Iran J Public Health, Vol. 49, No.6, Jun 2020, pp.1112-1119

Original Article

Diffusion Weighted Imaging of Brain Gliomas in the Differential Diagnosis Value

Jian JIANG, Liangcai BAI, Xueling ZHANG, Jianli LIU, *Junlin ZHOU

Department of Radiology, Lanzhou University Second Hospital, Lanzhou 730030, P.R. China

***Corresponding Author:** Email: jrj24t@163.com

(Received 13 Jul 2019; accepted 10 Sep 2019)

Abstract

Background: To evaluate the diagnostic value of diffusion weighted imaging (DWI) and apparent diffusion coefficient measurement (ADC) in glioma.

Methods: Thirty two low-grade glioma patients and 31 high-grade glioma patients who were confirmed by pathology in Lanzhou University Second Hospital, Lanzhou, China from February 2016 to January 2019 were selected. The other 30 patients with brain metastases were selected as a control group. DWI imaging data of the three groups were collected, and ADC, relative ADC (rADC) values in tumor parenchyma, peritumor edema area, and contralateral normal white matter area were measured, and the levels of n-acetyl aspartic acid (NAA), choline (Cho), creatine (Cr) of tumor metabolites were analyzed.

Results: rADC values in the peri-tumor edema areas of the high-grade glioma group were significantly lower than those in the low-grade group and the metastatic group (P=0.011) , and the low-grade group was significantly lower than that in the metastatic group ($P < 0.05$). NAA/Cho and NAA/Cr in parenchymal and peritumor edema areas of patients in the advanced group were significantly lower than those in the metastatic group ($P < 0.05$), and Cho /Cr was significantly higher than those in the metastatic group ($P < 0.05$).

Conclusion: the rADC value, NAA/Cho, NAA/Cr and Cho/Cr in parenchymal and peritumor edema areas of the tumor can help to distinguish high-grade glioma, low-grade glioma and brain metastases.

Keywords: Apparent dispersion coefficient measurements; Diffusion-weighted imaging; Glioma; Metabolites

Introduction

Glioma is a common primary intracranial malignant tumor, accounting for about 50% of all intracranial tumors. Due to the particularity and complexity of brain tissue structure, glioma can cause different degrees of functional changes in the brain, leading to psychological problems such as anxiety and depression. With high mortality and recurrence rate, poor prognosis and serious impact on quality of life (1).

At present, surgical resection is the first choice for the treatment of glioma disease, and the contour of the tumor can be determined and the resection operation can be performed by stereoscopic orientation and positioning with the help of microscopic technology (2). However, in most cases, the boundary between glioma and surrounding brain tissue is blurred, and some brain metastases have similar or overlapping signals on conventional Magnetic Resonance Imaging (MRI) images, which is not easy to distinguish accurately, thus causing some difficulties in treatment (3).

With the continuous development of neuroimaging technology, Diffusion Weighted Imaging (DWI), which focuses on reflecting the Diffusion of tissue water molecules, has gradually been

widely used in glioma (4). DWI is to identify different pathological tissues by studying the abnormal movement of free water particles in tissues at the molecular level with high accuracy (5), however, this technique is still lacking of sufficient clinical data support, and there are few relevant references.

Therefore, we aimed to explore the differential diagnosis value of DWI in patients with glioma and brain metastasis.

Methods

General information

Selection of the patients were made in February 2016 to January 2019 in Lanzhou University Second Hospital, China and confirmed by pathology, diagnosis and treatment of 63 cases of patients with brain glioma.

Patients signed informed consent forms (Lanzhou University Second Hospital Medical Ethics Committee), according to the world health organization classification system (6) were divided into low grade gliomas (Ⅰ-Ⅱ) group of 32 cases with high grade glioma (Ⅲ - Ⅳ) group of 31 cases.

In the low-grade glioma group, there were 19 males and 13 females, aged 6-70 years, with an average age of 54.92±10.37 years, including 12 cases of ganglionic glioma, 9 cases of hair cell astrocytoma, and 11 cases of diffuse astrocytoma. In the high-grade glioma group, there were 20 males and 11 females, aged 12-68 years, with an average age of 57.48±12.05 years old, including 10 cases of mesenchymal glioma, 15 cases of mesenchymal astrocytoma, and 6 cases of glioblastoma. Meanwhile, another 30 patients with brain metastases in our hospital were selected as the metastatic group, including 18 males and 12 females, aged 25-70 years, with an average age of 55.07±11.24 years. There was no significant difference in age, gender and other basic data between the three groups, which was comparable.

Inclusion and exclusion criteria

Inclusion criteria: 1)Patients with glioma or brain metastasis confirmed by pathology of our hospital; 2)all patients with brain tumor were found for the first time; 3) patients who had not affected the treatment of this study before the study was included; 4) agreed to this study, signed the informed consent patients. Exclusion criteria: 1) patients with incomplete clinical data; 2) patients with other immune system diseases; 3) patients with serious mental illness.

Research methods

Diffusion weighted MRI imaging and measurement methods

Using Siemens Verio 3.0 T superconducting MR scanner (Siemens medical systems co., LTD) to regular scans of patients, shaft a SE - T1W (TR 550 ms, TE 12 ms), axis FSE - T2W (TR 2 200 ms, TE 90 ms), axis of a fluid attenuated inversion recovery (fliud attenuated inversion recovery, FLAIR) T2W (TR 9 000 ms and 110 ms, TE TI 2 371 ms), field of view 320 mm×320 mm, matrix 256×256, axial layer thickness 5 mm. DWI adopted se-epi sequence, frequency selective fat suppression technique, TR 4 000 ms, TE 100 ms, layer thickness 9 mm, layer spacing 1 mm, FOV 260 mm×260 mm, matrix 256×192. The diffusion gradient was expanded from X, Y and Z directions. The values of two diffusion sensitive factors b were taken, b1=0s/mm2 and b2=1000s/mm2, respectively. MR scanning contrast agent was gd-dtpa (bayer pharmaceutical), the dosage per kg of body weight was 0.1mmol, the flow rate was 3ml/s, and the elbow was injected intravenously.

When selecting Regions Of Interest (ROI), firstly, tumor edges were determined according to T1WI and T2WI scans, and corresponding locations were marked on DWI , the contralateral normal white matter Of the tumor and tumor weeks edema area Of 40-80 was chosen ROI area respectively, each take 3-5 ROI, finally take measure average, including tumor edema area in tumor weeks less than 10 mm. In order to ensure a good representation of the selected ROI, attention should be paid to avoiding cerebral sulci and tumor necrotic tissue in practical operation to avoid volume effect. For patients with multiple tumors, the site with the largest tumor area and

obvious edema was selected as the target focus. The measurement of Apparent Diffusion Coefficient (ADC) in DWI images were all carried out in the workstation, version no. LEO3657, and the standardized ADC values in the tumor area and peri-tumor edema area (rADC) were calculated according to the following formula. The rADC value in the tumor area = tumor ADC value/ADC value in the contralateral normal white matter area. RADC value in the paratumoral edema area = ADC value in the paratumoral edema area/ADC value in the contralateral normal white matter area.

MR hydrogen proton spectrum analysis

Two-dimensional multibody spectral imaging was adopted, and point-resolved spectral analysis (PRESS) sequence scanning was used. TR 1510 ms, TE 150 ms, and the field of vision was 260mm ×260 mm. In the ROI area, spectral software automatically calculated the peak area of n-acetylaspartate (NAA), Choline (Cho), Creatine (Cr), etc., and calculated the ratios of NAA/ Cho, NAA/Cr and Cho /Cr.

Statistical software SPSS19.0 (Chicago, IL, USA) was used for data analysis, and measurement data were expressed as mean ± standard ($\chi \pm s$) deviation. F test was used for comparison between multiple groups, q test was used for pairwise comparison between multiple groups, and *t* test was used for comparison between two groups. $P< 0.05$, the difference was statistically significant.

Results

DWI imaging

In the low-grade group, tumors occurred in the right frontal cortex in 9 patients, the left frontal cortex in 4 patients, the right temporal in 5 patients, the left temporal in 3 patients, the left occipital in 4 patients, the left cerebellar hemisphere in 4 patients, and the right cerebellar hemisphere in 3 patients, including 27 patients with single lesion and 5 patients with multiple lesions. In the high-grade group, 9 cases occurred in the right frontal lobe, 9 cases in the left frontal lobe, 6 cases in the right temporal lobe, 5 cases in the left temporal lobe, and 2 cases in the pons, including 23 cases with single lesion and 8 cases with multiple lesions. The brain tumor parenchyma of the three groups usually showed T2WI high signal, DWI low signal, and ADC high signal, but the ADC signal of peritumoral edema area of metastatic tumor patients was lower than glioma patients (Fig. 1-3).

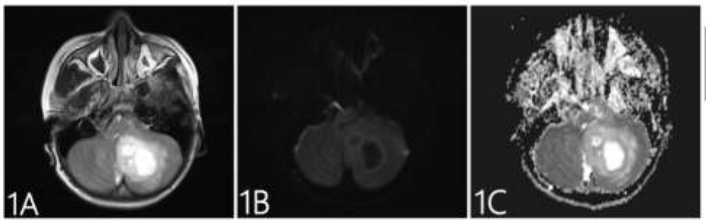

Fig. 1: male, 12 years old, a hair cell astrocytoma with a rounded cystic mass in the left cerebellar hemisphere. **A:** T2WI showed high signal and slight edema was observed around the tumor. **B:** DWI presented low signal, and peritumor edema presented equal signal; **C:** ADC in the sac solid area shows high signal

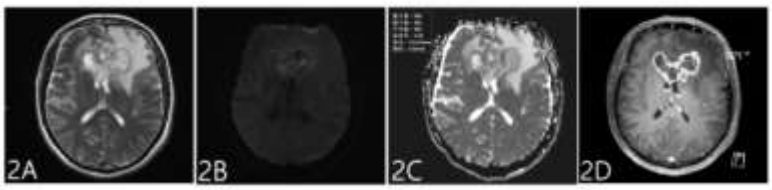

Fig. 2: a 46-year-old male with a glioblastoma with an irregular cystic mass on both foreheads. **A:** T2WI presented uneven and slightly high signal or equal signal, severe edema was observed around the tumor, and the edema area presented slightly high signal. **B:** DWI presented heterogeneous signals; **C:** ADC shows high signal or equal signal with clear boundary; **D:** T1 enhancement scan showed obvious irregular enhancement

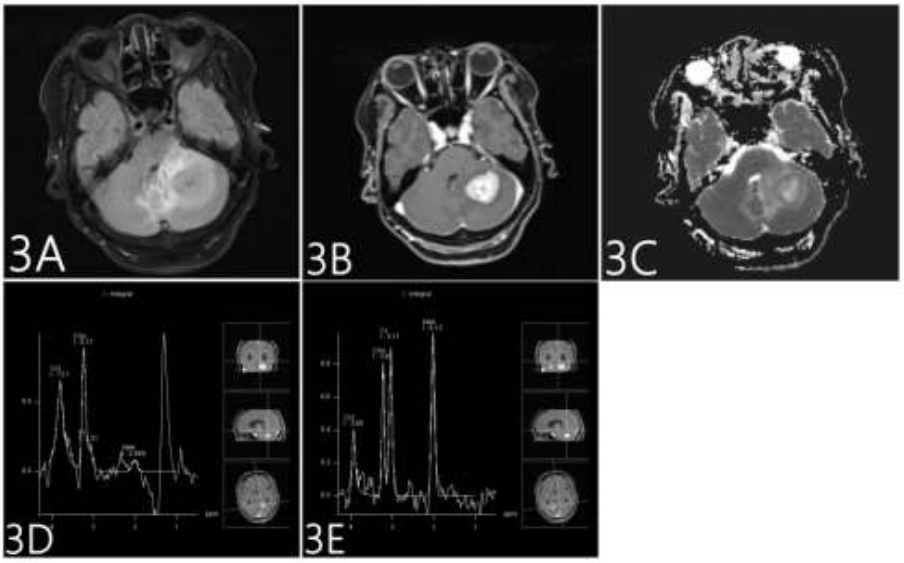

Fig. 3: female, 62 years old, with brain metastases from invasive ductal carcinoma of the breast. There is circular space in the left cerebellar hemisphere. **A:** T2-Flair presented equal signal **B:** T1WI enhanced scan showed obvious enhancement of tumor parenchyma.; **C:** ADC in the capsule solid area shows slightly high signal or equal signal; **D:** MRS in the tumor parenchyma showed a significant decrease in NAA, a slight increase in CHO, and a significant decrease in Cr. E: MRS in the normal white matter on the contralateral side of the tumor

Comparison of ADC and rADC values

The ADC values in the parenchymal and peri-tumor edema areas of the three groups were significantly higher than those in the normal white matter areas of the opposite sides ($P < 0.05$), and the rADC values in the peri-tumor edema areas of the high-grade glioma group were significantly lower than those in the low-grade group and the metastatic group ($P < 0.05$), and those in the low-grade group were significantly lower than those in the metastatic group ($P < 0.05$) (Table 1).

Table 1: comparison of ADC and rADC values among the 3 groups ($\bar{\chi}\pm s$, $\times 10^{-3}mm^2/s$)

Group	*Cases*	*Tumor parenchyma ADC*	*contralateral normal white matter area ADC*	*Tumor parenchyma rADC*	*Area of peritumor edema ADC*	*Edema of the contralateral white matter area ADC*	*Area of peritumor edema rADC*
Low-grade group	32	1.15±0.27[a]	0.76±0.12	1.53±0.32	1.23±0.21[b]	0.77±0.16	1.64±0.19[c]
High-grade group	31	1.75±0.33[a]	0.80±0.14	2.26±0.43	1.04±0.16[b]	0.73±0.11	1.46±0.16
Metastases group	30	1.84±0.39[a]	0.81±0.15	2.36±0.40	1.62±0.25[b]	0.75±0.13	2.29±0.40[c]
F		40.009	1.170	43.431	60.635	0.689	79.946
P		0.000	0.315	0.000	0.000	0.505	0.000

Compared with the contralateral white matter area of the tumor, a$P < 0.05$. BP < 0.05 compared with edema in the opposite white matter area. C$P < 0.05$ compared with the high-level group

Metabolite ratio analysis

The NAA/Cho and NAA/Cr ratios in the parenchymal area of the three groups were significantly lower than those in the peritumor edema area and the contralateral white matter area ($P < 0.05$), and Cho /Cr ratios were significantly higher than those in the peritumor edema area and the contralateral white matter area ($P < 0.05$). NAA/Cho and NAA/Cr in the peritumor edema area were significantly lower than those in the contralateral white matter area ($P < 0.05$), and Cho /Cr was significantly higher than those in the contralateral white matter area ($P < 0.05$). There was no significant difference in the NAA/Cho, NAA/Cr and Cho /Cr ratios in the contralateral white matter of the 3 groups. NAA/Cho and NAA/Cr in parenchymal and peritumor edema areas of patients in the advanced group were significantly lower than those in the metastatic group ($P < 0.05$), and Cho /Cr was significantly higher than those in the metastatic group ($P < 0.05$) (Table 2).

Table 2: comparison of metabolite ratios of patients in the 3 groups

Group		*Low-grade group*	*High-grade group*	*Metastases group*	*F*	P
NAA/Cho	Parenchyma area	0.47 ± 0.06^{abc}	0.24 ± 0.03^{ab}	0.39 ± 0.05^{abc}	182.336	0.000
	Area of peritumor edema	0.76 ± 0.12^{ac}	0.49 ± 0.07^{a}	0.68 ± 0.11^{ac}	57.408	0.000
	Contralateral white matter	1.40±0.21	1.43±0.17	1.41±0.26	0.014	0.986
NAA/Cr	Parenchyma area	1.22 ± 0.14^{abc}	0.91 ± 0.07^{ab}	1.28 ± 0.14^{abc}	82.695	0.000
	Area of peritumor edema	1.13 ± 0.11^{ac}	1.25 ± 0.12^{a}	1.37 ± 0.15^{ac}	27.506	0.000
	Contralateral white matter	1.49±0.12	1.50±0.13	1.52±0.15	0.402	0.670
Cho /Cr	Parenchyma area	2.59 ± 0.33^{abc}	3.80 ± 0.52^{ab}	3.27 ± 0.41^{abc}	63.801	0.000
	Area of peritumor edema	1.49 ± 0.15^{ac}	2.55 ± 0.28^{a}	2.01 ± 0.19^{ac}	194.354	0.000
	Contralateral white matter	1.02±0.08	1.06±0.13	1.03±0.11	1.154	0.320

Compared with the contralateral white matter area, aP < 0.05. BP < 0.05 and cP < 0.05 compared with the high grade group

Discussion

Glioma cell diseases are most common in young adults, when the patient has assumed important responsibilities in the family or society, and when faced with sudden disease pressure or even death threat, they will have a strong sense of despair. On the one hand, they worry that their reduced self-care ability will have an impact on their families, and they worry that they will be thrown away by the company and the society if they lose their ability to work. On the other hand, some patients are unable to correctly evaluate the severity of the disease they suffer from due to their low cognition of glioblastoma disease. They are blindly pessimistic and have a low level of psychological stress resilience. So in the face of patients with brain glioma, except for the treatment of patients with science, we should also pay close attention to patients' psychological emotional state changes, using the right means of persuation ease the patients psychological pressure, encourage patients to take an active part in social activities and give them enough social support, more attention should be paid to patients popularize basic knowledge of brain gliomas disease, distinguish between brain gliomas and brain metastases, and strengthen the rehabilitation training guidance, to reduce patients' stress reaction, improve the level

of mental flexibility, promote its better adapt to the situation.

Glioma and brain metastasis are two common brain tumors with different pathological basis. Glioma, especially high-grade glioma, is mainly manifested as infiltrating growth of tumor cells along dilating blood vessels and nerve fibers, blurry boundary between tumor parenchyma and normal brain tissue, T2 high signal in conventional MRI imaging examination, and generally does not disappear with tumor resection, with high recurrence (7). Brain metastases are primary tumors from other parts of the body that metastasized to the brain and often present as single or multiple lesions in the brain parenchyma. The boundaries between the tumor parenchyma and normal brain tissue are clear. Peritumor edema is vasogenic edema caused by tumor compression of blood vessels, and no tumor cells exist (8). However, some patients with single brain metastases may not find other extracranial tumors when detecting brain tumors. At this time, the manifestations of these tumors are very similar to those of glioma in CT and MRI images, and there is no characteristic signal change, so it often leads to misdiagnosis. The clinical treatment of brain glioma is usually dominated by surgery and radiotherapy, while the treatment of brain metastases is usually dominated by whole-brain radiotherapy. The two totally different treatment methods determine that if brain metastases are misdiagnosed as glioma, serious treatment accidents will be caused, directly affecting the prognosis of patients. Therefore, there is an urgent need for a technical method that can specifically distinguish glioma from brain metastases to diagnose diseases more accurately.

MRI was would impose to a certain frequency of rf pulse in a static magnetic field in the human body, make the hydrogen protons from the larmor precession to nutation, resonance with the radio frequency (rf) pulse, when the rf pulse stopped, hydrogen proton lost outside effect, the state gradually regression larmor precession, nutation and release energy, and the system is converted to electrical signals, finally presents to images in terminal screen (9). Among them, the time required for hydrogen protons to gradually return from nutation state to larmor is relaxation time, including longitudinal relaxation time T1 and transverse relaxation time T2 (10). MRI has many different focus sequences, such as T1WI reflecting T1 relaxation time contrast, T2WI reflecting T2 relaxation time contrast, and DWI reflecting water molecule exchange state between tissues (11). DWI is a new field of neuroimaging. With the support of planar echo imaging and other technologies, it can carry out non-injury measurement at the cell level in living organisms. By setting different diffusion sensitive gradients, moving protons generate different signals under the action of concentration difference and form images (12). However, in the process of actual measurement proton movement can be influenced by heating, pressure gradient, diffusion barrier permeability, blood flow and intercellular space or T2 penetration effect of various factors, DWI image signal height cannot accurately reflect the movement of water molecules, the lesion site but ADC figure can better remove T2 penetration effect, so use ADC to as a general quantitative indicators, rADC values can be used to eliminate the differences between the ADC values of the individual, to avoid to affect (13).

DWI and ADC signals are usually negatively correlated (14). The faster water molecules diffuse, the lower DWI signal is, and the higher ADC signal is. ADC values in the parenchymal and peritumor edema areas of the three groups were significantly higher than those in the normal white matter areas of the contralateral sides, which was consistent with another study (15). This is because when water molecules in human brain tissues disperse in the vertical direction of nerve fibers, they are limited by normal nerve fibers running parallel to each other, resulting in limited diffusion and low ADC value. However, in brain tumor tissues, the disordered arrangement of nerve fibers has no effect on the free diffusion of water molecules (16), so the ADC value is relatively high. The rADC value in the peri-tumor edema area of patients in the high-grade glioma group was significantly lower than that in the low-grade group and the metastatic

group, and the low-grade group was significantly lower than that in the metastatic group, suggesting that the rADC value in the peri-tumor edema area may be used to distinguish glioma from brain metastasis. Brain metastases are metastases from extracranial malignant tumor to intracranial by blood route. Generally, they are manifested as expansion and growth in the center. The peritumor edema is vasogenic edema without tumor cells, so water molecules spread faster and the rADC value is higher. The edema area of glioma is often filled with infiltrating tumor cells, which grow in the space near blood vessels and hinder the diffusion of water molecules (17), especially in patients with high-grade glioma, resulting in a low rADC value.

^{1}H-MRS is the only non-invasive technique to quantitatively analyze the degree of tissue damage in brain tumor patients, indicating the degree of tissue invasion by measuring the changes of tumor metabolites NAA, Cho and Cr (18). NAA is currently recognized by the medical community as a marker to reflect axonal density and neuronal activity, and its resonance peak appears at 2.03 PPM. NAA is usually low expressed in patients with impaired neuronal function (19). Cho peak located at 3.20 PPM is mainly used to reflect the cell proliferation ability or malignant degree of tumor. When the cell membrane conversion and metabolism change in tumor tissues of patients, Cho content will increase. Cr is the internal reference standard of nerve metabolism, which is stable at 3.04 PPM. As the methyl group of total creatine, Cr is low-expressed when energy metabolism of tumor patients increases (20).

The results of this study showed that the NAA/Cho and NAA/Cr ratios in the tumor parenchymal area of the three groups were significantly lower than those in the peritumor edema area and contralateral white matter area, and Cho /Cr ratios were significantly higher than those in the peritumor edema area and contralateral white matter area. NAA/Cho and NAA/Cr in the peritumor edema area of the 3 groups were significantly lower than that in the contralateral white matter area, and Cho /Cr was significantly higher than that in the contralateral white matter area, suggesting that the damage degree of neuronal axonal structure in the tumor parenchyma area was higher than that in the peritumor edema area. NAA/Cho and NAA/Cr in the parenchymal and peritumor edema areas of the high-grade group were significantly lower than those in the metastatic group, and Cho /Cr were significantly higher than those in the metastatic group, suggesting that NAA/Cho, NAA/Cr and Cho ratios had different manifestations in patients with glioma and brain metastasis.

Conclusion

There were significant differences in rADC, NAA/Cho, NAA/Cr and Cho /Cr levels between patients with high and low grade glioma and patients with brain metastases in the tumor parenchyma and peritumor edema areas, suggesting that the determination of rADC value and NAA/Cho, NAA/Cr and Cho /Cr levels could be used to distinguish patients with high and low grade glioma from patients with brain metastases.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

This study was supported by Gansu Health Industry Research Project (No. GSWSKY2016-06).

Conflicts of interest

The authors declare that there is no conflict of interest.

References

1. Schwartzbaum JA, Fisher JL, Aldape KD, et al (2006). Epidemiology and molecular patholo-

gy of glioma. *Na Clin Pract Neurol,* 2: 494-503.
2. Furnari FB, Fenton T, Bachoo RM, et al (2007). Malignant astrocytic glioma: genetics, biology, and paths to treatment. *Genes Dev,* 21: 2683-2710.
3. Suh CH, Kim HS, Jung SC, et al (2019). MRI as a diagnostic biomarker for differentiating primary central nervous system lymphoma from glioblastoma: A systematic review and meta-analysis. *J Magn Reson Imaging,* 50(2): 560-572.
4. Lu X, Xu W, Wei Y, et al (2019). Diagnostic performance of DWI for differentiating primary central nervous system lymphoma from glioblastoma: a systematic review and meta-analysis. *Neurol Sci,* 40(5): 947-956.
5. Werner JM, Stoffels G, Lichtenstein T, et al (2019). Differentiation of treatment-related changes from high-grade glioma progression: A direct comparison between FET PET and ADC values obtained by DWI MRI. *Eur J Nucl Med Mol Imaging ,* 46(9): 1889-1901.
6. Hervey-Jumper SL, Berger MS (2016). Maximizing safe resection of low-and high-grade glioma. *J Neurooncol,* 130(2): 269-282.
7. Fathi Kazerooni A, Nabil M, Zeinali Zadeh M, et al (2018). Characterization of active and infiltrative tumorous subregions from normal tissue in brain gliomas using multiparametric MRI. *J Magn Reson Imaging,* 48(4): 938-950.
8. Skogen K, Schulz A, Helseth E, et al (2019). Texture analysis on diffusion tensor imaging: discriminating glioblastoma from single brain metastasi. *Acta Radiol,* 60: 356-366.
9. Annen J, Heine L, Ziegler E, et al (2016). Function–structure connectivity in patients with severe brain injury as measured by MRI-DWI and FDG-PET. *Hum Brain Mapp,* 37(11): 3707-3720.
10. Qin J, Liu Z, Zhang H, et al (2017). Grading of gliomas by using radiomic features on multiple magnetic resonance imaging (MRI) sequences. *Med Sci Monit,* 23: 2168-2178.
11. Artzi M, Liberman G, Blumenthal D T, et al (2018). Differentiation between vasogenic edema and infiltrative tumor in patients with high-grade gliomas using texture patch-based analysis. *J Magn Reson Imaging,* 48: 729-736.
12. Wang MH (2018). Conventional MRI texture analysis of peritumoral edema in the differential diagnosis of glioblastoma and solitary metastatic brain tumor. *China Medical Abstracts,* 52: 756-760.
13. Zhang L, Min Z, Tang M, et al (2017). The utility of diffusion MRI with quantitative ADC measurements for differentiating high-grade from low-grade cerebral gliomas: evidence from a meta-analysis. *J Neurol Sci,* 373: 9-15.
14. Chenevert TL, Malyarenko DI, Galbán CJ, et al (2019). Comparison of Voxel-Wise and Histogram Analyses of Glioma ADC Maps for Prediction of Early Therapeutic Change. *Tomography,* 5(1): 7-14.
15. Ceschin R, Kocak M, Vajapeyam S, et al (2019). Quantifying radiation therapy response using apparent diffusion coefficient (ADC) parametric mapping of pediatric diffuse intrinsic pontine glioma: a report from the pediatric brain tumor consortium. *J Neurooncol,* 143(1): 79-86.
16. Zhang H, Ma L, Shu C, et al (2015). Diagnostic accuracy of diffusion MRI with quantitative ADC measurements in differentiating glioma recurrence from radiation necrosis. *J Neurol Sci,* 351(1-2): 65-71.
17. Shu C, Quan G, Yuan T, et al (2017). Application of multiple b-value DWI in assessment of early treatment response in postoperative patients with glioma. *Chinese Journal of Medical Imaging Technology,* 33(8): 1190-1196.
18. Tian HL, Zu YL, Wang CC, et al (2017). Major Metabolite Levels of Preoperative Proton Magnetic Resonance Sectroscopy and Intraoperative Fluorescence Intensity in Glioblastoma. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao,* 39(4): 511-517.
19. Crain ID, Elias PS, Chapple K, et al (2017). Improving the utility of 1 H-MRS for the differentiation of glioma recurrence from radiation necrosis. *J Neurooncol,* 133 (1): 97-105.
20. Gao W, Wang X, Li F, et al (2017). Cho/Cr ratio at MR spectroscopy as a biomarker for cellular proliferation activity and prognosis in glioma: correlation with the expression of minichromosome maintenance protein 2. *Acta Radiol,* 60(1): 106-112.