Processing of DTI data:
Images were post-processed using the Philips software for tractography.

The maps obtained were:
1- FA maps.
2- Directionally-encoded color FA maps.
3- 3D fiber tractography.

The direction and anatomy of the tracts are seen in the directionally encoded FA maps, where a specific color is assigned to tracts running in the three orthogonal planes: Red is for right to left tracts, green for antero-posterior tracts, and blue for cranio-caudal tracts.

The FA values were measured at the region of abnormality and were compared with the normal values on the unaffected contralateral side.
MR tractography of the white matter tracts was performed based on known anatomy. Regions of interest (ROI) were drawn as seeds in the uninvolved portions of the white matter tracts (multi-ROI technique), and the software algorithm tracked the white matter tracts that passed through these ROIs.

C- Interpretation of DTI data:
Color-coded DTI maps were analyzed, followed by tractography of individual tracts. DTI data and MR tractography of the involved white matter tracts were compared with the corresponding tracts of the contralateral normal hemisphere. The tracts were visually inspected for changes in size and orientation, and compared to those in the contralateral hemisphere. The tracts were characterized as either displaced or disrupted. They were considered displaced if they maintained normal anisotropy relative to the corresponding tract in the contralateral hemisphere but had abnormal location or orientation; disrupted if anisotropy was markedly reduced such that the tract could not be identified on the DTI based maps and/or by the failure of the fiber tracking algorithm.

The patients included in this study were categorized according to:
The FA value:
° Mild (0.2-0.3).
° Moderate (0.1-0.2).
° Severe (less than 0.1).
Tractography:
° Normal.
° Reduced caliber (if at least one tract shows reduced caliber with no other tracts show disruption).
° Disrupted (if at least one tract is disrupted).
Glasgow coma scale:
° Mild (13-15)
° Moderate (9-12)
° Severe (3-8).

Results
Forty patients (30 male and 10 female), with age range 14-67 (mean 34.7) who were subjected to head trauma were retrospectively evaluated.

Association between fractional anisotropy (FA) at lesion and Glasgow coma scale on admission was studied:
- Among the 20 patients in the moderate FA group, 8 patients (40%) were belonging to the moderate group and 8 patients (40%) were belonging to the severe group.
- In the mild FA group 4 patients (33%) were in the mild GCS group, 6 patients (50%) were in the moderate group and 2 patients (16.7%) were in the severe group.
- On the other hand, among the eight patients with normal FA at the site of the lesion, 4 patients (50%) were in the mild GCS group, 2 patients (25%) were in the moderate group and 2 patients (25%) were in the severe group.
- There was no statistically significant association between (FA) at lesion and Glasgow coma scale on admission ($p=0.738$).

![Bar chart](image)

The association between fractional anisotropy (FA) at lesion and fiber tract morphology changes was studied:
- Among the 20 patients in the moderate FA group, 16 patients (80%) showed fiber caliber reduction, 4 patients (20%) showed fiber disruption.
- Among the 12 patients in the mild FA group 6 patients (50%) showed fiber disruption, 4 patients (33.3%) showed fiber caliber reduction and 2 patients (16.7%) showed no gross fiber tract morphology changes.
- On the other hand, among the eight patients with normal FA at the site of the lesion, 6 patients (75%) showed fiber caliber reduction and 2 patients (25%) showed no gross fiber tract morphology changes.
- There was no statistically significant association between (FA) at lesion and fiber tract morphology changes ($p=0.192$).
FA normal FA mild FA moderate

### Association between fractional anisotropy (FA) at lesion and fiber tract morphology changes:

- Among the 20 patients in the moderate FA group, 14 patients (70%) were belonging to the GOS score 4, 4 patients (20%) were belonging to the GOS score 5 and 2 patients (10%) were belonging to GOS score 3.
- In the mild FA group 6 patients (50%) were in GOS score 4, 4 patients (33.3%) were belonging to the GOS score 5 and 2 patients (16.7%) was normal.
- On the other hand, among the eight patients with normal FA at the site of the lesion, 4 patients (50%) was in the GOS score 5, 2 patients (25%) were in the GOS score 4 and 2 patients (25%) were normal.
- There was no statistically significant association between (FA) at lesion and Glasgow outcome scale ($p=0.525$).

### Association between fractional anisotropy (FA) at lesion and Glasgow outcome scale was studied:

- Among the 26 patients fiber caliber reduction, 14 patients (53.8%) were belonging to the GOS score 4, 10 patients (38.5%) were belonging to the GOS score 5 and 2 patients (7.7%) were belonging to GOS score 3.
- Among the 10 patients with fiber disruption, 8 patients (80%) were in GOS score 4 and 2 patients (20%) was belonging to GOS score 5.
- There were four patients with normal caliber of fibers (100%) were normal.
- There was high statistically significant association between fiber tract morphology changes and Glasgow outcome scale ($p=0.002$).

### Statistical analysis:

- Results were expressed as mean ± SD or number (%).
- Comparison between categorical data was performed using Chi square test. Statistical analysis was performed with the aid of the SPSS computer program (version 19 windows).
- The data were considered significant if $p$-value was 0.05 and highly significant if $p$-value was <0.01.
Fig. (5): Male patient 36 years old, suffered motor car accident, presented with deep coma. Axial FLAIR WIs (a) and axial T2 WIs (b) show large well defined area of high signal at the right temporal cortical and subcortical region (c). 3D fiber tractography of both inferior longitudinal fasciculi overlaid over color coded 3D T1 image showing decreased caliber of the right one (red). On follow-up this patient showed severe motor disability and visual memory disturbance with GOS=4.

Fig. (6): Male patient 14 years old, suffered penetrating head trauma, presented with DCL and convulsions. Axial (a) and sagittal (b) T1 WIs showing large area of mixed intermediate and high signal at the splenium of corpus callosum (c). 3D fiber tractography of the corpus callosum overlaid over 3D T1 image showing disrupted fibers at its splenium. On follow-up this patient showed cognitive impairment yet no motor disability with GOS=4.

Fig. (7): Male patient 32 years old, suffered motor car accident, presented with DCL and convulsions. Axial T1 WIs (a) and T2* WIs (b) showing cortical hemorrhagic contusion and thin left temporal acute subdural hematoma (c). 3D fiber tractography of both uncinate fasciculi overlaid over color coded 3D T1 image showing decreased of caliber of the left one (blue). On follow-up this patient showed Patient shows memory impairment, yet no motor disability with GOS=5.
Discussion

Traumatic brain injury (TBI) is a major cause of death and severe disability under the age of 45 years in Western countries. Diffuse-type (non-focal) injuries are generally the most devastating, yet their assessment in vivo is hampered by the low sensitivity of conventional imaging [6].

Conventional MR imaging cannot provide reliable information about the integrity of white matter tracts, thereby limiting the ability to predict clinical outcome [7].

The advantage of MR tractography lies in the fact that it gives direct and superior visualization of the involved white matter tracts in-vivo, which is currently not possible by conventional imaging [7].

With diffusion tensor imaging (DTI), the microstructural organisation of white matter tracts can be obtained and provide important information about their integrity as well as orientation. The information so obtained may prove more sensitive to assess tract damage than the volume estimation of signal abnormality on conventional imaging [7].

DTI non-invasively provides quantitative pathophysiological information in vivo, and the prospect of tracking white matter microstructural changes over time holds the promise of measuring neuroplasticity and repair following head trauma, which eventually may offer a way of monitoring therapeutic response [8].

The aim of this work was to study the pattern of involvement of the white matter tracts and their integrity following head trauma and correlate this with the clinical outcome. We assessed our patients according to the GCS, GOS scores, degree of reduction of FA and pattern of WM tract affection. The study was conducted on 40 cases, 15 (75%) were males and 5 (25%) were females. Age of these patients ranged from 14 to 67 years (Mean age: 34.70±15.47).

The fiber tract morphology changes detected by fiber tractography revealed 26 patients (65%) with fiber caliber reduction, 10 patients (25%) with fiber disruption, and 4 patients (10%) with preserved tracts.

The association between fiber tract morphology changes detected by Fiber tractography and Glasgow outcome scale was studied and there was high statistical significant association between them (p=0.002). We classified our patients according to the fiber tract morphology changes into decreased caliber, disrupted and non-disrupted and according to the GOS score into five grades from 1 to 5. We found that among 13 patients with fiber caliber reduction, 7 patients (53.8%) were belonging to the GOS score 4, 5 patients (38.5%) were belonging to the GOS score 5 and 1 patient (7.7%) was belonging to GOS score 3, whereas among the 5 patients with fiber disruption, 4 patients (80%) were in GOS score 4 and 1 patient (20%) was belonging to GOS score 5.

This agreed with the study done by Wang et al. [9] who examined 28 patients with mild to severe traumatic axonal injury and 20 age- and sex-matched healthy control subjects. Fiber tractography was obtained 0-9 days post-injury for acute scans and 6-14 months post-injury for chronic scans. Long-term outcome by means of Glasgow outcome scale, was evaluated on the day of the chronic scan. It demonstrated that tractography-based measurements can detect deterioration of structural connectivity associated with TAI and determine long-term outcome from both acute and chronic measurements.

This also goes with Le et al., [10] who performed serial scans at 3 days and 12 weeks after injury on a patient with blunt head injury that exhibited posterior callosal disconnection syndrome. Tractography revealed interruption of the white matter fibers in the postero-inferior aspect of the splenium that correlated with the patient’s left hemialexia, suggesting that this approach may have prognostic value for evaluating cognitive and neurological sequelae associated with mild traumatic brain injury.

We studied the association between fractional anisotropy (FA) at lesion and fiber tract morphology changes and we didn’t find statistical significant association between them (p=0.192).

This goes with a study done by Rutgers et al. [11], who conducted 2 tractography investigations of patients and found that only a minority of sites with decreased FA were associated with fiber bundles showing evidence of discontinuity. This suggests that decreases in FA could be related to edema, hemosiderin deposition, axonal degeneration, or fiber misalignment rather than fiber disruption.

We studied the association between fractional anisotropy (FA) at lesion and Glasgow coma scale on admission. We classified our patients according to the degree of reduction of FA at the site of the lesion into mild, moderate and severe groups. We didn’t find statistical significant association between the degree of reduction of FA and the Glasgow coma scale on admission (p=0.738).
Association between the fractional anisotropy (FA) at lesion and Glasgow outcome scale was also studied and we didn’t find statistical significant association ($p = 0.525$).

The two aforementioned associations go with the study done by Vigneswaran et al., [12], in which sixty-one patients with mild traumatic brain injury who presented to the emergency department (ED) of University of Malaya Medical Center (Kuala Lumpur, Malaysia) for a consecutive 11-month period between April 1, 2013 and March 1, 2014, DTI and neuropsychological assessments were performed at admission and repeated again at 6 months post-trauma where most of the observed FA associations with neuro-cognitive status (acute and chronic) represented negative associations.

However, Annette et al. [13] who performed a prospective longitudinal study of 30 adult patients admitted for subacute rehabilitation following severe traumatic brain injury. DTI and conventional MRI were acquired at mean 8 weeks (5-11 weeks), and repeated in 23 of the patients at mean 12 months (9-15 months) post-trauma, and showed that At the initial scan, DTI parameters for patients with unfavourable outcome tended to deviate more from control values than for patients with favourable outcome.

There are few limitations in our study related to technical issues. Errors in calculating the trajectories can be caused by eddy current distortion, gradient nonlinearities and motion and susceptibility artifacts. There can be problems in mapping of crossing and/or branching fibers, where diffusion anisotropy can average out, causing loss of information or the production of false information about the fiber orientation at that site.

**Conclusion:**

DTI can visualize and quantify the changes in the integrity and orientation of the white matter tracts that are transected by focal brain contusions, which are otherwise not shown on conventional MR imaging or even conventional DWI scans. MR tractography can visualize the white matter tracts as being either disrupted, reduced caliber or preserved and offers a potential tool for clinical-imaging correlation of the involved white matter tracts and patient’s clinical recovery.

**References**

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دور الرنين المغناطيسي

الرنين المغناطيسي الانتشاري الموتر للألياف العصبية هو أحد الوسائل الحديثة في دراسة إتجاه وسلامة الألياف العصبية في الجسم.

وقد ركزت العديد من الدراسات البحثية الأخيرة على تطبيق تقنيات الرنين المغناطيسي الانتشاري في مرضى اصابات الرأس. ومع ذلك، فقد تناول عدد قليل من تلك الدراسات مشكلة تطبيق تقنيات الرنين المغناطيسي للتنبؤ بعوامل التحسن لألكليينكي لهذه المجموعة من المرضى.

وقد تمت هذه الدراسة على أربعين مريضاً ممن تعرضوا لأصابة بالرأس حيث تم دراسة مدى تأثر الألياف العصبية في فص الدم.

وقد تم في هذه الدراسة، تقسيم الحالات إلى ثلاثة أقسام: تأثير فعال، تأثير ضعيف، وتأثير غير محدد.

وقد وجد أيضاً علاقة أحيائية قوية بين نوع اصابة الألياف العصبية للمخ وعوامل التحسن ألكليينكي للمريض حيث وجدنا عند متابعة حالات الإصابة ان جميع المرضى المصابين بانقطاع الألياف العصبية تبقي لديهم نسبة من العجز العصبي بينما المرضى الذين لم يصابوا بانقطاع الألياف العصبية

أقرب نسبة تحسن جيد.