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### **ORIGINAL ARTICLE**

# 3-T high-b-value diffusion-weighted MR imaging in hyperacute ischemic stroke

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#### **KEYWORDS**

3 Tesla; MRI; DWI; High b-value; Hyperacute ischemic stroke

#### Summary

Background and purpose: In patients with hyperacute ischemic stroke, early demonstration of infarction is essential. Diffusion weighted imaging (DWI) is the key method for detecting hyperacute infarction. The value of high b-value DWI in hyperacute ischemic stroke is controversial at 1.5 T, and is unknown at 3 T. The aim of this study is to explore the value of high b-value versus standard b-value DWI at 3 T in hyperacute stroke with quantitative and qualitative analysis. Material and methods: This study prospectively included 104 consecutive patients with hyperacute stroke. At 3 T, conventional MR sequences and DWI were performed. The examination included a standard DWI (b =  $1000 \text{ s/mm}^2$ ) and two high b-value DWI (b =  $3000 \text{ s/mm}^2$  and b =  $5000 \text{ s/mm}^2$ ). Qualitative and quantitative analysis was performed.

Results: With increasing b value, DW images appeared noisier. The number of detected lesions was significantly higher on b = 3000 images than on the other DW images and higher on b = 5000 images than on b = 1000 images. The number of lesions greater than 1 cm was not significantly different. Lesion conspicuity was higher, boundary better seen, lesion extent bigger, and estimation of final infarct size was better on high b-value than on standard b-value DWI. Contrast-to-noise-ratio (CNR) and signal-to-noise-ratio (SNR) decreased and contrast ratio (CR) increased on high b-value DWI compared to standard b-value DWI.

Conclusion: At 3T, high b-value DWI was superior to standard b-value DWI in detection of hyperacute infarction and prediction of final infarct size in spite of increasing imaging artifacts. © 2013 Published by Elsevier Masson SAS.

# Introduction

In patients with hyperacute ischemic stroke, early demonstration of lesion location and extent is essential for guiding recanalization therapy [1-3]. Diffusion-weighted imaging (DWI) is the key method for detecting ischemic lesions within the first hours after stroke onset [4]. In stroke diffusion

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studies, the b values applied are usually in the range of  $800-1500 \text{ s/mm}^2$ , but recent progress in magnetic resonance imaging (MRI) technology now permits higher b values, which have already been used for imaging acute ischemic stroke at 1.5 T [5-7] and 3 T [8]. However, detecting hyperacute ischemic stroke ( $\leq 6 \text{ h}$  from onset) is particularly difficult because DWI is less sensitive with shorter MRI delay [9]. High b-value DWI has already been used at 1.5 T and 3 T in hyperacute ischemic stroke, but its value is controversial with the former value [5-7,10] and still unknown with the latter [8,11,12].

Thus, the aim of the present study was to explore the usefulness of high b-value *vs* standard b-value DWI at 3T in hyperacute stroke, using quantitative and qualitative analysis.

#### Material and methods

#### **Patients**

This study prospectively included, from October 2010 to December 2011, 104 consecutive patients (42 women and 62 men; mean age 68.9 years; age range 33—90 years) with hyperacute stroke. The delay from stroke onset was known, and ranged from 30 to 337 min (mean 148.4 min). Localization of infarction is shown in Table 1. Vessel occlusion was found in 63 patients. Intravenous lysis was performed in 48 patients, intra-arterial lysis in three patients, combined intravenous and intra-arterial lysis in two patients, and mechanical recanalization in 15 patients. Recanalization of vessel occlusion was documented in 29 patients. This study had the approval of the responsible ethics commission.

#### MRI examinations

All MRI studies were performed using a 3-T system (Trio; Siemens Medical Systems, Erlangen, Germany) with a receive-only eight-element head coil. Conventional MR sequences as well as echo-planar DWI were performed. The examination began with a standard DW sequence (b = 1000 s/mm<sup>2</sup>) followed by two high b-value DWI (b = 3000 s/mm<sup>2</sup>) and  $b = 5000 \text{ s/mm}^2$ ) sequences. These latter two sequences were based on the standard DW sequence. Alterations in repetition time (TR) and echo time (TE) were chosen to be as low as possible. In the b = 5000 DW sequence, the number of excitations was increased to maintain signal-to-noise ratio (SNR). Details of the imaging parameters are presented in Table 2. Follow-up computed tomography (CT) was performed in 60 patients and follow-up MR in two. The delay from time of stroke onset to follow-up imaging was 1-20 days with an interval of 1-6 days in most (n = 57) patients.

#### Qualitative analysis

All DW images were interpreted by two neuroradiologists whose experience with DW imaging was 14 and 5 years, respectively. All images were displayed on picture archiving and communication system (PACS) monitors. The artifacts for every sequence were graded on a four-point scale (none, mild, moderate and strong) and, after reading the images in a blinded manner, the observers assessed the DW images

for the numbers of lesions that were smaller and bigger than 1 cm. The observers then compared the b = 1000 images with the b = 3000 images and b = 5000 images side-by-side to determine lesion conspicuity, lesion boundaries and lesion extent. In addition, lesion extent was compared with the follow-up CT or MRI. Finally, the grades and rankings assigned were the result of a consensus opinion following discussion between the two observers.

#### Quantitative analysis

A single investigator performed the quantitative analysis for the 91 patients with measurable infarcts. In 104 lesions, regions of interest (ROIs) were positioned over the infarct, the contralateral normal brain and the background. Contrast ratio (CR), contrast-to-noise ratio (CNR) and SNR were calculated as CR = SI (infarct) -SI (brain)/SI (infarct) + SI (brain), CNR = SI (infarct) -SI (brain)/SD (background) and SNR = SI (infarct)/SD (background), where SI (infarct) and SI (brain) represented the signal intensity value in the ischemic infarction and contralateral normal brain, respectively, and SD (background) represented the standard deviation of the background noise.

Apparent diffusion coefficient (ADC) was derived from the ADC map, and the relative ADC (rel ADC) was calculated as rel ADC = ADC (infarct)/ADC (brain), where the ADC (infarct) and ADC (brain) represented the ADC of the ischemic lesion and contralateral normal brain, respectively.

#### Statistical analysis

Differences in the number of detected lesions and rel ADC were analyzed using the paired t test and a confidence interval (CI) of 95%. Correlations between delay after stroke onset and number of lesions, and CR, CNR, SNR and ADC, were analyzed using the chi-square test. A P value < 0.05 was considered statistically significant. For evaluation, a commercially available statistical software package (SPSS 19.0; SPSS Inc., Chicago, IL, USA) was used.

#### Results

Artifacts were mild in 99 patients and moderate in five patients on b = 1000 images, moderate in 100 patients and strong in four patients on b = 3000 images, and strong in all patients on b = 5000 images. The effect of artifacts on false-positive results could not be evaluated because, in most patients, CT was performed as follow-up imaging.

In 90 patients, lesions were greater than 1 cm. The numbers of lesions detected using the different DWI sequences are shown in Table 3. The number of detected lesions was significantly higher on b = 3000 images than on either b = 1000 images (P < 0.001) or b = 5000 images (P < 0.005), and was also higher on b = 5000 images than on b = 1000 images (P < 0.005; Fig. 1). The number of lesions greater than 1 cm was not significantly different among the different DW sequences. In three (2.9%) patients, no lesions greater than 1 cm were detected on b = 1000 images, but one lesion each greater than 1 cm were found on the b = 3000 and b = 5000 images. One of these patients had additional small lesions

Localization	Patients	Localization	Patients
A. cerebri media	76	A. cerebi anterior	2
A. basilaris (pons)	8	A. cerebri posterior (thalamus)	2
A. cerebri posterior	6	PICA, cerebellum	2
A. cerebri anterior and media	3	A. choroidea anterior	1
Border zone	3	A. cerebri posterior and PICA (cerebellum)	1

Parameter	Sequence					
	2D EPI	2D EPI	2D EPI			
B value (s/mm²)	1000	3000	5000			
Gradient directions	3	3	3			
TR (ms)	3100	4100	4300			
TE (ms)	79	108	118			
Flip angle (°)	90	90	90			
Section thickness (mm)	5	5	5			
Sections	23	23	23			
Distant factor (%)	20	20	20			
Bandwidth (Hz/pixel)	1347	1347	1347			
FOV (mm)	230 × 230	230 × 230	230 × 230			
Matrix	128 × 128	128 × 128	128 × 128			
Averages	3	3	4			
Acquisition time (min.sec)	0.48	0.55	1.15			

Delay min	1000 lesions all	1000 lesions < 1 cm	1000 lesions > 1 cm	3000 lesions all	3000 lesions < 1 cm	
0—360 <i>n</i> = 104	2.076	1.038	1.038	2.701	1.615	
0—90 <i>n</i> = 17	1.705	0.647	1.058	2.235	1.058	
91—180 <i>n</i> = 68	1.882	0.852	1.029	2.441	1.397	
181–270 <i>n</i> = 12	3	2.083	0.916	3.75	2.75	
271—360 <i>n</i> = 7	3.285	2	1.285	4.571	3.142	
Delay min	3000 lesions	> 1 cm 5000	lesions all 500	0 lesions < 1 cm	5000 lesions > 1 cm	
0-360 <i>n</i> = 104	1.086	2.40	3 1.32	26	1.076	
0—90 <i>n</i> = 17	1.176	2.05	5 0.94	<b>1</b> 1	1.176	
91—180 <i>n</i> = 68	1.044	2.23	5 1.20	)5	1.029	
181—270 <i>n</i> = 12	1	2.75	1.75	5	1	
271-360 n=7	1.428	4.14	2 2.71	14	1.428	

on all DW images. With increasing delay from stroke onset, the number of detected lesions increased, although there was no correlation between delay from stroke onset and lesions greater than 1 cm. Lesion conspicuity was greater, boundaries were better seen and their extents were larger

on b=5000 and b=3000 images compared with b=1000 images (Table 4, Figs. 2—4). Estimation of lesion extent in comparison to follow-up CT and MRI was better on b=5000 and b=3000 images than on b=1000 images (Figs. 2, 3). Compared with b=1000 images, CR increased on b=3000

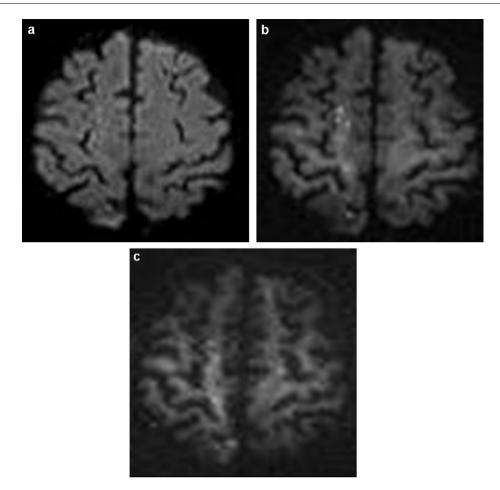


Figure 1 Multiple small ischemic lesions in the right border zone. Delay from stroke onset was 230 minutes. Lesion detection was better on b = 3000 images (b) than on b = 5000 images (c) followed by b = 1000 images (a).

images by 105% and by 124.9% on b=5000 images. CNR and SNR decreased on b=3000 images by 29.2% and 59.7%, respectively, and on b=5000 images by 42.3% and 69.5%, respectively, compared with b=1000 images (Table 5). There was no correlation between delay from stroke onset and CR, CNR and SNR. The rel ADC was significantly higher on b=5000 vs b=1000 (P<0.05) and vs b=3000 images (P<0.001), but was not significantly different between the b=1000 and b=3000 images. There was no correlation between delay from stroke onset and the rel ADC (Table 6).

#### **Discussion**

At our present, it is still uncertain whether high b-value DWI sequences can improve the detection of acute and hyperacute ischemic lesions as the published results are inconsistent. In our study, at 3 T, high b-value DW sequences were better at detecting hyperacute ischemic lesions than were standard b-value DW sequences in spite of images apparently having more noise with more artifacts, and lower SNR and CNR.

Lesion cons	picuity	Lesion boundary		Lesion extent		Lesion extent compared to follow-up CT/MRI	
5 > 3 > 1	37.5%	5 > 3 > 1	53.8%	5 > 3 > 1	50.9%	5 = 3 > 1	42.2%
5 = 3 > 1	27.8%	3 > 5 > 1	24%	5 = 3 > 1	32.6%	5 > 3 > 1	35.5%
3 > 5 > 1	23.1%	5 = 3 > 1	18.2%	3 > 5 > 1	11.5%	3 > 5 > 1	15.5%
1 = 3 = 5	4.8%	3 > 1 > 5	1.9%	3 = 1 > 5	2.8%	1 > 3 > 5	2.2%
3 > 1 > 5	3.8%	1 = 3 = 5	0.9%	3 > 1 > 5	0.9%	1 > 3 = 5	2.2%
3 > 5 = 1	2.8%	1 > 3 > 5	0.9%	1 > 3 > 5	0.9%	1 > 5 > 3	2.2%

1: b = 1000 s/mm<sup>2</sup>; 3: b = 3000 s/mm<sup>2</sup>; 5: b = 5000 s/mm<sup>2</sup>; >: a higher conspicuity, sharper boundary, bigger extent, and better prediction of extent of infarction compared to follow-up imaging; =: no difference.

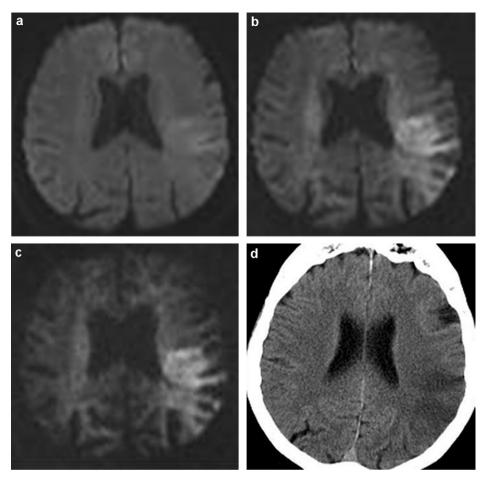


Figure 2 Occlusion of two branches of the left medial cerebral artery. Hyperacute infarction frontal and parietal. Delay from stroke onset was 195 minutes. Lesion conspicuity was higher, boundary was better seen and lesion extent was bigger on b = 5000 (c) and b = 3000 images (b) compared to b = 1000 images (a). Estimation of lesion extent compared to follow-up CT (d) 1 day later was best on b = 5000 images (c).

Table 5	Contrast rati	io, contrast-1	to-noise-ratio	, and signal-t	o-noise-ratio	in hyperacut	e ischemic les	ions.	
Delay min	1000 CR	3000 CR	5000 CR	1000 CNR	3000 CNR	5000 CNR	1000 SNR	3000 SNR	5000 SNR
0-360 n = 104	0.188	0.386	0.424	69.24	49.05	40.00	216.92	87.51	66.24
0—90 n = 18	0.161	0.325	0.367	54.73	34.84	30.45	196.99	72.50	57.30
91—180 n = 66	0.187	0.389	0.429	67.54	49.91	42.31	212.16	88.21	69.01
181—270 n = 12	0.242	0.456	0.490	88.70	54.39	42.39	227.91	88.77	64.39
271—360 n=8	0.177	0.397	0.411	86.77	66.01	38.87	284.59	113.53	66.29

1000: b = 1000 s/mm²; 3000: b = 3000 s/mm²; 5000: b = 5000 s/mm²; CR: contrast ratio; CNR: contrast-to-noise-ratio; SNR: signal-to-noise-ratio; Delay: delay from stroke onset; n: number of lesions.

At 1.5 T, Meyer et al. [5] and Burdette and Elster [6] performed high b-value DW sequences in patients with ischemic stroke within 14 days of the onset of neurological symptoms and found no diagnostic advantages compared with

the usual DW imaging. Toyoda et al. [7] performed high b-value DW sequences in patients with ischemic stroke within 3 to 48h after the onset of neurological symptoms, and found ischemic lesions to be more distinct and extensive

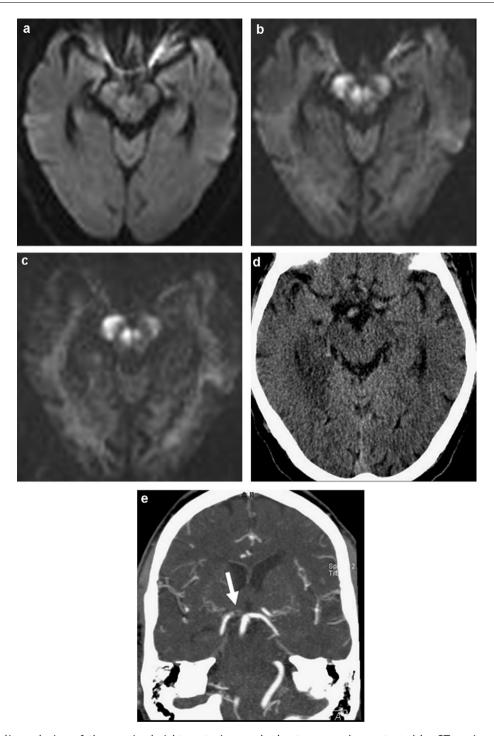


Figure 3 Embolic occlusion of the proximal right posterior cerebral artery was demonstrated by CT angiography (e, arrow). Hyperacute ischemic lesion in the right mesencephalon. Delay from stroke onset was 165 minutes. Lesion conspicuity was higher, and lesion extent was bigger on b = 5000 (c) and b = 3000 images (b) compared to b = 1000 images (a). On follow-up CT (d) 1 day later, hypodense infarction in the right mesencephalon and temporal lobe is shown.

with increased b values in 19 of 32 patients. The size of the final infarction was more predictable with high b-value DWI. In patients with hyperacute stroke ( $\leq$ 6 h from onset), Kim et al. [10] demonstrated that high b-value DW sequences were superior to the usual DW sequences for the detection and estimation of the extent of ischemic lesions.

Cihangiroglu et al. [8] performed DWI at 3 T in patients with acute ischemic stroke within 24 h of the onset of neurological symptoms. On high b-value DW images, ischemic lesions were more conspicuous, and more ischemic lesions were detected compared with the usual DW imaging. Lettau and Laible [12] found high b-value DW images helpful for diagnosing hyperacute ischemic lesions in the

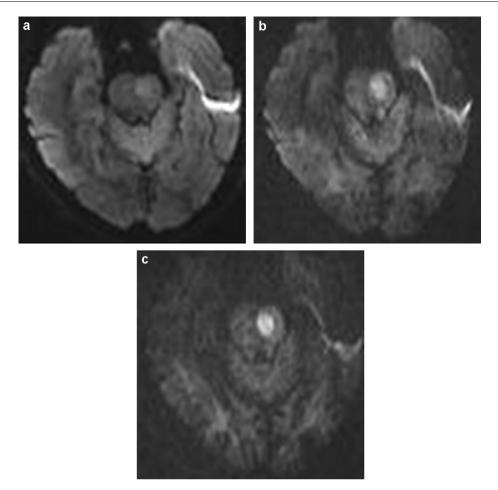


Figure 4 Hyperacute ischemic lesion in the pons. Delay from stroke onset was 160 minutes. Lesion conspicuity was higher, and lesion extent was bigger on b = 5000 (c) and b = 3000 images (b) compared to b = 1000 images (a). Lesion boundary was best shown on b = 5000 images (c).

Table 6 Mean	apparent	diffusion coef	ficient (ADC)	and mean	relative ADC i	in hyperacute	ischemic l	esions.	
Delay min	1000 ADC I	1000 ADC B	1000 rel ADC	3000 ADC I	3000 ADC B	3000 rel ADC	5000 ADC I	5000 ADC B	5000 rel ADC
0-360 n = 104	0.508	0.818	0.625	0.359	0.585	0.618	0.266	0.411	0.647
0—90 <i>n</i> = 18	0.496	0.778	0.639	0.339	0.558	0.608	0.255	0.407	0.628
91–180 <i>n</i> = 66	0.516	0.829	0.627	0.370	0.590	0.630	0.273	0.413	0.664
181—270 <i>n</i> = 12	0.481	0.851	0.568	0.345	0.612	0.576	0.253	0.419	0.604
271—360 <i>n</i> = 8	0.508	0.768	0.661	0.340	0.564	0.600	0.248	0.399	0.622

1000: b = 1000 s/mm²; 3000: b = 3000 s/mm²; 5000: b = 5000 s/mm²; ADC I: mean apparent diffusion coefficient (ADC) in infarction; ADC B: mean ADC in contralateral normal brain; rel ADC: mean relative ADC = ADC I/ADC B; Delay: delay from stroke onset; n: number of lesions.

vertebrobasilar territory. The high b values used were 2000 [7,10], 2500 [5], 3000 [5–8,12], 4000 [11] and 5000 [12]  $s/mm^2$ .

In acute ischemic stroke, false-negative findings in DWI studies are a well-known problem. Oppenheim et al. [13] performed the usual DW sequences at 1.5 T in 139 patients with ischemic stroke within 48 h of the onset of neurological symptoms and found eight (5.8%) cases of false-negative

DWI studies. On the other hand, the detection of additional acute or hyperacute ischemic lesions on high b-value DW images is a well-known benefit. Kim et al. [10] found three further hyperacute ischemic lesions in 94 patients, Cihangiroglu et al. [8] found four additional acute ischemic lesions in 27 patients, and Lettau and Laible [12] identified one further hyperacute ischemic lesion in six patients. Our present study found additional hyperacute ischemic lesions

in 32 out of 104 patients and lesions greater than 1 cm in five out of 104 patients. The most lesions were found on b = 3000 images. The number of detected lesions on high bvalue DW images was statistically significantly higher on high b-value DW images compared with standard DW sequences (Fig. 1), although the number of detected lesions greater than 1 cm was not significantly different (Table 3). Kim et al. [10] found hyperacute ischemic lesions to be more conspicuous and larger on high b-value DW images in 23 and 11 of 94 patients, respectively. Toyoda et al. [7] found that acute ischemic lesions were more distinct and more extensive with increased b values in 19 out of 32 patients, and Cihangiroglu et al. [8] found that all acute ischemic lesions were more conspicuous with increasing b values. On the high b-value images in our present study, hyperacute ischemic lesions were more conspicuous in 92 patients, larger in 99 patients and the boundaries more clearly shown in 100 of 104 patients (Figs. 2-4). Also, Toyoda et al. [7] suggested that the size of the final infarction was more predictable on high b-value images. In our study, the size of infarction was more predictable on high b-value images in 42 of 45 patients with follow-up imaging (Table 4; Figs. 2 and 3).

One potential limitation of high b-value DWI, however, is false-positive results due to the relative hyperintensity of white-matter tracts. As in most of our patients follow-up imaging was performed by CT, false-positive results could not be evaluated.

As reported by Burdette et al. [14], more artifacts were found and white-matter tracts became progressively more hyperintense with increasing b values. Another major problem of high b-value DW sequences is the reduction in SNR and CNR. Kim et al. [10] found that, with increasing b values, SNR was decreased in ischemic lesions by 17%, whereas CNR in ischemic lesions was increased by 23%. Cihangiroglu et al. [8] and Burdette and Elster [6] found SNR to be decreased by 46.9% and 41%, and CNR by 25.3% and 35%, respectively. In our present patients, SNR and CNR were decreased on b = 3000 images by 59.7% and 29.2%, respectively, and on b = 5000 images by 69.5% and 42.3%, respectively, compared with b = 1000 images (Table 5).

Delay from the time of stroke onset may be influencing SNR and CNR in acute and subacute ischemic lesions. On performing normal DW sequences at 1.5 T, Kim et al. [10] demonstrated that the values of SNR (38.7) and CNR (8.7) within hyperacute ischemic lesions were lower than the SNR (59) and CNR (34) within acute and subacute ischemic lesions reported by Burdette and Elster [6]. However, on b = 1000 images at 3 T, Cihangiroglu et al. [8] found SNR (134) and CNR (58) values within acute ischemic lesions that were lower than the SNR (216) and CNR (69) in hyperacute ischemic lesions in our present patients. In addition, in our hyperacute ischemic lesions, there were no correlations between delay of stroke onset and SNR, CNR and CR.

As SNR and CNR both increase with higher field strength, higher SNR and CNR values were found in our study on  $b = 3000 \ (87.5/49)$  and  $b = 5000 \ (66.2/40)$  images at 3 T than those reported by Kim et al. [10] and Burdette and Elster [6] on b = 1000 images at 1.5 T. Also, in our b = 5000 DW sequence, the number of excitations was increased to maintain SNR. As CR increases in acute ischemic lesions on high b-value DW sequences, lesions appear to be more hyperintense, which can result in greater conspicuity. Cihangiroglu

et al. [8] demonstrated higher CR on b = 3000 images (0.42) than on b = 1000 images (0.26). Our present study found increasing CR on high b-value DW images — specifically, 0.18 with b = 1000, 0.38 with b = 3000 and 0.42 with b = 5000 (Table 5).

As reported by Cihangiroglu et al. [8], lower ADC values were also found on high b-value DW sequences vs standard DW images. In addition, for better comparison of ADC values, the rel ADC was calculated, and was higher on b = 5000 images than on the other DW images. The differences in ADC between b = 3000 and b = 1000 images, however, were not significant. Furthermore, there was no correlation between delay from stroke onset and rel ADC (Table 6). As Sorensen et al. [15] demonstrated a significant decrease of ADC in acute ischemic gray and white matter, these different structures were not evaluated separately in our study. Although signal intensity of brain water showed non-monoexponential decay when measured over a b-factor range of up to 5000 s/mm<sup>2</sup>, clinical ADC measurement is based on the concept of monoexponential signal decay using two or three measurements of signal intensity with different b values [16]. Thus, to extract ADC, our study used two measurements with different b values (b = 0 and the maximum b value in each sequence).

As the clinical use of 3T MRI has become more widespread, more patients with acute and hyperacute ischemic stroke are now being examined at 3T. For this reason, Rosso et al. [9] compared the sensitivity and specificity of 1.5 T and 3 T DWI in detecting hyperacute ischemic stroke lesions. Using the usual DW sequences, 1.5 T MR imaging was found to be superior to 3 T: sensitivity was 99.1% at 1.5 T and 92.5% at 3 T, and specificity was 97.8% at 1.5 T and 84.1% at 3T. Higher magnetic field strength and shorter MRI delay were predictors of a false-negative diagnosis. In contrast, using the usual DW sequences and perfusion imaging in patients with hyperacute ischemic stroke, Kosior et al. [17] found that MR imaging at 3T was at least as good as and, in some ways, superior to 1.5 T. Higher SNR at 3 T compared with 1.5 T could be beneficial for DW imaging with high b values, but there are no reports comparing high b-value DW sequences in acute or hyperacute cerebral infarction at different field strengths.

Our present study used high b-value imaging at  $3\,T$  in hyperacute ischemic stroke, and found better detection of infarction and prediction of final infarct size than with standard b-value imaging in spite of an increase in imaging artifacts. On b=3000 images, more small (<1cm) hyperacute ischemic lesions were detected, probably as a result of lower SNR and CNR in b=5000 images (Table 5), whereas b=5000 images were superior in demonstrating both lesion boundaries and lesion extent (Table 4). As b=3000 images detected the most hyperacute ischemic lesions, and artifacts were prominently evident in all b=5000 images, b=3000 imaging can be recommended as the DWI modality for hyperacute ischemic strokes.

Our present study had the following limitations: in all patients, the order of the various DW sequences was the same, but resulted in differences in delay from stroke onset of about 1 to 2 min; follow-up imaging was performed in only 62 out of 104 patients; false-positive results were not evaluated; and there was no intraindividual comparison of DWI at 3 T with 1.5 T.

#### Conclusion

At 3T, high b-value imaging of hyperacute ischemic stroke suggested better detection of infarction and prediction of final infarct size than standard b-value imaging in spite of the increase in imaging artifacts.

#### Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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