



Differentiation of high-grade-astrocytomas from solitary-brain-metastases: Comparing diffusion kurtosis imaging and diffusion tensor imaging

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ABSTRACT

Objective: To compare the value of MRI diffusion kurtosis imaging (DKI) and diffusion tensor imaging (DTI) in differentiating high-grade-astrocytomas from solitary-brain-metastases.

Methods: Thirty-one high-grade-astrocytomas and twenty solitary-brain-metastases were retrospectively identified. DKI parameters [mean kurtosis (MK), radial kurtosis (Kr), and axial kurtosis (Ka)] and DTI parameters [fractional anisotropy (FA) and mean diffusivity (MD)] values with and without correction by contralateral normal-appearing white matter (NAWM) in the tumoral solid part and peritumoral edema, were compared using the *t*-test. Receiver operating characteristic (ROC) curves were used to test for the best parameters.

Results: The DKI values (MK, Kr, and Ka) and DTI values (FA and MD) in tumoral solid parts did not show significant differences between the two groups. Corrected and uncorrected MK, Kr, and Ka values in peritumoral edema were significantly higher in high-grade-astrocytomas than solitary-brain-metastases, and MD values without correction were lower in high-grade astrocytomas than solitary-brain-metastases. The areas under curve (AUC) of corrected Ka (1.000), MK (0.889), and Kr (0.880) values were significantly higher than those of MD (0.793) and FA (0.472) values. The optimal thresholds for corrected MK, Kr, Ka, and MD were 0.369, 0.405, 0.483, and 2.067, respectively.

Conclusion: DKI and directional analysis could lead to improved differentiation with better sensitivity and directional specificity than DTI.

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1. Introduction

High-grade astrocytomas and solitary brain metastasis are the two most common malignant brain tumors in adults. Preoperative differentiation between them may contribute to more appropriate treatment plans and follow-up, especially when solitary brain metastases are detected before the primary cancer [1]. Conventional MRI has a very limited ability to distinguish between the two, DTI has shown promise in differentiating between high-grade astrocytomas from solitary brain metastases, but it cannot differentiate accurately enough, and mixed results have been obtained [2–4].

DTI is based on the assumption that water molecule diffusion follows a Gaussian distribution [5,6]. Diffusion kurtosis imaging (DKI) is the extension of DTI, which is an MRI technique depicting the non-Gaussian water molecule diffusion. The diffusion of water molecules in normal tissue and tumor tissue always follows a non-Gaussian distribution. So DKI may be more closely reflecting the real situation of water molecule movement in tumor tissue than DTI [7,8]. A few studies have been conducted using DKI for grading of cerebral astrocytomas, and reported that DKI parameters were more sensitive than conventional diffusion methods to grade cerebral astrocytomas [9–11].

There are no studies on the value of DKI in differentiating high-grade astrocytomas from solitary brain metastasis. DKI can be of particular interest for noninvasively differentiating high-grade astrocytomas from solitary brain metastasis. Here, the value and diagnostic accuracy of DKI parameters in differentiating high-grade

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astrocytomas from solitary brain metastasis were evaluated and compared to results for DTI.

2. Materials and methods

2.1. Patients

The institutional review board of our hospital approved this study. Written informed consent was obtained from every patient before participation. We recruited high-grade astrocytomas patients and brain metastases patients. Inclusion criteria included solitary enhancing lesions with peritumoral edema and no previous therapy before MRI examination. Exclusion criteria were cystic and recurrent tumors. Fifty-one patients were recruited between January 2012 and March 2014. The patients were divided into two groups which included high-grade astrocytomas group ($n=31$) and brain metastases group ($n=20$). Patients with high-grade astrocytomas were confirmed by pathology. Tumor grading was performed as proposed by the criteria of the World Health Organization Classification of Tumors of the Nervous System 2007, and twenty patients with solitary metastatic brain tumors were confirmed by pathology and clinical diagnosis. Of the 20 patients with brain metastases, the primary sites of cancer were found to be the lung ($n=12$), breast ($n=4$), thyroid ($n=1$), kidney ($n=1$), and colon ($n=2$).

2.2. MRI data acquisition

All examinations were performed with a 3.0T MRI scanner (GE Signa HDxt, U.S.) by using an 8-channel head coil for signal reception. The scanning sequences included conventional MRI sequences [T1-weighted imaging (T1WI), contrast enhanced T1WI (CE-T1WI), T2-weighted images (T2WI), and T2 fluid attenuated inversion recovery (T2FLAIR) images] and DKI sequences which included DTI sequence. The parameters used for conventional MRI sequences were repetition time (TR) 195 ms and echo time (TE) 4.76 ms for gradient-echo (GRE) T1WI and CE-T1WI, TR 4000 and TE 98 ms for fast spin-echo (FSE) T2WI, and TR 8000 ms, TE 95 ms, and inversion time (TI) 2371.8 ms for T2FLAIR. Slice thickness and slice interval were 5.0/1.5 mm. Field of view (FOV) was $240 \times 240 \text{ mm}^2$; matrix: 256×256 . 0.1 mmol/kg of gadolinium chelate contrast was injected for contrast-enhanced imaging. Echo planar imaging (EPI) sequence was used to perform diffusion-weighted imaging (DWI) and DKI data. Implemented b values of DKI were 0, 1000, and $2000 \text{ mm}^2/\text{s}$. These were applied in 30 uniformly distributed directions [6]. Another 10 images without diffusion sensitization were also produced. The following other imaging parameters were kept constant throughout the DKI data acquisition sequences: TR/TE: 6500/115 ms; FOV: $240 \times 240 \text{ mm}^2$; matrix for acquired: 128×128 ; number of excitations (NEX): 2; slice thickness: 6 mm; slice interval: 1 mm. DKI scan time was about 7 min. Parameters for DWI data: TR/TE: 3000/87 ms; FOV: $240 \times 240 \text{ mm}^2$; matrix for acquired: 160×160 ; slice thickness, 6 mm; slice interval, 1 mm; NEX=2; $b=0, 1000 \text{ mm}^2/\text{s}$. These were applied along three orthogonal directions. DWI scan time was about 45 s. DKI and DWI scan were before the contrast enhanced T1WI scan.

2.3. MRI data processing and analysis

Before the DKI data calculation all the raw images were corrected for head motion and eddy current distortions using global affine transformations (DKI tool package developed by GE Research team). The diffusion weighted images and kurtosis images were calculated on a voxel-by-voxel basis (DKI tool package developed by GE Research team). The diffusion tensor and diffusion kurtosis were calculated simultaneously, and all the data ($b=0, 1000$, and $2000 \text{ mm}^2/\text{s}$) were used. They were fitted to the following Eq.

(1), which was derived from Tabesh's and Basser's studies [12,13]. After the kurtosis and diffusion tensor were estimated by fitting all data into Eq. (1), five metrics could be derived from the two tensors which included mean kurtosis (MK), radial kurtosis (Kr), axial kurtosis (Ka), fractional anisotropy (FA) and mean diffusivity (MD).

$$\ln[S(n, b)/S_0] = -b \sum_{i=1}^3 \sum_{j=1}^3 n_i n_j D_{ij} + \frac{1}{6} b^2 \bar{D}^2 \sum_{i=1}^3 \sum_{j=1}^3 \sum_{k=1}^3 \sum_{l=1}^3 n_i n_j n_k n_l W_{ijkl} \quad (1)$$

Here, $S(n, b)$ is the signal intensity for b value b ($b \neq 0$) along direction n , S_0 is the signal intensity for b_0 image, $\bar{D}$ is the MD, n_i ($i=1, 2, 3$) is the component of the diffusion direction vector n , W_{ijkl} , and D_{ij} are the components of the kurtosis and diffusion tensor, respectively.

Conventional MRI sequences were here used to observe the basic features of tumors, such as cystic, necrotic, and hemorrhagic components, tumoral solid parts, tumor boundaries, and edema range, all of which determined the edge of ROIs. With supporting workstation processing software (GE Functool 9.4.05a), ROIs were manually drawn around the solid parts of the tumor, peritumoral edema, contralateral normal-appearing white matter (NAWM) and contralateral normal-appearing dorsal thalamus (NADT). Directionally encoded (DEC) FA maps were inspected and ROIs were reliably identifiable in all parameter images, which could help partial volume effects be minimized [14].

ROIs of the enhanced part of the tumor which represented the solid parts of the tumors, were delineated on the transverse CE-T1WI, by excluding the cystic, necrotic, hemorrhagic components and adjacent normal tissue to avoid a partial volume effect (Figs. 1 and 2). If the intensity of the solid part of the tumor was uneven on DWI, the lowest ADC value area would be the ROIs. ROIs of peritumoral edema were delineated on the transverse CE-T1WI according to transverse T2FLAIR image, and the ROIs of edema were delineated in the middle part of peritumoral edema by excluding adjacent normal tissue and cerebrospinal fluid (CSF) to avoid a partial volume effect and CSF contamination (Figs. 1 and 2). Two independent radiologists (a neuroradiologist with 6 years of experience; and a neuroradiologist with 13 years of experience) blinded of pathological results performed image analysis, respectively drawn three different ROIs and obtained three parameter values per patient, and calculated the total mean $\pm$ standard deviation. If the DKI (MK, Kr, and Ka) and DTI (FA and MD) parameter values in contralateral NAWM were different between high-grade-astrocytomas and solitary-brain-metastases, which could have introduced a bias because of the individual differences which were attributed to the influence of age, tumor location, and underlying diseases, such as hypertension. So the DKI (MK, Kr, and Ka) and DTI (FA and MD) parameter values in the tumoral solid parts and peritumoral edema were corrected by contralateral NAWM at the same level. For example, corrected MK value = the MK value / the MK value in contralateral NAWM [10].

2.4. Statistical analysis

SPSS18.0. statistical analysis software was used. The DKI parameters (MK, Kr, and Ka) and DTI parameters (FA and MD) values of contralateral NAWM, contralateral NADT, tumoral solid parts, peritumoral edema, and patient age were compared between high-grade astrocytomas and solitary brain metastasis using the t -test. $P < 0.05$ was considered statistically significant. Receiver operating characteristic (ROC) curves were generated for DKI and DTI parameter values with and without correction by contralateral NAWM to assess the areas under curves (AUC) and determine optimal cutoff points for each parameter.

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