

Research Progress of MRI Diffusion Tensor Imaging in the Diagnosis and Grading of Brain Glioma

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Abstract: Brain glioma is a prevalent neoplasm within the central nervous system. Due to its highly invasive growth pattern, it is often indistinct from normal brain tissue, which complicates accurate diagnosis and grading of the tumour. Diffusion tensor imaging (DTI) is a method of microscopically monitoring the dispersion movement of water molecules. It can conduct both qualitative and quantitative analysis, reflecting pathological changes to the microstructure of brain tissue and non-invasively revealing white matter fibre bundles. This article reviews the research progress in the diagnosis and classification of glioma by means of quantitative study parameters and white matter fiber bundle display by diffusion tensor imaging.

Keywords: Magnetic Resonance Imaging; Diffusion Tensor Imaging; Brain Glioma; Diagnosis; Fractionation.

1. Introduction

The fifth edition of the World Health Organization (WHO) classification of central nervous system tumours in 2021 categorises central nervous system tumours into 12 distinct categories, one of which is glioma, glial neuron tumour and neuronal tumour [1]. The concept of glioma, first proposed by Virchow in 1846, is that of a primary intracranial tumour originating from glial cells, with a high annual incidence worldwide [2]. The growth of glioma cells can be carried out along the vascular space and nerve fibre bundles, with strong infiltration ability. The WHO classifies glioma into grades V to VI, of which grade V and VI are low-grade glioma (LGG) and grade VII and VIII are high-grade glioma (HGG).

In 1994, Basser et al. [3] proposed the concept of diffusion tensor imaging (DTI), which is based on diffusion weighting imaging (DTI). This technology is a functional Magnetic Resonance Imaging (fMRI) technique that has been developed on the basis of DWI technology. Utilising the anisotropy of water molecule dispersion, DTI technology employs multiple gradient magnetic fields to obtain information regarding the dispersion intensity of water molecules in multiple directions within tissues. This enables quantitative analysis of the dispersion movement of water molecules and non-invasive detection of the integrity of white matter fibre bundles. The technology has been used to infer the damage degree of brain tumours to white matter fibre tracts, to show the invasion scope of brain tumours and the relationship between brain tumours and white matter fibre tracts [4-5]. Diffusion tensor tractography (DTT) represents a significant advancement in the field of DTI technology, offering a more comprehensive study of white matter fiber tracts within the brain. This technology facilitates the visualisation of the anatomical relationship between brain tumours and fiber tracts through three-dimensional reconstruction of nerve fiber tracts [6]. The advantages of DTI, including its capacity for quantitative analysis of water molecule diffusion movement and visual display of white matter fiber bundles, are particularly valuable in the diagnosis

and classification of brain glioma, given the aggressive nature of this condition and the unclear boundary with normal peritumor white matter fiber bundles.

2. Basic Principle and Parameters of DTI

2.1. Basic Principles of DTI

The random motion of particles suspended in a liquid or gas that never stops is known as Brownian motion. The degree of diffusion of water molecules in all directions is the same in a homogeneous medium, which is known as isotropic diffusion. In human tissues, the diffusion movement of water molecules is affected by many factors such as tissue temperature, cell space, and cell membrane physiological barrier, so that there are differences in the degree of diffusion in all directions, which is known as anisotropic diffusion. In the context of the white matter of the brain, the diffusion of water molecules is predominantly influenced by the density of nerve fibres and their arrangement direction, myelin integrity, and other intricate structural elements. The resistance of water molecules in the direction parallel to the white matter fibre bundle is significantly lower compared to the resistance in the direction perpendicular to the white matter fibre bundle. DTI employs these characteristics by utilising gradient magnetic fields in at least six distinct linear directions to acquire diffusion degree information for water molecules in each direction, facilitating quantitative analysis. Employing quantitative analysis parameters and computerised reconstruction technology, white matter fibre beam imaging (DTT) can also be performed.

2.2. Common Parameters of DTI

The quantitative parameters of DTI are calculated on the basis of the following three eigenvalues: λ_1 , λ_2 and λ_3 . If the dispersion tensor is regarded as an ellipsoid, then the three eigenvalues are the dispersion coefficients of the ellipsoid in the direction of the three perpendicular principal axes. The maximum dispersion coefficient, λ_1 , is oriented along the

direction of the white matter fiber bundle, while the transverse dispersion coefficients, λ_2 and λ_3 , are denoted as the intermediate dispersion coefficient and the lowest dispersion coefficient, respectively. It is noteworthy that λ_1 is also referred to as the axial diffusivity (AD/DA), and the average value of λ_2 and λ_3 is designated as the radial diffusivity (RD/DR).

2.2.1. ADC and MD

The apparent diffusion coefficient (ADC) value is widely regarded as the most fundamental quantitative index of diffusion-weighted imaging (DWI), with the capacity to reflect the diffusion of water molecules within tissues, and is directly proportional to the diffusion capacity of water molecules. However, it should be noted that the ADC value is constrained in its ability to reflect the diffusion characteristics of water molecules solely in the direction that is applied by the gradient magnetic field. The mean diffusivity (MD) value represents the average of the three eigenvalues, that is, the average of the dispersion tensor in all directions. The MD value can be expressed as the average ADC value, reflecting the diffusion of water molecules as a whole and providing a more comprehensive assessment than ADC. However, it is important to note that both the ADC and MD values are influenced by the size of the water molecule diffusion, but not its direction.

2.2.2. FA

FA (fractional anisotropy) is defined as the ratio of dispersion anisotropy to the whole dispersion, with a value ranging from 0 to 1. It has been established that a tendency towards 1 in the value of FA is indicative of increased anisotropy in the dispersion movement of water molecules in tissues. Conversely, as the value approaches 0, the dispersion tends to be isotropic. FA values can be used to obtain a gray level and colour-coded map. Utilising this framework, the connectivity of adjacent voxels in the direction of fibre bundles can be displayed in three dimensions by employing tracer technology, thereby yielding three-dimensional images of white matter fibre bundles [7-8].

3. Application of DTI in the Diagnosis and Grading of Brain Glioma

3.1. Application of DTI Quantitative Parameters in the Diagnosis and Grading of Brain Glioma

3.1.1. DTI Quantitative Study Parameters Were Used to Diagnose Brain Glioma

A number of studies have demonstrated that the ADC value of glioma is elevated in comparison to that of normal brain tissue, and that the FA value is reduced relative to that of normal brain tissue. DUY et al. [9] discovered that the rADC value of glioma tumour body and peritumoral oedema zone was elevated in comparison to that of a healthy control, while the rFA value was diminished relative to that of a healthy control. BRAHIMAJ et al. [10] found that the ADC value in the enhanced glioma region was greater than that in the contralateral normal white matter region, while the FA value was smaller than that in the contralateral normal white matter region. In a separate study, EL OUADH et al. [11] found that ADC value was glioma tumor > peritumoral > contralateral normal white matter, and FA value was glioma tumor < peritumoral < contralateral normal white matter. Some studies also directly introduced eigenvalues. For instance, KUMAR

et al. [12] discovered that the λ_2 value, λ_3 value, MD value, AD value, RD value, and FA value were, in order of decreasing order, glioma parenchyma area < healthy brain tissue area < peritumoral edema area < glioma parenchyma area. In the study by PAPAGEORGIOU et al. [13], the glioma lesion area, peritumoral edema area and contralateral normal brain tissue area was selected. It was found that the FA values of LGG and HGG were as follows: contralateral normal brain tissue area > peritumoral edema area > glioma lesion area. The MD values and DR values of LGG were as follows: The contralateral normal brain tissue area was found to be less than the peritumoral edema area and the glioma lesion area. The MD value, AD value, DR value and DA value of LGG were found to be lower than those of HGG, with the contralateral normal brain tissue area being less than the peritumoral edema area and the glioma lesion area. Other studies have revealed the relationship between ADC value, FA value and pathological classification of glioma. For instance, TIMOCIN et al. [14] found that ADC value of glioma patients was higher than that of the healthy control group, while FA value was lower than that of the healthy control group. Furthermore, ADC value was found to be: extrusion brain glioma < infiltrating brain glioma < destructive brain glioma, and FA value was: compressive glioma > invasive glioma > destructive glioma.

3.1.2. DTI Quantitative Study Parameters Were Used to Grade Brain Glioma

In recent years, a number of studies have utilised ADC value and FA value to grade glioma. However, the conclusions drawn by these studies regarding the relationship between these two quantitative parameters and glioma grade have been inconsistent. Some of these conclusions can be summarised as follows: an increase in glioma grade was accompanied by a decrease in ADC value, while FA value increased in the opposite manner. ZHANG et al. [15] found that the ADC value of glioma was as follows: Grade IV > Grade IV > Grade V, and FA value was Grade IV < Grade V. Conversely, STOPA, VAMVAKAS and TAKAHASHI et al. found that ADC value of glioma was LGG > HGG [16-18] and FA value was LGG < HGG. Some results showed that ADC value was negatively correlated with glioma grade, but there was no clear correlation between FA value and glioma grade. A number of studies have found that the relative apparent diffusion coefficient (rADC) of glioma tumour body and peritumoral edema area LGG > HGG. However, the relative fractional anisotropy (rFA) of the two regions showed no statistically significant difference between high and low grade gliomas [19]. LIN et al. [20] found that ADC value LGG was higher than HGG in the tumour body and peritumoral edema area of glioma, but there was no statistically significant difference in FA value between high and low grade gliomas. The relationship between FA value and glioma grade is also described differently in this study compared to the above ones. For instance, RAJA and LI et al. found that the FA value of glioma was LGG > HGG [21-22].

Furthermore, it was determined that the correlation between ADC and FA values and glioma grade was significantly influenced by the designated areas of interest. For instance, JIANG et al. [23] observed that rADC values within the parenchyma area and tumour margin diminished with the escalation of tumour malignancy, while rADC values in the peritumoral edema area exhibited a LGG < HGG trend. The rFA values of the tumor margin (LGG < HGG), the rFA values of the peritumoral edema area (LGG > HGG), and the

rFA values of the parenchyma area were found to be statistically insignificant between high and low grade gliomas. Conversely, SHAN et al. [24] observed that the ADC value and MD value of glioma tumor LGG were greater than HGG. However, no statistical significance was found in the difference between high and low grade gliomas in peritumoral ADC value, MD value, tumor FA value and peritumoral FA value. In addition to the quantitative parameters mentioned in the above studies, some studies also directly use eigen values for glioma classification, such as KU-MAR et al. [12] found relative mean diffusivity (rMD), λ_1 , λ_2 , λ_3 values of LGG > HGG. Conversely, the LGG < HGG value of λ_1 in the peritumoral edema area, and rFA value in the parenchyma area, rFA value in the peritumoral edema area, and rMD value in the peritumoral edema area exhibited no statistical significance between high and low grade gliomas. In contrast, PAPAGEORGIOU et al. [13] found that the DA value of glioma lesions and the MD value, DA value and DR Value in the peritumoral edema area were LGG < HGG.

3.1.3. DTI Quantitative Parameters Were Used for Differential Diagnosis of Brain Glioma

Quantitative parameters of diffusion tensor imaging (DTI) have been shown to distinguish high-grade glioma (HGG) from brain metastases. MAO et al. [25] found that apparent diffusion coefficient (ADC) values in the peritumour oedema area and fractional anisotropy (FA) values in the tumour margin area were HGG < brain metastases, and FA values in the tumour parenchyma area were HGG > brain metastases. NGUYEN et al. [26] found that the FA value, MD value, DA value and DR Value in the peritumor area were HGG < brain metastases. In a separate study, SHUKLA and CHO [27-28] found that the minimum and average MD values in the peritumoral area were HGG < brain metastases, and the average FA values in the peritumoral area were HGG > brain metastases. They also found that the minimum MD value had the best identification effect. Quantitative parameters of DTI can also be used to distinguish HGG, brain metastases and tuberculomas: SONI et al. [29] found that the FA value around the tumour parenchyma of HGG was higher than that of brain metastases and tuberculomas. DTI quantitative research parameters can also be used to distinguish glioblastoma, lymphoma and metastatic tumours. ZHANG et al. [30] found that the FA value in the tumour parenchymal area of glioblastoma was the highest among the three. DTI quantitative study parameters can also be used to distinguish HGG recurrence from spurious progression. For example, WU et al. [31] found that rMD value in the edema area around the lesion was significantly reduced when HGG recurred compared with spurious progression.

3.2. Application of DTI Combined with other Techniques in the Diagnosis and Grading of Brain Glioma

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3.3. Application of DTT in the Diagnosis and Grading of Brain Glioma

3.3.1. Morphological Changes of Fiber Bundles and Classification of Brain Glioma

The invasive growth of brain glioma frequently results in alterations to the morphology of the surrounding white matter fiber bundles, with varying degrees of severity. The literature on this subject is inconclusive, with different studies offering divergent descriptions of these morphological changes. However, a number of studies have identified a correlation between the grade of brain glioma and the morphological changes of the surrounding white matter fiber bundles, with more malignant tumors being associated with more severe damage to the fiber bundles. The proportion of peritumoral white matter fiber bundle destruction was higher in HGG than LGG [19]. LEROY et al. [40] found that the peritumoral white matter fiber bundles of LGG were mostly normal or displaced, while those of HGG were mostly sparse or interrupted. A similar observation was made by LATINI et al. [41], who reported that the morphology of peritumoral white matter fiber bundles was predominantly displaced and separated in LGG, and absent and interrupted in HGG. CAMINS et al. [42] further demonstrated that the morphology of white matter fiber bundles in tumor focal areas and peritumoral edema areas were primarily infiltrated in LGG and destroyed in HGG. In other studies, the concept of neuronal entanglement was proposed when describing the morphological changes of fiber bundles. For example, SEOW and MATO et al. found that LGG peritumor neuronal fibers mostly manifested as moving, while HGG mostly manifested as neuronal entanglement and mostly appeared in temporal and frontal lobes [43-44].

3.3.2. The Morphological Changes of Fiber Bundles Were Used for the Differential Diagnosis of Brain Glioma

The morphological changes of white matter fibre bundles have been shown to reflect the grade of glioma to a certain extent, and to provide a reference for the differentiation of glioma from other brain tumours. In a study by LEROY et al. [40], the white matter fibre bundles in the peri-tumour area of HGG were found to mostly show destruction, while the white matter fibre bundles in the peri-tumour area of BMS mostly showed infiltration and displacement. CAMINS et al. [42] found that the peritumoral white matter fiber bundles in astrocytoma and metastatic tumors were mostly partially

interrupted, compressed, shifted or deformed and displaced, while those in meningiomas were mostly sparse and displaced.

4. Conclusion and Prospect

The primary benefits of DTI comprise the non-invasive demonstration of white matter fibre bundles and the quantitative analysis of water molecular dispersion movement. This enables the establishment of the relationship between subtle structural changes in brain tissue and brain tissue lesions, facilitating accurate lesion characterization and providing a valuable reference for surgical planning and prognosis assessment. However, it should be noted that DTI is not without certain limitations. Firstly, there is a lack of consensus on quantitative research parameters for diagnosing and grading brain glioma. This is particularly evident in the significant variability of FA values across different studies, which may be attributable to the use of a plane echo sequence in DTI technology, which is sensitive to motion and susceptible to motion and deformation artefacts due to its magnetic sensitivity. This results in the instability of the measurement parameters, which may also be related to the selection of the region of interest and the number of samples. Furthermore, DTI's low resolution in displaying cross-connected fiber bundles may lead to an inaccurate representation of fiber bundle direction.

In the future, further elucidation is required to elucidate the reasons for the varying standards of DTI quantitative research parameters in the diagnosis and grading of brain glioma. Thereafter, improvements or new parameters should be introduced to establish a unified standard for the diagnosis and grading of brain glioma. Furthermore, the potential of integrating DTI with other technologies should be investigated to leverage the strengths of DTI and enhance the diagnostic precision.

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