Physica Medica 66 (2019) 119–123

Contents lists available at ScienceDirect

Physica Medica

journal homepage: www.elsevier.com/locate/ejmp

Technical note

Optimal *b*-values for diffusion kurtosis imaging of the liver and pancreas in MR examinations

Katarzyna Pasicz[a], Joanna Podgórska[b,c,*], Jakub Jasieniak[b], Ewa Fabiszewska[a], Witold Skrzyński[a], Agnieszka Anysz-Grodzicka[b], Andrzej Cieszanowski[b], Paweł Kukołowicz[a], Iwona Grabska[a]

[a] Medical Physics Department, The Maria Sklodowska-Curie Institute – Oncology Center, 5 Roentgena Street, Warsaw, Poland
[b] Department of Radiology I, The Maria Sklodowska-Curie Institute – Oncology Center, 5 Roentgena Street, Warsaw, Poland
[c] 2nd Department of Clinical Radiology, Medical University of Warsaw, 1a Banacha Street, Warsaw, Poland

ARTICLE INFO

Keywords:
Magnetic resonance
Diffusion kurtosis imaging

ABSTRACT

Purpose: The objective was to optimise the number of *b*-values for diffusion kurtosis imaging (DKI) of the liver and pancreas in MR examinations to ensure reliable results with the shortest possible acquisition time.
Methods: Twenty healthy volunteers underwent DKI at 3.0 T Siemens Magnetom Skyra using 7 *b*-values (b = 0, 200, 500, 750, 1000, 1500, 2000 s/mm^2). The regions of interest (ROIs) were placed in the liver (right lobe, left lobe) and pancreas (head, tail). DKI parameters (D_{app}, K_{app}) for ROIs were calculated for 7 *b*-values utilising the nonlinear least-squares (NLLS) Marquardt-Levenberg algorithm. All calculations were repeated for ten subsets of data, with the number of *b*-values reduced to 4. DKI parameters calculated for subsets were compared with parameters calculated for all 7 *b*-values.
Results: The correlation coefficient between DKI parameters calculated for 7 *b*-values and subsets ranged from 0.65 to 1.00. The coefficient of variation (CoV) of DKI parameters calculated for a group of volunteers varied from 8% to 42% and was not affected by the reduction of the *b*-values number. Only one subset of data (b = 0, 500, 1500 and 2000 s/mm^2) simultaneously met two criteria: no statistical difference ($p < 0.05$) from results obtained for 7 *b*-values and very good correlation with them.
Conclusions: DKI acquisition with 4 *b*-values (b = 0, 500, 1500 and 2000 s/mm^2), compared to DKI acquisition utilising 7 *b*-values, allowed for the reduction of acquisition time by 36%, without affecting the calculated DKI parameters.

1. Introduction

Diffusion-weighted imaging (DWI), a form of magnetic resonance imaging, is one of the most dynamically developing imaging techniques. The widest application was found in oncology, where it not only helps in tumour detection and differential diagnosis but also in assessing the effectiveness of treatment (chemotherapy and radiotherapy) and tumour recurrence. The principle of DWI is to measure the diffusion of water molecules (not only in the intracellular space but also in the intravascular space). Factors influencing the reduction of the extracellular space, such as an increased number of cells, cell oedema, neoangiogenesis, necrosis or tissue proliferation, lead to restriction of water diffusion in this space. Standard DWI relies on apparent diffusion coefficient (ADC) calculated using a monoexponential analysis, which assumes Gaussian behaviour of water diffusion [1,2]. Linear fit applied in the monoexponential model is reasonable in *b*-values to 600–1000 s/mm^2 [2]. For higher *b*-values, due to barriers that water molecules encounter in the tissue, the normal distribution does not accurately describe diffusion process [3]. The deviation from Gaussian distribution can be quantified using a parameter called “excess kurtosis” which represents the microstructure in the tissue environment. Diffusion Kurtosis Imaging (DKI) is a new, rapidly developing magnetic resonance (MR) DWI technique [4–9]. In order to capture the diffusion kurtosis effect, the acquisition of several *b*-values, including very high *b*-values (b > 1000 s/mm^2), is needed. As DKI takes into account the influence of tissue barriers (cell membranes, organelles) on diffusion, it is presumed to better reflect the actual water diffusion processes than standard DWI. Therefore, DKI gives hope for a more accurate assessment of water diffusion in tissues. Several limitations, however, hinder the use of DKI in routine practice, including lack of standardisation and long

* Corresponding author at: Department of Radiology I, The Maria Sklodowska-Curie Institute – Oncology Center, 5 Roentgena Street, 02-781 Warsaw, Poland.
E-mail address: joanna.podgorska@coi.pl (J. Podgórska).

https://doi.org/10.1016/j.ejmp.2019.09.238
Received 5 May 2019; Received in revised form 19 September 2019; Accepted 22 September 2019
Available online 07 October 2019
1120-1797/ © 2019 Associazione Italiana di Fisica Medica. Published by Elsevier Ltd. All rights reserved.

Table 1
The acquisition parameters of applied DKI sequence.

T_R (repetition time)	7400 ms
T_E (echo time)	67 ms
Number of slices	33
Slice thickness	5 mm
Echo spacing	0.54 ms
Number of gradient directions	3
Gradient Direction	3-scan-Trace weighting
Distortion correction	On
Bandwidth	2332 Hz/px
FOV Read	380 mm
FOV Phase	80.6%
Voxel size	1.4 mm × 1.4 mm × 5 mm
Partial Fourier Factor	Off
Diffusion Acquisition Scheme	Monopolar
Fat Supression Technique	SPAIR
Flip angle	90°

Table 2
The number of signal averages (NSA) for particular *b*-values acquisition.

b [s/mm^2]	NSA
0	1
200	2
500	3
750	4
1000	5
1500	7
2000	8

acquisition time (due to additional *b*-values). For clinical applications, there is a need to achieve the shortest possible scan time, which can be obtained by decreasing the number of *b*-values. Past studies have reported DKI sequences using different numbers of *b*-values. For example, in the brain, *b*-values of about 2000 s/mm^2 have been reported to be sufficient [5]. Another study reported that DKI of the liver was successful using six *b*-values and three directions of the motion-probing gradient [3]. The aim of this study was to optimise the DKI method to ensure reliable results in the shortest possible time.

2. Methods

2.1. Study population

Between January 2017 to March 2017, 20 healthy volunteers (10 male and 10 female; mean age: 39 years; age range: 25–62 years) were enrolled for this single-centre prospective study. The research protocol was approved by the local ethics committee, and written consent was obtained from all patients prior to the study.

Inclusion criteria were age ≥18 years and willingness and ability to undergo MRI and participate in the study. Exclusion criteria were age < 18 years and contraindications to MR imaging, such as pacemakers, metal implants and severe claustrophobia.

3. MR imaging protocol

MR imaging was performed with the 3.0 T unit (Magnetom Skyra, Siemens Medical Solutions, Erlangen, Germany) using explorer gradients (maximum amplitude of 45 mT/m and slew rate of 200 mT/m/ms) and phased-array multicoil system (18 elements) with spine array. The examination protocol contained the following sequences: breath-hold (BH) T_1-weighted gradient-echo (GRE) DIXON and respiratory triggered (RT) T_2-weighted half -Fourier acquisition single-shot turbo spin echo (HASTE), both performed in the axial plane. Then, DKI in the axial plane was acquired using a standard spin-echo echo-planar sequence. Selected parameters of applied DKI sequences are shown in Table 1. The Integrated Parallel Acquisition Techniques (IPAT) imaging option with a factor of 3 was used. DKI sequences were acquired with the seven *b*-values: b = 0, 200, 500, 750, 1000, 1500 and 2000 s/mm^2. In order to maintain a sufficient signal-to-noise ratio, a different number of signal averages (NSA) was chosen (NSA for each *b*-value are presented in Table 2).

3.1. Data analysis

The MR images were assessed by two radiologists respectively with 6 and 4 years of experience in body MR imaging, respectively (JP, AAG). All measurements were performed at commercial workstations (Syngovia, Siemens Medical Solution, Erlangen). For the calculation of DKI parameters (D_{app}, K_{app}), the regions of interest (ROIs) were placed on chosen slices of b = 0 s/mm^2 images, independently for each DWI sequence for the right liver lobe, left liver lobe, head of the pancreas and tail of the pancreas. Blood vessels were avoided. Then, ROIs were copied and pasted from these images to corresponding scans acquired with higher *b*-values. Each ROI was placed two times by each observer then ROI data (signal intensity and standard deviation (SD)) was exported to the text file and the values were averaged.

3.2. Parameter estimation

The DKI parameters (D_{app}, K_{app}) were calculated using the following equation (1):

$$\frac{S(b)}{S(0)} = \exp(-b \bullet D_{app} + 1/6 \bullet b^2 \bullet D_{app}^2 \bullet K_{app})$$

where S is the signal intensity as a function of b, $S(0)$ is a signal intensity at b = 0 s/mm^2, b is a factor dependent on the pulse duration and strength of the diffusion gradients, D_{app} is the corrected apparent diffusion accounting for the observed non-Gaussian behaviour, and K_{app} is a unitless parameter called apparent kurtosis coefficient.

For the calculations of DKI parameters, we applied our own program, utilising the method of the nonlinear least-squares (NLLS) Marquardt-Levenberg algorithm (function fit, Gnuplot version 5.0, patch level 4). Normalized standard deviation of the corresponding *b*-value value to signal intensity at b = 0 s/mm^2 (NSD = SD(b_i)/S(0)) was used to compute a weight for the datum, 1/(NSD)^2. The fit was judged on the basis of the sum of the squared differences or 'residuals' between

Table 3
Different sets of *b*-values used for diffusion kurtosis calculation with a presumed time of acquisition.

Subset of data	7 *b*	4 *b* (0)	4 *b* (1)	4 *b* (2)	4 *b* (3)	4 *b* (4)	4 *b* (5)	4 *b* (6)	4 *b* (7)	4 *b* (8)	4 *b* (9)
b-value [s/mm^2]	0	0	0	0	0	0	0	0	0	0	0
	200	–	–	200	200	–	–	–	–	200	200
	500	–	500	–	–	500	500	–	–	–	500
	750	–	–	–	750	750	–	750	750	–	–
	1000	1000	–	–	–	–	1000	–	1000	1000	–
	1500	1500	1500	1500	–	–	–	1500	–	–	–
	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000
Acquisition time [min:s]	11:23	8:04	7:19	6:58	5:51	6:13	6:35	7:42	5:51	5:29	5:29

Table 4
Median values and standard deviation of DKI parameters for 20 volunteers in each region of interest.

Subsets of data	7 *b*	4 *b* (0)	4 *b* (1)	4 *b* (2)	4 *b* (3)	4 *b* (4)	4 *b* (5)	4 *b* (6)	4 *b* (7)	4 *b* (8)	4 *b* (9)
Position of ROI	Median value of D_{app} [10^{-3} mm^2/s]										
RLL	1.67 ± 0.17	1.47 ± 0.15	1.64 ± 0.21	1.79 ± 0.30	1.81 ± 0.23	1.74 ± 0.16	1.64 ± 0.18	1.56 ± 0.14	1.60 ± 0.13	1.71 ± 0.23	2.13 ± 0.31
LLL	2.02 ± 0.52	1.75 ± 0.41	2.08 ± 0.53	2.29 ± 0.7	2.08 ± 0.64	2.05 ± 0.50	1.94 ± 0.51	1.93 ± 0.44	1.85 ± 0.41	1.98 ± 0.68	2.58 ± 0.72
PH	1.96 ± 0.78	1.75 ± 0.59	1.79 ± 0.89	1.99 ± 0.72	2.02 ± 0.75	1.95 ± 0.90	1.86 ± 0.86	1.91 ± 0.56	1.91 ± 0.60	2.03 ± 0.72	2.24 ± 1.06
PT	1.77 ± 0.38	1.66 ± 0.32	1.7 ± 0.44	1.75 ± 0.44	1.91 ± 0.44	1.85 ± 0.43	1.79 ± 0.41	1.73 ± 0.29	1.75 ± 0.30	1.81 ± 0.41	2.04 ± 0.57
Position of ROI	Median value of K_{app}										
RLL	0.92 ± 0.15	0.88 ± 0.18	0.91 ± 0.16	0.92 ± 0.16	0.90 ± 0.13	0.90 ± 0.14	0.9 ± 0.15	0.89 ± 0.18	0.88 ± 0.17	0.9 ± 0.14	0.87 ± 0.12
LLL	0.87 ± 0.28	0.87 ± 0.31	0.85 ± 0.29	0.81 ± 0.29	0.84 ± 0.26	0.84 ± 0.26	0.87 ± 0.27	0.86 ± 0.3	0.87 ± 0.29	0.86 ± 0.27	0.79 ± 0.21
PH	0.70 ± 0.17	0.71 ± 0.19	0.69 ± 0.17	0.70 ± 0.24	0.69 ± 0.16	0.70 ± 0.16	0.66 ± 0.18	0.73 ± 0.17	0.72 ± 0.17	0.68 ± 0.20	0.67 ± 0.16
PT	0.74 ± 0.15	0.74 ± 0.18	0.73 ± 0.16	0.76 ± 0.16	0.75 ± 0.15	0.75 ± 0.15	0.74 ± 0.16	0.75 ± 0.16	0.75 ± 0.17	0.75 ± 0.16	0.72 ± 0.14

RLL – right liver lobe, LLL – left liver lobe, PH – pancreatic head, PT – pancreatic tail.

the input data points and the function values, evaluated at the same places. The algorithm attempted to minimize WSSR (Weighted sum-of-squares residual), as the residuals were 'weighted' by the input data errors before being squared.

All calculations were systematically repeated for subsets of data, with the number of *b*-values reduced to 4 (presented in Table 3). In the first step, all combinations (i.e. 35 subsets) of 4 *b*-values were analysed. Only the subsets containing the *b* value equal 0 s/mm^2 and 2000 s/mm^2 were compared in order to find the optimal distribution of *b*-values, for which:

- determined values of DKI parameters were not significantly different compared with the initial model (7 *b*-values);
- the acquisition time was shortest.

3.3. Statistical analysis

All statistical analyses were performed in R (version 3.3.2, The R-Foundation, Austria) [10]; $p < 0.05$ was considered statistically significant. The Shapiro-Wilk test was used to test the normality of data. DKI parameters calculated for subsets were compared with the parameters calculated for all 7 *b*-values (Wilcoxon signed rank test). Results were expressed as median ± standard deviation. The repeatability of D_{app} and K_{app} calculated from particular subsets was assessed by the coefficient of variation (CoV). The relationships between DKI parameters were analysed using Spearman correlation coefficients. A correlation coefficient was considered to be very good (r = 0.75–1.00), moderate to good (r = 0.50–0.74); fair (r = 0.25–0.49), minimal (r = 0.01–0.24) or none (r < 0.01).

4. Results

The median values and standard deviation of DKI parameters of the right liver lobe, left liver lobe, pancreatic head and tail calculated for 20 volunteers using a different number of *b*-values are summarised in Table 4. In all studied regions D_{app} and K_{app} derived from all seven *b*-values did not show a significant difference in comparison with D_{app} and K_{app} derived from one subset of 4 *b*-values: 4 *b* (1) (*b* = 0, 500, 1500, 2000 s/mm^2) (Table 5). Additionally, for the pancreatic tail, no significant differences were observed for the subset of data 4 *b* (3) (*b* = 0, 200, 750, 2000 s/mm^2) and 4 *b* (4) (*b* = 0, 500, 750, 2000 s/mm^2). Moreover, no significant differences were found for the pancreatic head for the subset of data 4 *b* (2) (*b* = 0, 200, 1500, 2000 s/mm^2) .

The coefficient of variation (CoV) of DKI parameters varied from 8% to 41% (Table 6). The lowest agreement was noted for pancreatic head (D_{app} parameter) and for left lobe of the liver (K_{app} parameter).

Spearman correlation of DKI parameter for the association of 7 *b*-values with different combinations of 4 *b*-values is presented in Table 7. A very good correlation for all analysed regions (r = 0.82–1.00) was observed in all subsets of data except 4 *b* (3) and 4 *b* (6).

Results obtained for only one subset of data (4*b* (1)) simultaneously met two criteria: no statistical difference from results obtained for 7 *b*-values and very good correlation with them.

5. Discussion

By performing multiple *b*-value acquisitions and subsequent calculations of diffusion kurtosis derived parameters from several combinations of reduced to four number of *b*-values, we attempted to find an optimal combination in terms of accuracy and acquisition time. For all analysed regions, we found no significant differences between D_{app} and K_{app} calculated from seven *b*-values and one combination of four *b*-values: 4 *b* (1) (*b* = 0, 500, 1500, 2000 s/mm^2). Additionally, for pancreatic tail, no significant differences were observed for subset of *b*-values: 0, 200, 750 and 2000 s/mm^2. Other listed combinations showed

Table 5
p-Values obtained from Wilcoxon signed rank test of DKI parameters in each region of interest.

Subsets of data	7 *b* vs. 4 *b* (0)	7 *b* vs. 4 *b* (1)	7 *b* vs 4 *b* (2)	7 *b* vs. 4 *b* (3)	7 *b* vs. 4 *b* (4)	7 *b* vs. 4 *b* (5)	7 *b* vs. 4 *b* (6)	7 *b* vs. 4 *b* (7)	7 *b* vs. 4 *b* (8)	7 *b* vs. 4 *b* (9)
Position of ROI		*p*-value of D_{app}								
RLL	< 0.05	0.78	< 0.05	< 0.05	0.01	0.14	< 0.05	< 0.05	< 0.05	< 0.05
LLL	< 0.05	0.47	< 0.05	< 0.05	0.05	0.67	< 0.05	< 0.05	0.06	< 0.05
PH	< 0.05	0.76	0.87	0.07	0.25	0.52	< 0.05	< 0.05	0.70	< 0.05
PT	< 0.05	0.81	< 0.05	0.12	0.70	0.76	< 0.05	< 0.05	0.31	< 0.05
Position of ROI		*p*-value of K_{app}								
RLL	0.05	0.05	0.10	< 0.05	< 0.05	< 0.05	0.10	< 0.05	< 0.05	< 0.05
LLL	0.17	0.50	< 0.05	< 0.05	< 0.05	< 0.05	0.41	0.28	< 0.05	< 0.05
PH	0.31	0.18	0.57	< 0.05	< 0.05	< 0.05	0.50	0.12	< 0.05	< 0.05
PT	0.22	0.08	0.90	0.13	0.10	< 0.05	0.09	< 0.05	0.05	< 0.05

RLL – right liver lobe, LLL – left liver lobe, PH – pancreatic head, PT – pancreatic tail.

Table 6
The coefficient of variation (CoV in %) of DKI parameters in each region of interest.

Subsets of data	7 *b*	4 *b* (0)	4 *b* (1)	4 *b* (2)	4 *b* (3)	4 *b* (4)	4 *b* (5)	4 *b* (6)	4 *b* (7)	4 *b* (8)	4 *b* (9)
Position of ROI		CoV of D_{app} [%]									
RLL	10	10	12	16	12	9	11	9	8	13	15
LLL	25	24	25	31	29	24	25	24	22	31	27
PH	36	30	42	34	34	41	40	28	29	34	44
PT	20	19	23	22	23	23	22	17	17	22	27
Position of ROI		CoV of K_{app} [%]									
RLL	16	19	17	17	15	15	16	19	18	15	14
LLL	29	32	29	30	28	28	29	31	30	29	25
PH	24	27	24	36	22	23	26	24	24	30	25
PT	20	24	20	20	19	20	21	21	22	20	18

RLL – right liver lobe, LLL – left liver lobe, PH – pancreatic head, PT – pancreatic tail.

Table 7
Spearman correlation of DKI parameters in each region of interest for the association of 7 *b*-values with different combinations of 4 *b*-values, respectively.

Subsets of data	7 *b* vs. 4 *b* (0)	7 *b* vs. 4 *b* (1)	7 *b* vs. 4 *b* (2)	7 *b* vs. 4 *b* (3)	7 *b* vs. 4 *b* (4)	7 *b* vs. 4 *b* (5)	7 *b* vs. 4 *b* (6)	7 *b* vs. 4 *b* (7)	7 *b* vs. 4 *b* (8)	7 *b* vs. 4 *b* (9)
Position of ROI		Spearman correlation of D_{app}								
RLL	0.86	0.84	0.91	0.72	0.87	0.93	0.65	0.87	0.98	0.82
LLL	0.90	0.98	0.95	0.97	0.99	0.96	0.96	0.97	0.95	0.94
PH	0.87	0.94	0.89	0.95	0.96	0.97	0.85	0.88	0.95	0.92
PT	0.89	0.96	0.86	0.91	0.96	0.95	0.91	0.97	0.93	0.95
Position of ROI		Spearman correlation of K_{app}								
RLL	0.99	0.99	0.95	0.95	1.00	1.00	0.99	0.99	0.98	0.89
LLL	0.99	1.00	0.98	0.99	0.99	1.00	0.98	0.99	0.98	0.97
PH	0.85	0.98	0.98	0.96	0.95	0.98	0.93	0.93	0.97	0.97
PT	0.93	0.99	0.95	0.94	0.97	0.97	0.94	0.95	0.97	0.93

RLL – right liver lobe, LLL – left liver lobe, PH – pancreatic head, PT – pancreatic tail.

significant differences. Determined values of DKI parameters for the following subsets of data: 4 *b* (3), 4 *b* (4), 4 *b* (5), 4 *b* (7), 4 *b* (8) and 4 *b* (9) were significantly different compared with the initial model (seven different *b*-values) (Table 5).

In order to quantify non-Gaussian water diffusion in DKI sequence higher maximum *b*-value must be used compared to DWI sequence [12]. For MRI of the brain maximum *b*-values of about 2000 to 3000 s/mm^2 for DKI are appropriate [12]. A dataset with a large number of *b*-values, a large number of diffusion directions, high maximum *b*-values, and high SNR provides more accurate calculations of DKI parameters [11]. In some investigations of DKI of the brain 6 *b*-values ranging from 0 to 2500 s/mm^2 in increments of 500 s/mm^2 were used [5]. Other studies reported that DKI of the brain requires at least 3 *b*-values and 15 diffusion directions [12,13]. Kurtosis models for prostate were best estimated using five to seven *b* values, including 0 s/mm^2, 100 s/mm^2 and 1900–2000 s/mm^2 [14]. However, a study in DKI of the liver was successful using six *b* values and three directions of the motion-probing gradient [3]. DKI parameters can be calculated from data containing 3 *b*-values at a minimum [11].

DKI may provide more accurate information about diffusion [15,16]. Previous studies reported that DKI should be added to the routine imaging protocol for screening cancer, with the highest diagnostic accuracy of diffusion coefficients [17]. Since DKI imaging relies on the quantitative analysis of D_{app} and K_{app}, reproducibility of calculated DKI parameters remains crucial. For that reason, it is necessary to standardise the imaging protocol. In the literature, some studies reported different numbers of *b*-values and distinct diffusion gradient directions required for the DKI sequence [3,4,8,15,18–21]. Studies focused on abdominal organs using three to thirteen *b*-values. The scanning time varied from 4 min and 56 s to 20 min. Our study systematically evaluated the effect of the number of *b*-values on the results of DKI-derived parameters. For this purpose, we compared the consecutive results obtained for various combinations of *b*-values. Results obtained for seven *b*-values were taken as reference. Application of more *b*-values would prolong the examination time and could be difficult to implement in the clinical practice. However, further reduction of *b*-values to estimate DKI parameters would be insufficient to capture the non-Gaussian distribution behavior of molecular motion and therefore,

received parameters would be potentially incorrect. Furthermore, an inadequate number of applied *b*-values may negatively impact the acquired DKI maps. Insufficient signal to noise ratio (SNR) and high noise on the parametric maps may be an important barrier in the clinical application of DKI [2]. In our study, the DKI parameters were calculated from ROI data, which were placed on particular *b*-value images. This is though time-consuming. In routine practice, the parametric maps would be more useful.

The main limitations of this study were as follows. Firstly, the study group was relatively small. Secondly, the study considered only healthy patients and was limited to two organs: liver and pancreas. Third, we used a maximum *b*-value of 2000 s/mm^2. In practice, the optimum choice of maximum *b*-value, for DKI, is a compromise between precision and accuracy. In the future, combinations with maximum *b*-value of 1500 s/mm^2 should be investigated. Fourth the presented study minimalize *b*-value up to four values. Future studies should be made to further evaluate goodness of fit for different *b*-values.

In most papers (e.g. [4,8]) a non-linear fit to S(*b*) is performed without additional weighting, which can be considered as using equal weights. In this paper a different weighting was employed. It was assumed in our study, that uncertainty of *S*(*b*) value measured in ROI was equal to the standard deviation of *S*(*b*) in that ROI. Since ROIs were placed in non-uniform areas, standard deviation included not only statistical noise, but also differences in the signal caused by the presence of the anatomical structures. Information on the noise level could be obtained from another ROI, placed in a uniform area of the image. This would be, however, affected by spatial non-uniformity of the noise level [22]. A better estimate of noise could be taken from multiple acquisitions [22,23]. Unfortunately, this approach would be counterproductive, since the aim of the work was to shorten the acquisition time. Proposed weighting scheme in our study may result in higher weights for high *b*-values. This may be desirable since in DKI we are particularly interested in quantifying kurtosis effect, which is observable for high *b*-values. It should be also reminded, that NSA for large *b*-values was increased. Clinical studies on oncology patients have already been carried out in our institute to validate the proposed fitting scheme. Preliminary results are promising and will be the subject of another publication.

In conclusion, we think that the proposed optimal set of four *b*-values: 0, 500, 1500 and 2000 s/mm^2 may be applied in routine practice. Reduction of the number of applied *b*-values significantly saves time by up to 36% compared to the full study protocol without affecting DKI parameters.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejmp.2019.09.238.

References

[1] Sheng RF, Wang HQ, Yang L, Jin KP, Xie TH, Chen CZ, et al. Diffusion kurtosis imaging and diffusion-weighted imaging in assessment of liver fibrosis stage and necroinflammatory activity. Abdom Radiol (New York) 2017;42:1176–82. https://doi.org/10.1007/s00261-016-0984-4.

[2] Rosenkrantz AB, Padhani AR, Chenevert TL, Koh D-M, De Keyzer F, Taouli B, et al. Body diffusion kurtosis imaging: basic principles, applications, and considerations for clinical practice. Magn Reson Imaging 2015;42:1190–202. https://doi.org/10.1002/jmri.24985.

[3] Goshima S, Kanematsu M, Noda Y, Kondo H, Watanabe H, Bae KT. Diffusion kurtosis imaging to assess response to treatment in hypervascular hepatocellular carcinoma. AJR Am J Roentgenol 2015;204(5):W543–9. https://doi.org/10.2214/AJR.14.13235.

[4] Rosenkrantz AB, Sigmund EE, Winnick A, et al. Assessment of hepatocellular carcinoma using apparent diffusion coefficient and diffusion kurtosis indices: preliminary experience in fresh liver explants. Magn Reson Imaging 2012;30(10):1534–40. https://doi.org/10.1016/j.mri.2012.04.020.

[5] Jensen JH, Helpern JA, Ramani A, Lu H, Kaczynski K. Diffusional kurtosis imaging: the quantification of non-gaussian water diffusion by means of magnetic. Magn Reson Med 2005;53:1432–40. https://doi.org/10.1002/mrm.20508.

[6] Pentang G, Lanzman RS, Heusch P, Müller-Lutz A, Blondin D, Antoch G. Diffusion kurtosis imaging of the human kidney: a feasibility study. Magn Reson Imaging 2014;32:413–20. https://doi.org/10.1016/j.mri.2014.01.006.

[7] Wittsack HJ, Lanzman RS, Mathys C, Janssen H, Mödder U, Blondin D. Statistical evaluation of diffusion-weighted imaging of the human kidney. Magn Reson Med 2010;64:616–22. https://doi.org/10.1002/mrm.22436.

[8] Kartalis N, Manikis GC, Loizou L, Albiin N, Zöllner FG, Del Chiaro M, et al. Diffusion-weighted MR imaging of pancreatic cancer: a comparison of mono-exponential, bi-exponential and non-Gaussian kurtosis models. Eur J Radiol Open 2016;3:79–85. https://doi.org/10.1016/j.ejro.2016.04.002.

[9] Rosenkrantz AB, Sigmund EE, Winnick A, Niver BE, Spieler B, Morgan GR, et al. Assessment of hepatocellular carcinoma using apparent diffusion coefficient and diffusion kurtosis indices: preliminary experience in fresh liver explants. Magn Reson Imaging 2012;30(10):1534–40. https://doi.org/10.1016/j.mri.2012.04.020.

[10] R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.URL https://www.R-project.org/; 2016.

[11] Yokosawa S, Sasaki M, Bito Y, Ito K, Yamashita F, Goodwin J, et al. Optimization of scan parameters to reduce acquisition time for diffusion kurtosis imaging at 1.5T. Magn Reson Med Sci 2016;15(1):41–8. https://doi.org/10.2463/mrms.2014-0139.

[12] Jensen JH, Helpern JA. MRI quantification of non-Gaussian water diffusion by kurtosis analysis. NMR Biomed 2010;23(7):698–710. https://doi.org/10.1002/nbm.1518.

[13] Zhou IY, Guo Y, Igarashi T, Wang Y, Mandeville E, Chan S-T, et al. Fast diffusion kurtosis imaging (DKI) with Inherent COrrelation-based Normalization (ICON) enhances automatic segmentation of heterogeneous diffusion MRI lesion in acute stroke. NMR Biomed 2016;29:1670–7. https://doi.org/10.1002/nbm.3617.

[14] Merisaari H, Jambor I. Optimization of b-value distribution for four mathematical models of prostate cancer diffusion-weighted imaging using b values up to 2000 s/mm (2): simulation and repeatability study. Magn Reson Med 2015;73:1954–69. https://doi.org/10.1002/mrm.25310.

[15] Budjan J, Sauter EA, Zoellner FG, Lemke A, Wambsganss J, Schoenberg SO. Attenberger UI Diffusion kurtosis imaging of the liver at 3 Tesla: in vivo comparison to standard diffusion-weighted imaging. Acta Radiol 2018;59(1). https://doi.org/10.1177/0284185117706608.

[16] Huang L, Li XH, Huang SY, Zhang ZW, Yang XF, Lin JJ, et al. Diffusion kurtosis MRI Versus conventional diffusion-weighted imaging for evaluating inflammatory activity in Crohn's disease. J Magn Reson Imaging 2018;47(3):702–9. https://doi.org/10.1002/jmri.25768.

[17] Wang WT, Yang L, Yang ZX, Hu XX, Ding Y, Yan X, et al. Assessment of microvascular invasion of hepatocellular carcinoma with diffusion kurtosis imaging. Radiology 2018;286(2):571–80. https://doi.org/10.1148/radiol.2017170515.

[18] Muhi A, Ichikawa T, Motosugi U, Sano K, Matsuda M, Kitamura T, et al. High-b-value diffusion-weighted MR imaging of hepatocellular lesions: estimation of grade of malignancy of hepatocellular carcinoma. J Magn Reson Imaging 2009;30(5):1005–11. https://doi.org/10.1002/jmri.21931.

[19] Hu G, Liang W, Wu M, Chan Q, Li Y, Xu J, et al. Staging of rat liver fibrosis using monoexponential, stretched exponential and diffusion kurtosis models with diffusion weighted imaging- magnetic resonance. Oncotarget 2018;9(2):2357–66. https://doi.org/10.18632/oncotarget.23413.

[20] Shen L, Zhou G, Tang F, Lin Y, Zhou J, Lv P, et al. MR diffusion kurtosis imaging for cancer diagnosis: a meta-analysis of the diagnostic accuracy of quantitative kurtosis value and diffusion coefficient. Clin Imaging 2018;9(52):44–56. https://doi.org/10.1016/j.clinimag.2018.06.005.

[21] Maximov II, Tonoyan AS, Pronin IN. Differentiation of glioma malignancy grade using diffusion MRI. Phys Med 2017;40:24–32. https://doi.org/10.1016/j.ejmp.2017.07.002.

[22] Dietrich O, Raya JG, Reeder SB, Reiser MF, Schoenberg SO. Measurement of signal-to-noise ratios in MR images: influence of multichannel coils, parallel imaging, and reconstruction filters. J Magn Reson Imaging 2007;26:375–85. https://doi.org/10.1002/jmri.20969.

[23] Landman BA, Bazin P, Smith SA, Prince JL. Robust estimation of spatially variable noise fields. Magn Reson Med 2009;62:500–9. https://doi.org/10.1002/mrm.22013.