Journal of Neuroradiology (2011) **38**, 214—222

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ORIGINAL ARTICLE

A systematically designed study to investigate the effects of contrast medium on diffusion tensor MRI☆

Une étude conçue pour évaluer les effets du produit de contraste en IRM du tenseur de diffusion

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Available online 7 January 2011

KEYWORDS
Diffusion tensor;
Contrast medium;
Time dependence;
Isotropic and anisotropic diffusion;
Malignant brain tumour

Summary
Objective. — This study investigated whether or not the effect of contrast medium on diffusion tensor magnetic resonance imaging (DTI) is time-related in patients with malignant brain tumours.
Patients and methods. — Twelve patients who only had malignant brain tumours were included in the study. DTI acquisitions were performed five times consecutively: twice before, once during, then twice after contrast injection. Diffusion indices were mapped and regions of interest (ROIs) were placed in the tumour, peritumoral edema and contralateral normal brain tissue. Repeated-measures ANOVA was used to investigate the effects of time on contrast medium in relation to diffusion indices.
Results. — Precontrast DTI was redefined as ''pre'' by averaging the two before-contrast scans, as there were no statistically significant differences between them. There were statistically significant differences at four time points for only the edema ROI for fractional anisotropy and the first-largest eigenvalue, but not for trace and the second-largest eigenvalue.
Conclusion. — The effects of contrast medium on DTI were time-dependent for diffusion anisotropic indices. DTI obtained at > 6 min after contrast injection does not cause significant changes in diffusion isotropic and anisotropic values.

Abbreviations: DTI, diffusion tensor MR imaging; ROI, regions of interest; FA, fractional anisotropy; ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; BBB, blood—brain barrier; EPI, echo-planar imaging; SENSE, sensitivity encoding; T2WI, T2-weighted images; T1WI, T1-weighted images; FLAIR, fluid-attenuated inversion recovery; ANOVA, analysis of variance; MRI, magnetic resonance imaging; Gd-DTPA, gadolinium-DTPA; PET—CT, positron emission tomography—computed tomography; CSF, cerebrospinal fluid; SD, standard deviations.

☆ This study was supported by the Program of Kyung Hee University for the Young Researcher in Medical Science (KHU- 2009-1395, 2010-0708, GHJ).

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doi:10.1016/j.neurad.2010.11.004

Introduction

The diffusion tensor model is an ellipsoid with six degrees of freedom such that a minimum of six diffusion-encoded measurements are required to describe the tensor matrix, which is subject to a set of three eigenvectors and their corresponding eigenvalues (λ_1, λ_2, λ_3). Using these eigenvalues, the isotropic and anisotropic diffusion values can be obtained from the rotationally invariant indices. The representative indices are trace for the mean diffusivity and FA (FA = scaled standard deviation divided by the norm of the tensor) for anisotropic diffusion. DTI has recently been investigated for a wide variety of pathological conditions of the brain, including infarctions [1,2] and brain tumours [3—11]. Applications for DTI in tumour imaging have been used to differentiate pathological differences in brain tumours [12,13], peritumoral edema from tumour infiltration [3], radiation effects from tumour recurrence or progression [10,11,13,14] and tumour grades [15,16]. However, the applications of DTI in tumour imaging can be further expanded.

Contrast agents are routinely used in a conventional protocol to study brain tumours to improve both diagnostic specificity and sensitivity. When DTI is performed with conventional MRI in patients with brain tumours, the scans are usually obtained before contrast injection. However, DTI after contrast injection followed by routine MRI may be necessary in certain circumstances. In this case, identifying any alterations in DTI data after contrast injection is required. However, DTI data cannot be used if the contrast medium alters isotropic and/or anisotropic diffusion. Controversial findings have been reported concerning the effect of contrast medium on isotropic diffusion (the mean ADC or trace) when the DWI technique was used to assess patients with brain abnormalities [2,11,12]. In particular, an investigation by Firat et al. [11] was performed with three measurements of DWI — one taken before Gd-DTPA injection, and two taken after contrast medium injection — in subjects with either normal brain or brain lesions, including stroke, showing different pathological areas. They found that these scans were non-specific in patients with brain tumours. They also found that ADC values in the early post-contrast phase were significantly decreased after contrast medium injection compared with those in the precontrast phase, although ADC values in the late post-contrast phase had reverted (normalized) to levels of the precontrast phase. However, these authors did not explore the effects of contrast medium on anisotropic diffusion, as they were using DWI rather than DTI.

Recently, we performed DTI in a small sample of patients with heterogeneous brain tumours [17] to investigate the previously controversial findings on the effects of contrast medium, and to further evaluate the changes in anisotropic diffusion after contrast injection. In that study, only two DTI datasets were acquired, from before and after Gd-DTPA injection. Our results revealed that both the trace and FA values in specific areas showed statistically significant differences between pre- and post-contrast DTI. However, anisotropic diffusion in that study may have been influenced not only by contrast-medium injection, but also by the time at which the DTI scan was acquired. Also, the population sample in that study was too heterogeneous to analyse as a single group, especially given the small numbers of subjects involved. In addition, as a second precontrast DTI was not done in that study, it was not possible to ascertain whether or not the timing of the FA and trace was causally related to the influence of the contrast. This led to the realization that it is important to investigate the influences of both the contrast medium per se and its time-related variations for diffusion isotropy and anisotropy.

It was also evident that any new study had to be designed to initially evaluate reliable measurements according to the passage of time and the effects of injecting contrast during DTI. Thus, the aim of the present systematic study was to investigate any DTI signal alterations, using time-related measurements both during and after the administration of contrast medium. In this study, only patients with malignant brain tumours such as high-grade glioma or metastases, which are usually associated with breakdown of the BBB, were included to allow data evaluation from a more homogeneous group. On the basis of our previous findings, it was hypothesized that contrast medium can alter the values of diffusion tensor parameters for malignant brain tumours compared with the values acquired without contrast injection. Also, any changes in those values might depend on the time interval between contrast injection and the DTI scan.

Materials and methods

Study patients

The present study only included patients with malignant brain tumours that might have disturbed the BBB. Cases were included if the tumours were classified into either of two categories, according to conventional MRI or pathological confirmation: high-grade glioma, such as glioblastoma multiforme or anaplastic astrocytoma; or intra-axial metastatic neoplasm. Using these criteria, 12 patients (eight men and four women; average age: 63 years; age range: 47—85 years; Table 1) were recruited into the study. The primary tumours of six metastases were four lung cancers, one renal cell carcinoma and one hepatocellular carcinoma. Of the high-grade gliomas, only two tumours were confirmed by pathology, whereas the others were diagnosed by conventional brain MRI or by PET—CT. Except for the brain tumours, the subjects' radiological findings suggested no neurological disorders.

The study was approved by the local ethics committee, and all the patients or their legal guardians provided their written informed consent.

MRI acquisition

All MRI data were obtained with a 3-T scanner (Philips Achieva; Best, The Netherlands). Each patient underwent a conventional MRI examination that included T1-weighted (TW1) sagittal images (repetition time/echo time, TR/TE: 450/10 ms), T2-weighted (T2W) axial images (TR/TE: 5304/110 ms) and FLAIR axial images (TR/TE/inversion time: 6000/120/2000 ms). In addition, contrast-enhanced fat-suppressed T1W images (TR/TE: 438/12 ms) were also acquired in both axial and coronal sections after completing