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FULL PAPER

A comparison of high b -value vs standard b -value diffusion-weighted magnetic resonance imaging at 3.0 T for medulloblastomas

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Objective: To investigate the utility of diffusion-weighted (DW) MRI using high b -value vs standard b -value for patients with medulloblastoma (MB). Minimum apparent diffusion coefficient (ADC_{MIN}) values were also compared with tumour cellularity.

Methods: High and standard b -value DW images were obtained for 17 patients with MB. The number and location of the lesions, signal intensities (SIs), signal-to-noise ratios (SNRs), contrast-to-noise ratios, contrast ratios (CRs) and ADCs of the lesions were compared. Tumour cellularity was also measured and compared with ADC_{MIN} values.

Results: All 20 lesions were hyperintense on the DW MR images with high and standard b -values. Four additional lesions were revealed on high b -value, and all 24 lesions were more conspicuous at high b -value. SI, SNR and ADC

values for the lesions were lower in the high b -value images than in the standard b -value images. The ADC_{MIN} value at $b = 3000 \text{ s mm}^{-2}$ was more significantly associated with tumour cellularity than that at $b = 1000 \text{ s mm}^{-2}$. CR values were significantly higher in the high b -value images than in the standard b -value images.

Conclusion: DW imaging using high b -value may be beneficial for detecting additional, less prominent lesions and may improve the contrast between MB lesions and normal tissue. A stronger inverse correlation with tumour cellularity was identified using the ADC_{MIN} values at high b -value.

Advances in knowledge: This study demonstrates the superiority of high b -value DW imaging compared with standard b -value imaging for the detection of MB lesions, especially those with subtle foci.

INTRODUCTION

Medulloblastoma (MB) is a highly malignant neuro-epithelial tumour of the posterior fossa that predominantly develops in children. However, it can also develop in adults. MB is thought to arise from primitive, undifferentiated, small round cells that are located in the superior medullary velum (at the roof the fourth ventricle) early in life, and later in life, these cells may migrate laterally.¹ The cerebellum is the most common location for MB, and most cases arise in the midline cerebellar vermis. However, in older children, adolescents and adults, MB manifests in more lateral locations within the cerebellar hemisphere. MB consists predominantly of small cells with minimal cytoplasm and oval, round or wedge-shaped homogeneously dark nuclei, and MB exhibits a high signal intensity (SI) on

diffusion-weighted (DW) imaging, possibly reflecting the small-cell histology of this tumour.² In general, MBs exhibit either classic histological features or histological features of one of the following non-classic variant subtypes: desmoplastic MB, MB with extensive nodularity, or large cell or anaplastic MB.³

DW MRI detects the diffusion of water in biological tissues. However, water distribution is complicated by bulk flow within capillaries and the active transport of water. Water diffusion is also affected by tumour cellularity, with the motion of water in the interstitium being the main contributor to higher apparent diffusion coefficient (ADC) values.² Highly cellular tumours incorporate less interstitial space and, therefore, are characterized by reduced water

diffusion and lower ADC values. Accordingly, DW imaging may be useful for evaluating gliomas since cellularity is a key factor in determining the tumour grade. For lymphomas,^{4,5} meningiomas⁶ and other tumours with high cellularity, a correlation between ADC values and cellularity has been observed. However, DW imaging does have limitations. For example, the sensitivity of DW imaging is low for small lesions such as leptomeningeal metastatic MB nodules, for various regions of the brainstem, and for imaging performed in the early stages following acute ischaemic stroke.

Theoretically, high b -value DW imaging provides better contrast owing to its sensitivity to tissue diffusivity and its reduced T2 shine-through effect.⁷ Accordingly, DW imaging at 3.0 T enables images to be captured at higher b -values with greater sensitivity. Moreover, this has been found to improve pre-operative histological grading of cerebral gliomas⁷ and meningiomas.⁸ DW imaging using a higher b -value has also been used for the diagnosis of acute stroke^{9,10} and Creutzfeldt–Jakob disease,^{11,12} and has produced better contrast between lesions and normal tissue in neurodegenerative diseases¹³ and primary central nervous system lymphoma (PCNSL).¹⁴

To our knowledge, only standard DW imaging has previously been used to investigate MBs.^{1,2,15–20} The b -value that is commonly used in conventional DW imaging is 1000 s mm^{-2} , while b -values $\geq 3000 \text{ s mm}^{-2}$ are considered high. A disadvantage of using a high b -value for DW imaging is that the signal-to-noise ratio (SNR) is reduced owing to the application of larger diffusion gradients.²¹ As a result, the MR signal decays. Therefore, the aim of the present study was to compare the use of high b -value ($b = 3000 \text{ s mm}^{-2}$) vs standard b -value ($b = 1000 \text{ s mm}^{-2}$) 3.0-T DW MRI for patients with MB. A possible correlation between ADC values and the cellularity of MB was also investigated.

METHODS AND MATERIALS

Patients

The present retrospective study was approved by our institutional review board. MRI and DW imaging were performed for patients diagnosed with MB between June 2009 and July 2013. The 17 patients included in this study (11 males and 6 females) with a mean age of 7 years were diagnosed with MB based on the pathological examinations of surgical specimens as defined by the World Health Organization (WHO). There was no more than 7 days between the imaging examinations and the surgeries performed. All of the human and animal studies performed were approved by the review board of the First Affiliated Hospital of Xiamen University and were performed in accordance with the ethical standards established in the 1964 Declaration of Helsinki and its subsequent amendments. In addition, all of the participating patients provided informed consent prior to inclusion in this study.

MRI

All MRI studies were performed using a 3.0-T superconducting MRI system (Magnetom® Verio Tim; Siemens Healthcare, Erlangen, Germany). Single-shot echoplanar DW imaging was performed with b -values of 1000 s mm^{-2} and 3000 s mm^{-2} . The

effective gradient was 40 mTm^{-1} , and the slew rate was $150 \text{ mTm}^{-1} \text{ ms}^{-1}$. An eight-channel phased-array head coil was used with a repetition time (TR) of 8200 ms and an echo time (TE) of 91 ms. For standard and high b -value images, the TR and TE values were 8200 and 100 ms, respectively. The field of view (FOV) was $22 \times 22 \text{ cm}^2$ and the matrix was 128×128 . The section thickness was 6 mm, and there were 24 sections and average of 2. The scan times were 2 min 5 s and 2 min 10 s to obtain standard b -value and high b -value images, respectively.

Conventional MRI (cMRI) studies were performed in three orthogonal planes, and they included non-enhanced T_1 weighted images [250 ms TR, 2.48 ms TE, $22 \times 22 \text{ cm}^2$ FOV, 320×256 matrix size, 6-mm section thickness (average, one)], T_2 weighted images [6000 ms TR, 96 ms TE, $22 \times 22 \text{ cm}^2$ FOV, 320×320 matrix size, 6-mm section thickness (average, one)] and fluid-attenuated inversion recovery (FLAIR) imaging [4000 ms TR, 94 ms TE, $22 \times 22 \text{ cm}^2$ FOV, 320×256 matrix size, 6-mm section thickness (average, one)]. Transverse, sagittal and coronal spin echo T_1 weighted images and FLAIR images were acquired after an intravenous administration of 0.1-mmol kg^{-1} body weight gadopentetic acid, a gadolinium-based contrast medium (Magnevist®; Bayer Schering Pharma AG, Berlin, Germany).

Image analyses

Two neuroradiologists blinded to patient history and information evaluated the DW images, ADC maps and cMRI images to detect and localize the areas exhibiting restricted diffusion. Matching DW images and ADC maps were presented in a random order. In the case of a disagreement, the third neuroradiologist assessed the images in question, and a final decision was made. For each case, the number of lesions detected using $b = 1000 \text{ s mm}^{-2}$ and $b = 3000 \text{ s mm}^{-2}$ DW imaging were counted and compared with the number of lesions revealed by gadolinium-based, T_1 weighted imaging and contrast-enhanced FLAIR. The latter is considered a reference standard and has been shown to improve the detection of leptomeningeal metastatic spread of MB and cerebral metastasis compared with routine contrast-enhanced T_1 weighted imaging.^{22,23}

Quantitative analyses

All DW images were measured and analysed using a Siemens workstation. Regions of interest (ROIs) in lesion sites and normal contralateral brain tissue were measured on both high b -value and standard b -value image sets and ADC maps. The pons was selected to represent normal brain tissue when MB lesions were vermis lesions, or in cases involving bilateral lesions present in both cerebellar hemispheres. As much as possible, these measurements were made on similarly sized ROIs of the same region. ROIs were also placed as centrally as possible within the enhanced lesions present on contrast-enhanced T_1 weighted images, were selected according to the size of the lesion and were placed to avoid the lesion capsule and cystic, necrotic and hemorrhagic regions that might influence the ADC values. MRI SIs, SNRs, contrast-to-noise ratios (CNRs), contrast ratios (CRs) and ADC values for each of the $b = 1000 \text{ s mm}^{-2}$ and $b = 3000 \text{ s mm}^{-2}$ DW images were calculated. The ADC values for each lesion were calculated based on ADC maps at

Table 1. Characteristics of the additional leptomeningeal medulloblastoma lesions that were detected

Patient number	Tumour shape	Tumour location	Gadolinium-based T_1 weighted imaging	Contrast-enhanced (gadolinium) fluid-attenuated inversion recovery	Standard b -value DW imaging	Higher b -value DW imaging
N3	Round	Left frontal lobe	No	Yes	No	Yes
N6	Oval	Right central sulcus	No	Yes	No	Yes
N11	Dotted	Right temporal lobe	No	Yes	No	Yes
N14	Dotted	Left occipital lobe	No	Yes	No	Yes

DW, diffusion-weighted.

$b = 1000 \text{ s mm}^{-2}$ and $b = 3000 \text{ s mm}^{-2}$. Minimum ADC (ADC_{MIN}), maximum ADC (ADC_{MAX}) and mean ADC (ADC_{MEAN}) absolute values were recorded. Image noise was measured from a large area outside the brain parenchyma, and this was defined as the background SI.

The SI and ADC values were measured for $b = 1000 \text{ s mm}^{-2}$ and $b = 3000 \text{ s mm}^{-2}$ DW images, and both mean and standard deviation (SD) values were calculated. SNRs, CNRs and CRs were also calculated using the following equations:^{9,14}

Figure 1. A classic medulloblastoma in a 4-year-old male with a 2-month history of ataxic gait. (a) An axial T_2 weighted MR image reveals slight hyperintensity in the cerebellar vermis. (b) A contrast-enhanced axial T_1 weighted MR image demonstrates a slightly heterogeneous, yet intense enhancement of the lesion. (c) A diffusion-weighted (DW) image that was obtained using a b -value of 1000 s mm^{-2} . (d) An apparent diffusion coefficient (ADC) map that shows the slightly restricted diffusion values that were observed in the lesion. (e) A DW image that was obtained using a b -value of 3000 s mm^{-2} . (f) An ADC map that shows a slight increase in signal intensities in the cerebellar vermis.

Figure 2. A 4-month-old male diagnosed with medulloblastoma with extensive nodularity. (a) An axial T_2 weighted MR image demonstrates an eccentric posterior fossa tumour present in the right cerebellar hemisphere. (b) In a post-contrast T_1 weighted image, marked heterogeneous enhancement was observed. (c) A diffusion-weighted (DW) image obtained using a b -value of 1000 s mm^{-2} . (d) An apparent diffusion coefficient (ADC) map that shows slightly restricted diffusion values for the lesion. (e) A DW image obtained using a b -value of 3000 s mm^{-2} . (f) An ADC map that shows increased signal intensities in the right cerebellar.

$$\text{SNR} = S_{\text{lesion}} / \sigma_{\text{noise}}$$

$$\text{CNR} = |S_{\text{lesion}} - S_{\text{brain}}| / \sigma_{\text{noise}}, \text{ and}$$

$$\text{CR} = |S_{\text{lesion}} - S_{\text{brain}}| / |S_{\text{lesion}} + S_{\text{brain}}|$$

where S_{brain} is the average SI of the contralateral normal brain tissue, S_{lesion} is the average of SI of the lesion and σ_{noise} is the SD of the background noise.

Histopathological studies

All pathological specimens were evaluated by a single experienced reviewer (SZ, a paediatric pathologist with 15 years' experience). Tumours were classified according to the latest WHO classification of tumours of the central nervous system.²⁴ Briefly, following surgical resection, tumour specimens were fixed in 10% phosphate-buffered formalin, embedded in paraffin and representative slides were stained with haematoxylin–eosin reagent for standard histological diagnosis according to WHO criteria. Tumour cellularity was evaluated as described previously.²⁵ Briefly, at least four separate fields containing high cellularity regions were selected from areas of each solid tumour sample. The cellularity of each field was calculated by manually counting the total number of cells present in each photomicrograph obtained at $\times 400$ magnification. The mean number of cells observed was recorded for each case.

Statistical analyses

Statistical analyses were performed using a commercially available software package, Medcalc v. 9.3 (Medcalc Software, Mariakerke, Belgium). Student's t -test was used to compare mean SI, SNR, CNR and ADC values between $b = 1000 \text{ s mm}^{-2}$ and $b = 3000 \text{ s mm}^{-2}$ DW images. A simple linear regression analysis was used to evaluate the relationship between tumour cellularity and ADC values. A p -value < 0.05 was considered statistically significant.

RESULTS

17 patients (11 males and 6 females) with a mean age of 7 years (range: 1/3–17 years) were included in this study. A total of 24 lesions were detected by cMRI. 14 patients had one lesion each (classic MB), 1 patient had two lesions (MB with extensive nodularity), another patient had three lesions (classic MB) and another patient had five lesions (desmoplastic MB). Of these lesions, 12 were located in the vermis, 8 were located in the cerebellar hemisphere and 4 small lesions ($< 0.5 \text{ cm}$ in diameter) were located in the right central sulcus, left frontal lobe, right temporal lobe and left occipital lobe, respectively (Table 1).

Qualitative analyses

Lesions were detected in DW images obtained using high and standard b -values, and areas of restricted diffusion were more conspicuous in the high b -value images (Figures 1 and 2). Correspondingly, the total number of lesions detected at

Figure 3. A 6-year-old male diagnosed with classic medulloblastoma in the cerebellar vermis. There was no lesion detected on an axial fluid-attenuated inversion recovery (FLAIR) MR image (a), a post-contrast T_1 weighted image (b) or with standard diffusion-weighted (DW) imaging (d). However, DW imaging using a high b -value (e) and contrast-enhanced FLAIR (c) showed that restricted diffusion and nodular enhancement was present in the right central sulcus, thereby indicating the presence of a small metastatic lesion (arrows).

$b = 1000 \text{ s mm}^{-2}$ and $b = 3000 \text{ s mm}^{-2}$ were 20 and 24, respectively. The two reviewers of these images (HH and CH, with 7 and 8 years' experience, respectively) agreed on the identification of 19 lesions in the standard b -value DW images and only had to resolve by consensus one disagreement regarding a single lesion. By contrast, both reviewers agreed on the presence of all 24 lesions that were identified in the high b -value images. Moreover, all of the lesions visualized in the standard b -value DW images were also detected in the high b -value DW images. For the four additional lesions that were identified in the high b -value DW images (Figure 3), these were not characterized by pathological examination, whereas the other 20 lesions were. Artefacts also appeared to be more pronounced in the high b -value images.

Mean $\pm$ SD values for SIs, SNRs, CNRs, CRs and all ADC values are summarized in Tables 2 and 3. All of the results were statistically significant ($p < 0.05$), except for the CNRs. The SNRs calculated from the high b -value images were lower than those for the standard b -value images. Moreover, the ADC_{MIN} , ADC_{MAX} and ADC_{MEAN} values were all significantly lower for the high b -value images compared with the standard b -value images.

In the high b -value images, the SI decreased by 44.4% (185.33 ± 69.59 vs 333.54 ± 80.32 at $b = 3000 \text{ s mm}^{-2}$ and $b = 1000 \text{ s mm}^{-2}$,

respectively). The SNR also decreased by 34.6% (237.19 ± 103.10 vs 363.11 ± 95.16 , respectively). By contrast, the CR was significantly higher in the high b -value images (0.374 ± 0.134 vs 0.204 ± 0.067 , respectively; $p < 0.004$). The ADC_{MIN} , ADC_{MAX} and ADC_{MEAN} values calculated from the high b -value images were also lower by 30.2%, 31.2% and 28.5%, respectively, compared with the standard b -value images.

Cellularity and minimum apparent diffusion coefficient values of the tumour tissues examined
The mean cell density per field was 439 cells (range: 300–612 cells), and a negative correlation between tumour cellularity and ADC_{MIN} values was observed for the MBs examined. Moreover, a stronger negative correlation was associated with the high b -value images ($r = -0.846$, $p < 0.001$) compared with the low b -value images ($r = -0.686$, $p = 0.003$) (Figure 4).

DISCUSSION

DW imaging is a technique which uses phase-defocusing and phase-refocusing gradients to determine the rates of water diffusion within tissues. Other MRI techniques cannot measure diffusion, and often water diffusion is altered in various diseases, including MB. The b -value of an MR image depends on the strength, duration and timing of the applied diffusion-sensitizing

Table 2. Signal intensity (SI), signal-to-noise (SNR), contrast-to-noise (CNR) and contrast ratio (CR) values for $b = 1000 \text{ s mm}^{-2}$ and $b = 3000 \text{ s mm}^{-2}$ diffusion-weighted images

Parameters	$b = 1000 \text{ s mm}^{-2}$	$b = 3000 \text{ s mm}^{-2}$	p -value
SI	333.54 ± 80.32	185.33 ± 69.59	<0.0001
SNR	363.11 ± 95.16	237.19 ± 103.10	0.0002
CNR	120.36 ± 43.49	127.73 ± 78.43	0.7216
CR	0.204 ± 0.067	0.374 ± 0.134	<0.0004

Table 3. Apparent diffusion coefficient (ADC) values from $b = 1000 \text{ s mm}^{-2}$ and $b = 3000 \text{ s mm}^{-2}$ diffusion-weighted images

ADC values	$b = 1000 \text{ s mm}^{-2}$	$b = 3000 \text{ s mm}^{-2}$	p -value
Minimum ADC	0.549 ± 0.058	0.383 ± 0.044	<0.0001
Maximum ADC	0.665 ± 0.072	0.457 ± 0.037	<0.0001
Mean ADC	0.596 ± 0.043	0.426 ± 0.033	<0.0001

gradients. While DW imaging using a higher b -value can be achieved using a 1.5-T MR system, the SNR is very low for the images obtained. Consequently, the use of higher b -values for DW imaging is limited when a 1.5-T MR system is used. However, a 3.0-T MR system can achieve a higher SNR, and thus, higher b -values for DW imaging can be used with a 3.0-T MR system.²⁶ Moreover, DW imaging with a 3.0-T MR system provides greater diffusion sensitivity.

Altered diffusion within a tumour can demarcate tumour tissue from normal tissue. Specifically, when MB tumours block water diffusion, they appear hyperintense on DW images and appear hypointense on ADC maps. In the low b -value DW images of the present study, most of the lesions exhibited slightly and moderately restricted diffusion ($n = 20$), although a few lesions ($n = 4$) were not hyperintense relative to the surrounding cortical grey matter. Furthermore, the SI, SNR and ADC values were lower in the high b -value images, while the CR values were significantly higher. As a result, the lesions present were more conspicuous. Additional lesions were also revealed in the high b -value images, indicating that the use of a higher b -value for DW imaging may be better for detecting small lesions. All of the additional lesions detected in the present study were leptomeningeal MB lesions, and they were surrounded by the grey matter or CSF. The contrast between the lesions with adjacent CSF and the lesions with adjacent grey matter was greater when the grey matter signals were suppressed, except when the CSF signals were nullified with the higher b -value DW imaging. These findings are in concordance with those from previous studies where high b -value DW imaging was applied to patients

with ischaemic stroke^{9,10} and patients with PCNSL.¹⁴ In both studies, high b -value images were also better at visualizing small lesions and multiple lesions in patients with stroke and PCNSL. To our knowledge, this is the first study to compare standard b -value and high b -value DW imaging in the detection of MB lesions.

In the present study, the ADC_{MIN} , ADC_{MAX} and ADC_{MEAN} values obtained from the high b -value DW images were consistently lower than those obtained from the standard b -value images. In previous studies,^{15–19} the ADC_{MEAN} values obtained at a b -value of 1000 s mm^{-2} ranged from 0.47×10^{-3} to $0.75 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ in patients with MB, and these data are consistent with the present results.

Comparisons between the ADC_{MIN} value at $b = 1000 \text{ s mm}^{-2}$ and cellularity in the MBs examined showed that ADC values are inversely associated with tumour cellularity. Thus, high cellularity leads to more restricted diffusion. Other studies have also reported an inverse correlation between tumour cellularity and the ADC values for meningiomas⁶ and gliomas,²⁷ and the results of the present study are in concordance with these. However, the results of the present study further demonstrate that the inverse correlation is stronger when the b -value is 3000 s mm^{-2} rather than 1000 s mm^{-2} for DW imaging.

In general, ADC values decrease when b -values increase above 1000 s mm^{-2} . If the relationship between the MR signal and the b -value is monoexponential, then the ADC values would be constant for any two-point calculation as the b -values increased.

Figure 4. A negative correlation between minimum apparent diffusion coefficient (ADC) values and tumour cellularity in a medulloblastoma [$r = -0.686$, $p = 0.003$ vs $r = -0.846$, $p < 0.001$ at $b = 1000 \text{ s mm}^{-2}$ (a) and $b = 3000 \text{ s mm}^{-2}$ (b), respectively].

However, ADC values have been found to decrease as *b*-values increase, thereby suggesting that bi-exponential SI decay may occur.^{28,29} Fast and slow diffusion components have been described in brain models, and at low and high *b*-values, SI is dominated by fast and slow diffusion, respectively. In future studies, the use of different *b*-values during DW imaging could be used to explore whether bi-exponential SI decay occurs in MB lesions.

To our knowledge, the present study is the first to evaluate the use of standard vs high *b*-values for MRI of patients with MB. However, the sample size in the present study was small since cases of MB are relatively rare. Therefore, in order to confirm the present results, additional DW images and ADC values from a larger prospective study are needed. In addition, most of the MBs examined exhibited a classical histology, while only two

non-classic variant subtypes of MB were available. Correspondingly, differences between classic MB and MB subtypes were not explored. The present study also did not address contributions from bulk capillary flow, active transport mechanisms and partial volume effects on ADC values.³⁰ Future large-scale studies should also include these types and considerations.

In conclusion, although a quantitative analysis demonstrated that higher SI, SNR and ADC values were associated with standard *b*-value DW imaging, the use of a higher *b*-value ($b = 3000 \text{ s mm}^{-2}$) facilitated the detection of more subtle lesions, and it also improved the contrast between lesions and normal tissue. In particular, a stronger inverse correlation between ADC_{MIN} at a *b*-value of 3000 s mm^{-2} from 3.0-T MRI and tumour cellularity was identified.

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