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Accelerated Segmented Diffusion-Weighted Prostate Imaging for Higher Resolution, Higher Geometric Fidelity and Multi-b Perfusion Estimation

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Abstract

Purpose: To improve the geometric fidelity and spatial-resolution of multi-b diffusion-weighted MRI of the prostate.

Materials and Methods: An accelerated segmented diffusion imaging sequence was developed and evaluated in 25 patients undergoing multi-parametric MRI exams of the prostate. A reduced field-of-view was acquired using an endo-rectal coil. The number of sampled diffusion weightings, or b-factors, was increased to allow estimation of tissue perfusion based on the intra-voxel incoherent motion (IVIM) model. Apparent diffusion coefficients (ADCs) measured with the proposed segmented method were compared to those obtained with conventional single-shot echo-planar imaging (EPI).

Results: Compared to single-shot EPI, the segmented method resulted in faster acquisition with two-fold improvement in spatial resolution and a greater than three-fold improvement in geometric fidelity. ADC values measured with the novel sequence demonstrated excellent agreement with those obtained from the conventional scan ($R^2=0.91$ for $b_{max}=500$ s/mm² and $R^2=0.89$ for $b_{max}=1400$ s/mm²). IVIM perfusion fraction was $4.0\pm2.7\%$ for normal peripheral zone, $6.6\pm3.6\%$ for normal transition zone and $4.4\pm2.9\%$ for suspected tumor lesions.

Conclusion: The proposed accelerated segmented prostate diffusion imaging sequence achieved improvements in both spatial resolution and geometric fidelity, along with concurrent quantification of IVIM perfusion.

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Keywords

diffusion MRI; echo planar imaging; acceleration; perfusion imaging; prostate cancer

Introduction

Prostate cancer (PC) is prevalent and affects approximately one in every nine men (1). Diffusion-weighted imaging (DWI) is an essential component of multi-parametric MRI, for the diagnosis and staging of PC (2–4). Indeed, with the PI-RADS v2 reporting and data system (5), the DWI sequence is given highest weight in the assessment of peripheral zone lesions. DWI with a high b value $\sim 1400 \text{ s/mm}^2$ has become the single most important sequence for detection of clinically significant prostate cancer (6). Single-shot echo-planar imaging (EPI), which is the most-commonly used technique for DWI, is typically associated with geometric distortions, inferior spatial resolution and low signal-to-noise ratio (SNR).

Geometric distortions result from the inherently low phase encoding bandwidth of single-shot EPI. Higher field strength and increased spatial resolution tend to aggravate the distortion problems (7). With multi-coil acquisitions, parallel imaging is typically the first choice to reduce distortion artifacts (8). For greater reductions, parallel imaging can be combined with the reversed gradient method (9, 10), or with segmentation along either the readout (11, 12) or phase encode (13) direction, and such combinations of methods have been applied to prostate diffusion imaging (14–17). An increase by a few-fold in scan time and the need for correction of motion-related phase errors are the primary downsides of segmented diffusion imaging.

Reduced field-of-view imaging is another approach to reduce distortion artifacts without parallel coil acceleration. The smaller number of k-space lines leads to greater line-to-line separation in k-space, which translates into better geometric fidelity (18, 19). Most reduced field-of-view applications in prostate have been based on selective excitation (20). The attained distortion correction has been reported to be comparable (21) to distortion correction that results with parallel imaging. For a narrower field-of-view along the phase encode direction, higher correction has been observed (22, 23) or such improved correction was exchanged for higher spatial resolution (24). Higher distortion correction also resulted in overall improved image quality (22, 23, 25, 26), which can be explained by the shorter echo-train and associated reduction in T_2^* -blurring.

A segmented acquisition method is proposed that allows for acceleration even in a single (endo-rectal) coil configuration, typically used in reduced field-of-view PC imaging. The acceleration strategy exploits the sparsity of diffusion-encoded data in the x - y - k_b - k_d space, where k_b and k_d are Fourier-transform duals of b and d , i.e., the b-factor and the diffusion direction, respectively. The approach essentially shifts some of the spatial encoding typically performed along the phase-encoding direction to k_b and k_d directions, thus reducing the number of phase-encoding steps required per image. A minimum of three diffusion encoding directions is needed to obtain a directionally invariant measure of diffusion, and the sampling of multiple b-factors permits the analysis of non-monoexponential diffusion decays invariably present in biological tissues. At high b-factors, the departure from a

monoexponential decay is attributed to the presence of different tissue compartments (27–30), while at low b-factors, such departure may be attributed to the intra-voxel incoherent motion (IVIM) of blood (30–33).

In general, the proposed acceleration method would tend to favor acquisition schemes that involve multiple b-factors and multiple diffusion encoding directions. In the present work, three orthogonal diffusion directions were sampled over a range of diffusion-weightings extending from very low to intermediate b-factors. Diffusion-weighted images were obtained for the proposed method as well as for a commercially-available method. Apparent diffusion coefficient (ADC) pixelmaps were generated and values were compared for both normal and presumed cancerous regions-of-interest (ROIs). Advantages in terms of geometric fidelity and spatial resolution were quantified, and tissue blood perfusion fractions were further estimated through IVIM analysis.

Materials and Methods

Patients

Twenty-five men, mean age 66 ± 7 years, with high suspicion for prostate cancer, scheduled to undergo multi-parametric prostate MRI exam, were recruited. Patients were scanned according to an IRB-approved protocol after providing informed consent. Review of medical records was performed in all cases to determine prior and post-MRI prostate biopsies, prior and post-MRI treatment, as well as all pathology results.

Twenty of the twenty-five patients enrolled had not received any prior therapy. Of the remaining five patients, three had received external beam radiation and androgen-deprivation therapy, one had brachytherapy seeds implanted, and one had undergone non-estrogenic herbal therapy.

MR Imaging

MR imaging was performed on a 3 Tesla Discovery MR750w system (GE Healthcare, Waukesha WI) with 40 mT/m maximum gradient strength and a maximum slew rate of 200 T/m/s. All patients underwent a standard multi-parametric MR exam (2) and an additional scan with the proposed segmented diffusion imaging sequence. The multi-parametric MRI protocol included: a 3-plane localizing scan; high-resolution anatomical 2D axial, coronal and sagittal multi-slice T₂-weighted scans at 0.6 mm isotropic in plane resolution and 3 mm slice thickness without gap; an axial spoiled gradient recalled T₁-weighted scan; axial diffusion scans at low and intermediate diffusion weighting; and a dynamic contrast-enhanced MRI (DCE-MRI) scan. For all scans, except the diffusion-weighted ones, signal reception was performed using a combination of endo-rectal coil (Medrad, Pittsburgh, PA) and pelvic phased array coils (GE Healthcare, Waukesha WI). In contrast, signal reception for the conventional and segmented diffusion scans was performed with the endo-rectal coil only.

Glucagon (Eli Lilly, Indianapolis, IN) was administered subcutaneously prior to the examination to minimize bowel peristalsis. Detailed protocol parameters (2) employed for conventional and segmented diffusion imaging are listed in Table 1. For the segmented

diffusion scan, a protocol with variable density b-factor sampling was employed (see Table 1). This protocol was designed to generate axial diffusion-weighted images at b-factors that matched the clinical exam, i.e., $b=500$ and 1400 s/mm^2 , but also further samples at b-factors suitable for multi-exponential analysis. With concurrent diffusion encoding along the three magnet principal axes, a shortening of diffusion encoding time and consequently echo-time was achieved, which in turn ensured an improved overall SNR. For the conventional diffusion scan, the built-in option for combining gradients in three orthogonal configurations was used, i.e., $[x \ y \ z]$ with relative amplitudes of $[1 \ 1 \ 0]$, $[\sqrt{0.5} \ -\sqrt{0.5} \ 1]$ and $[-\sqrt{0.5} \ \sqrt{0.5} \ 1]$. For the accelerated sequence, the optimal gradient combination $[1 \ 1 \ -0.5]$, $[1 \ -0.5 \ 1]$, $[-0.5 \ 1 \ 1]$ was used (34). The resulting diffusion encoding timings are provided in Table 1.

At low b-factors, the relative contribution of crusher gradients to the diffusion weighting can be substantial and may, if not accounted for, lead to errors in the IVIM signal analysis. For this reason, for the accelerated segmented sequence, a crusher gradient-free design was employed, where diffusion-encoding with a minimum b-factor of 12.5 s/mm^2 ensured adequate alternate signal crushing (34). Since the endo-rectal coil is a single coil configuration, multi-coil acceleration could not be applied with the conventional EPI diffusion sequence. For the segmented diffusion sequence a segmentation factor of 4 was chosen. The acceleration factor, R , equaled the segmentation factor, i.e., $R=4$. Consequently, with 128 phase encoding steps, for each diffusion encoding direction and each b-factor, 32 lines in k-space were sampled. In addition, with each shot, a fully sampled 2D navigator with a 32×32 matrix size was collected in a separate, refocused spin-echo at an echo time of 128 ms.

For each diffusion-imaging sequence, SNR was measured in a water-filled phantom placed next to the endo-rectal coil. The transversal relaxation time of the doped water was determined with a multi-spin-echo sequence. As is typically done for ADC map calculation, signal ratio maps were formed from the images obtained at respective $b_{\min}$ and $b_{\max}$. However, to avoid a skewed signal distribution, the logarithm operation was not applied. By measuring the average signal and the standard deviation within an ROI of such ratio maps, estimates of signal and noise and consequently SNR were determined.

Image Reconstruction

The raw data obtained with the experimental sequence was transferred to a work station and reconstructed according to a previously reported procedure (13). More specifically, the magnitude and phase of the concurrently acquired low-resolution 2D navigator echo was used for Tikhonov regularization and correction of motion-related phase variations, respectively. As is standard for manufacturer provided sequences, truncation artifacts in the diffusion-weighted images were mitigated with a Fermi-based apodization filter. Reconstruction times with a Matlab (Matlab Inc, Natick, MA) script running on a workstation equipped with an Intel I7-4770S (Intel, Santa Clara, CA) processor and 32 GB of memory amounted to about 30 minutes per slice.

Parameter Computation

For the conventional single-shot diffusion scans, ADC maps were reconstructed by the software provided by the scanner vendor. For the accelerated segmented diffusion scans, the signals measured at $b=12.5$ (4 excitations), 500 (4 excitations) and 1400 s/mm^2 (8 excitations) were complex averaged for each of the three orthogonal directions acquired. Subsequently, after geometric averaging of the three directionally dependent magnitude signals for each b-factor, ADC maps were calculated by pixel-wise computation of the slope of the logarithmized signals at $b=12.5$ and 500 s/mm^2 , $b=12.5$ and 1400 s/mm^2 respectively. The IVIM analysis was performed for the aggregate signal within regions of interest (ROIs). An estimate of the perfusion fraction was obtained by performing separate mono-exponential non-linear least-square fits for the perfusion-signal comprising b-factor range 12.5–150 s/mm^2 (6 b-factors) and for the largely perfusion signal-free b-factor range 150–500 s/mm^2 (5 b-factors). The latter fit resulted in the perfusion-free diffusion component, also known as tissue diffusivity D . The perfusion fraction f_p was obtained by calculating the relative difference $(S_{0(0 \leq b \leq 150)} - S_{0(150 \leq b \leq 500)})/S_{0(0 \leq b \leq 150)}$ with the signal values that resulted at $b=0$. Finally, for visual analysis, diffusion-weighted images were prepared for $b=500 \text{ s/mm}^2$ and 1400 s/mm^2 .

Setting the Regularization Parameter λ

The regularization parameter λ employed in the reconstruction (13) was varied over a wide range, from 0.001 to 0.1. The effects of these variations on the measured ADC values were evaluated, and a single value was selected for λ . This optimization was meant as a one-time exercise, and the selected value was used to reconstruct all slices from all patients in the present study. More specifically, the effect of λ on the correlation between ADC values produced by the conventional single-shot EPI sequence and the proposed approach were considered here, as measured for b settings of 500 and 1400 s/mm^2 . In general, strong regularization with high λ values leads to advantages such as strong artifact suppression and higher achievable acceleration, but λ settings that are too high could lead to errors in the diffusion-weighted images that would produce deviations in measured ADC values. Varying λ over a large range, a λ value was sought that was as large as possible, without visibly degrading the measured ADC values.

Region of Interest Selection and Assessment of Prostate Dimensions

All MR examinations were performed as part of the patient's clinical care and prospectively interpreted and reported. Index lesions deemed the most suspicious lesion in terms of size or potential aggressiveness were identified by a radiologist with three years post-fellowship experience in abdominal imaging and delineated on the conventional single-shot and accelerated multi-shot diffusion-weighted images. The radiologist also outlined ROIs of normal appearing peripheral zone (PZ) and transition zone (TZ). Prostate dimensions along the anterior-posterior direction, i.e., the direction coinciding with the distortion-prone phase encoding direction, were measured on a single slice at mid-gland level on high-resolution anatomical T₂-weighted images, as well as on matching $b=0$ images of the conventional single-shot and segmented diffusion scans.

Statistical Analysis

The effect of regularization strength on the agreement between conventional single-shot and accelerated segmented ADC values measured within ROIs was evaluated with linear regression analysis. Furthermore, Bland-Altman plots were generated to visualize the geometric agreement between methods. The improvement in geometric fidelity F was assessed by using the prostate dimension d on high-resolution anatomical T_2 -weighted images as reference:

$$F = \frac{d_{\text{conventional}} - d_{T2\text{-weighted}}}{d_{\text{segmented}} - d_{T2\text{-weighted}}}$$

Student's t-tests were performed to compare between mean ADC values and between mean ROI perfusion parameters and differences were considered significant for $P < 0.05$. To evaluate each parameter's potential to differentiate normal from cancerous tissue, the receiver operating characteristic (ROC) curve was obtained and the area under the curve (AUC) was calculated. The standard deviation of the AUC was estimated according to the method of Hanley and McNeil (35). Additionally, for each parameter, a two sided t-test was performed to test for a significant difference between the two groups sorted according to a combined Gleason score of below 7 or 7 and greater.

Results

Of the twenty-five patients enrolled in this study, seventeen had focal suspicious prostate lesions. Fifteen lesions were located in the PZ and four lesions in the TZ, i.e., two of the patients had focal lesions in both zones. Ten of the nineteen suspicious lesions detected (10/19) had a Prostate Imaging Reporting and Data System (PI-RADS v2) score of 5 and another nine (9/19) a PI-RADS score of 4. Average Prostate Specific Antigen (PSA) levels measured in 23 of the 25 patients were 19.1 ± 51.9 ng/mL (range 0.36–255 ng/mL). TRUS biopsies were obtained in 23 of the 25 patients. Biopsy was negative for one patient who presented no index lesion. In the other patients, Gleason grades of 3+3 ($n=7$), 3+4 ($n=7$), 4+3 ($n=1$), 7 ($n=2$), 4+4 ($n=1$), 4+5 ($n=2$), and 9 ($n=2$) were determined. In two of three patients who received MR-guided follow-up biopsies, the Gleason grade was updated from 7 to 4+5 and from 3+3 to 3+4, respectively. Of the patients without a suspicious focal lesion ($n=8$), one (1/8) was not biopsied, one (1/8) had a negative biopsy, (3/8) had a Gleason grade of 3+3, one (1/8) a grade of 3+4, and two (2/8) a grade of 9. The absence of an index lesion in one of the patients with Gleason grade 9 was due to prior therapy and since normal PZ and TZ ROIs also could not be defined, the data of this patient was not considered in the analysis.

The improvement in geometric fidelity with the accelerated segmented sequence is presented in Fig. 2. The average geometric fidelity improvement factor F at mid-gland level equalled 3.2 ± 1.1 . Examples of diffusion-weighted images and ADC maps of four patients with PI-RADS score 5 lesions are shown in Figure 3.

The effect of the regularization scaling parameter λ on the agreement between the ADC of conventional single-shot scans and accelerated segmented scans is shown in Fig. 4. Based on results such as presented in Fig. 4, a value of $\lambda=0.01$ was considered near optimal, and this setting was subsequently employed to reconstruct all slices from all patients. The slope for the $b = 1400 \text{ s/mm}^2$ case in Fig. 4a proved particularly important for this determination, as it shows $\lambda=0.01$ to be about as large a λ setting that can be chosen without sizably affecting correlation results. Image quality, on the other hand, was not visibly affected over the entire range of λ values covered here.

Scatter plots of conventional single-shot versus accelerated segmented ADC values measured in normal PZ, normal TZ, and lesion ROIs and resulting regression lines, for $\lambda=0.01$ and $b_{\max}=500$ and 1400 s/mm^2 are presented in Figure 5. Average ADC within normal PZ, normal TZ, and index lesion ROIs measured with the conventional single-shot and the segmented sequence at $b_{\max}=500$ and 1400 s/mm^2 are reported in Table 2.

Average IVIM perfusion fractions as well as the perfusion-free diffusion coefficients, obtained by fitting the b-factor sub-range $150\text{--}500 \text{ s/mm}^2$, for normal PZ, normal TZ, and lesion ROIs are also reported in Table 2. Figure 6 shows examples of the sub-range fitting that was used to determine the perfusion fraction and scatter plots of all perfusion fractions and perfusion-free diffusion coefficients measured.

The measured T_2 relaxation time of the water phantom was 70.7 ms. Signal-to-noise ratio was determined inside a rectangular ROI 436 mm^2 in size. For $b_{\max}=500 \text{ s/mm}^2$ the resulting SNR was 57 for the conventional sequence and 78 for the segmented sequence. For $b_{\max}=1400 \text{ s/mm}^2$ the resulting SNR was 40 for the conventional sequence and 17 for the segmented sequence.

Discussion

Diffusion images provide the most critical information for cancer diagnosis in a multiparametric prostate exam, yet conventional diffusion image quality in comparison to typical T_1 and T_2 -weighted images is clearly inferior. Therefore, perfecting geometric fidelity and spatial resolution of the diffusion scan promises to be of great diagnostic value, but also very desirable for more accurate biopsy and intervention guidance (15, 36). The present study demonstrates that a segmented acquisition can improve geometric fidelity and at the same time enhance spatial resolution of the diffusion imaging sequence in a multiparametric prostate exam. The integration of acceleration based on the reconstruction of sparsely sampled data shows that segmentation does not necessarily have to be traded for a hefty increase in scan time or considerable sacrifice in SNR.

For the purpose of superior SNR, prostate imaging may be performed with an endo-rectal radio-frequency coil. The use of a single coil proves essentially incompatible with parallel imaging. Even though the approach employed here can further incorporate parallel imaging (13), it can also function without it, and as such it can operate even in single-coil scenarios. For this reason, it may prove especially useful in combination with endo-rectal coils, because alternative methods that may depend on parallel imaging would be unavailable in

such cases. While the proposed approach is not limited to endo-rectal coils in any way, its affinity and potential usefulness for use with these coils was recognized and explored here.

With the implemented four-fold segmentation ($R=4$), the theoretically expected improvement in geometric fidelity would equal 4. However, some of the potential improvement in geometric fidelity was traded here for improved spatial resolution instead: improved resolution led to slightly longer echoes, and slightly larger echo spacing, which in turn reduced the gains achieved in geometric fidelity. In this configuration, the theoretically expected improvement in geometric fidelity was 3.3-fold (i.e., 4.4 kHz vs 1.3 kHz phase encode bandwidth), in good agreement with the average value of 3.2-fold that was measured at mid-gland level. The present method does allow for higher segmentation, but at a cost in scan time, noise amplification, or both (37). The proposed method affords much flexibility in terms of b - d coverage. One constraint in the present realization was to generate data that could be directly compared to the existing clinical protocol at our institution, i.e., three orthogonal diffusion encoding directions at $b_{\max}$ of 500 and 1400 s/mm². The SNR estimation with a water phantom indicated a superior SNR for the segmented sequence at $b_{\max}=500$ s/mm² and inferior SNR at $b_{\max}=1400$ s/mm². The SNR performance should be viewed in the context of total scan time, i.e., 6 min 4 sec for the experimental segmented sequence and 9 min 3 sec for the aggregate scan time of the clinical sequences. One novelty, compared to the previously published applications of this segmented diffusion imaging method in brain (13, 38), is the non-uniform sampling along b . This allows for higher image quality at the clinically most relevant b -factors of 500 and 1400 s/mm², while additional data is sampled to reveal the deviation from monoexponential diffusion signal decay. For the present comparison, in agreement with the clinical protocol, the ADC was computed with the slope of the logarithmized signals at $b_{\min}$ and $b_{\max}$, meanwhile non-linear least square fitting of all available values along b might have resulted in superior ADC estimation.

The clinical protocol acquired diffusion data for the computation of ADC with $b_{\max}$ 500 and 1400 s/mm² in separate scans with different echo time, meanwhile with the experimental sequence, all data was acquired in a single scan with identical echo time. Thus, some contrast disparity in the $b=500$ s/mm² images may be attributed to differences in T_2 -weighting. The differences in diffusion time, however, are probably too small to have any significant impact on ADC (39, 40). Obviously, a clinical protocol that acquires $b=0$, 500, and 1400 s/mm² at equal diffusion and echo time in a single scan would also have been practical. For a typical prostate cancer tissue T_2 -decay time of 85 ms (41) the increase in echo time from 64 to 79 ms (see Table 1) would have resulted in a minor, 16% loss of signal. Due to the longer repetition time, the aggregate scan time of the clinical protocol would have increased from slightly over 9 min (see Table 1) to 10 min. Such long time for a single scan would imply increased motion sensitivity.

Even without the additional acquisition of low b -factors, the experimental segmented sequence exceeds the conventional sequence in terms of geometric fidelity, spatial resolution, and scan efficiency. The integrated acquisition of low b -factors permitted an IVIM-based estimation of the perfusion fraction and the perfusion-free tissue diffusion component. The perfusion-free diffusion component, i.e., the tissue diffusivity D , holds the potential for better pathology differentiation (42, 43). Estimation of the small perfusion

fraction was hampered by fitting instability and succeeded only by two-step fitting of the cumulative signal within the ROIs. In view of the prevailing SNR, particularly of the highly under-sampled b-factors 25 to 400 s/mm², and perfusion fractions on the order of a few per cent, this is no surprise. Perfusion parameters are in reasonably good agreement with the limited available literature (31–34). The fast diffusion coefficient D^* , which tends to exhibit notoriously high variability, was not computed.

The necessary adjustment of the scaling of the regularization parameter adds to the complexity of the accelerated sequence protocol implementation. The analysis of over two magnitudes of variation of the scaling parameter revealed a relatively benign behaviour in terms of ADC agreement with conventional diffusion imaging. This appears also to agree with the range, where image quality tends to be superior, i.e., no presence of either excessive noise suppression or amplification. Meanwhile, initial analysis with limited data over an even wider range revealed a clear departure of ADC agreement for exceedingly low or high scaling values. A minor concern, that has been reported previously (38), is that the navigator that is used for regularization does not share the same echo time and thus T_2 -weighting with the actual data. In a multi-coil scenario, this limitation can be avoided with MUSE-style self-navigation, which, however, would discourage segmentation beyond 4 (38, 44).

The present method uses complex signal averaging. Typically, with diffusion imaging, motion-related shot-to-shot phase fluctuations preclude complex signal averaging and magnitude averaging is used instead. Complex signal averaging and thus bias-free improvement of SNR can be performed if the data is phase-corrected (45). The present method employs a navigator-based correction of motion-related phase variations.

A limitation of the present implementation is the presence of ghosting artifacts. With the selected field of view and segmentation factor, the high signal within the rectal wall next to the peripheral zone tends to produce a ghosting artifact close to the ventral surface of the prostate. In this area the coil sensitivity is low and the artifact is therefore much more prominent. Due to the asymmetric design of the endo-rectal coil, ghosting of the posterior rectal wall was not evident. A slight increase of the field of view or a reduction of the segmentation factor could be employed to shift the artifact more consistently outside the prostate. Swapping of phase and frequency encoding direction might also result in better control of ghosting, but would place residual distortions orthogonal to the symmetry axis of the prostate anatomy. In the present approach, it was observed that complex averaging of the data after phase correction with the navigator phase quite effectively but not completely suppressed ghosting. It should be noted that the conventional single-shot EPI diffusion sequence also showed ghosting artifacts. However, these were mostly observed in diagnostically irrelevant low signal areas surrounding the prostate.

Based on ADC, the present evaluation revealed similar tissue differentiation ability for the clinical and experimental sequence. AUCs were slightly higher for the segmented diffusion imaging sequence. This improvement reached statistical difference. There was also an improvement in the ability to predict low vs high Gleason score. A limitation is that in some patients only blind TRUS biopsies were available and, therefore, it cannot always be expected that the suspected tumor area reflects the biopsied area. This simple assessment, in

a limited group of patients, does not disclose the true diagnostic value of the experimental segmented sequence. It can be assumed, however, that improvements in terms of geometric fidelity, spatial resolution, SNR, and information content that come at no or reduced cost in scan time are diagnostically advantageous. The SNR measured in a water phantom is only an estimate and actual SNR will depend on tissue properties and location. Nevertheless, since the noise estimation was performed for all sequences with a consistent experimental setup at the same location, the SNR estimation is helpful to assess the relative performance of the different sequences.

In conclusion, a novel segmented accelerated diffusion imaging sequence, that permits faster scanning than a comparable conventional scan protocol, was applied to reduced field of view scanning with a single-coil in prostate cancer patients. The resulting diffusion-weighted images proved to be superior to images obtained with the conventional single-shot EPI sequence not only in terms of higher geometric fidelity, but also in terms of higher spatial-resolution and scan efficiency. Ghosting artifacts present in the images obtained with the novel sequence posed a relatively minor problem. Imaging of multiple b-factors provided added diagnostic value.

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Figure 1:

(a) Appearance of conventionally acquired data in x - y - k_b - k_d space (b) Appearance of data obtained with an accelerated, i.e., partially sampled acquisition in x - y - k_b - k_d space before applying regularized reconstruction. (c) Pulse sequence diagram. (d) Segmented multi-shot acquisition order for multiple directions. Background shades represent the three diffusion encoding directions: light-gray = direction 1, medium-gray = direction 2, dark-gray = direction 3. Circles indicate the sampling pattern, where a filled circle means sampled and an empty circle not sampled.

Figure 2:

(a-f) T₂-weighted anatomical and b=0 images obtained with conventional single-shot and segmented DWI of the prostate. Sagittal views, reformatted from the axial slices, are shown in images a-c and the original axial scan plane at mid-gland level in images d-f. The boundary between the prostate and the rectal wall that results from the largely undistorted T₂-weighted anatomical scan is indicated by a white dotted line overlaid on images a-c. The corresponding boundary for the b=0 images obtained with conventional single-shot and segmented DWI is indicated by a yellow line. Considerable reduction of distortion for the accelerated multi-shot sequence is evident by the better match between the yellow and white line. Similarly, on the axial views d-f, the prostate and the rectum geometry resulting from the T₂-weighted anatomical scan is indicated by overlaid white lines and for the b=0 images the rectum outline is represented by a yellow line. The improved match of organ geometry for the accelerated multi-shot axial image is obvious. (g) Bland-Altman plots of the extent of geometric distortions in the b=0 images of the diffusion weighted acquisition relative to T₂-weighted anatomical images, at mid-gland level for all subjects. Solid line shows mean difference and the dotted lines above and below the 95% confidence intervals at ± 1.96 standard deviations. The ratio of the length differences, i.e., the geometric fidelity improvement factor, amounted to 3.2 ± 1.1 .

Figure 3:

Examples of focal lesions from four patients with clinically significant prostate cancer: Shown are 76 mm x 76 mm sub-images of conventional single-shot (DWI_C) and segmented (DWI_S) diffusion-weighted images obtained at $b_{max}=500$ s/mm² and $b_{max}=1400$ s/mm² and corresponding ADC maps (ADC_C and ADC_S). The lower ADC that results with higher diffusion-weighting can readily be appreciated both on the conventional and the segmented diffusion-weighted images.

Figure 4:

Effect of regularization on the agreement between conventional single-shot ADC and segmented ADC values. The dependence of (a) Slope, (b) Offset, and (c) Coefficient of determination R^2 that result from the linear regression analysis are shown as a function of the regularization parameter λ .

Figure 5:

Agreement between conventional single-shot and accelerated multi-shot ADC values for all patients and ROIs for (a) $b_{\max}=500 \text{ s/mm}^2$ and (b) $b_{\max}=1400 \text{ s/mm}^2$. For each method the resulting standard deviation within each ROI is indicated by gray lines. The bottom figures show corresponding Bland-Altman plots for (c) $b_{\max}=500 \text{ s/mm}^2$ and (d) $b_{\max}=1400 \text{ s/mm}^2$. Solid line shows mean difference and the dotted lines above and below the 95% confidence intervals at ± 1.96 standard deviations.

Figure 6:

(a) Example of sub-range fits to the signal vs. b-factor data of a tumor ROI. The continuous and dotted lines extend over the respective fitted b-factor range, i.e. 12.5–150 s/mm² and 150–500 s/mm². (b) Example of sub-range fits to the signal vs. b-factor data of a normal PZ ROI. In this case the two mono-exponential fits almost overlap and the resulting perfusion fraction estimate is very small. (c) Perfusion fraction estimates from all patients in tumor (o), normal PZ (x) and normal TZ (+) ROIs. (d) Perfusion-free diffusion estimates from all patients in tumor (o), normal PZ (x) and normal TZ (+) ROIs.

Table 1:

Conventional single-shot and segmented DWI parameters

	Conventional Axial Single-Shot DWI ($b_{\max} = 500 \text{ s/mm}^2$)	Conventional Axial Single-Shot DWI ($b_{\max} = 1400 \text{ s/mm}^2$)	Axial Segmented DWI
Spatial Resolution	1.9 mm $\times$ 1.9 mm	1.9 mm $\times$ 1.9 mm	1.4 mm $\times$ 1.4 mm
Slice Thickness + Gap	4 mm + 0 mm	4 mm + 0 mm	4 mm + 0 mm
Matrix (Read $\times$ Phase)	96 $\times$ 77	96 $\times$ 77	128 $\times$ 128
Segmentation / Acceleration	No	No	4 / 4
Partial Fourier	71%	71%	no, i.e., 100%
FOV	180 mm $\times$ 144 mm	180 mm $\times$ 144 mm	180 mm $\times$ 180 mm
Number of Slices / Groups	22 / 1	22 / 1	22 / 1
BW (Read / Phase)	167 kHz / 1.3 kHz	167 kHz / 1.3 kHz	167 kHz / 4.4 kHz
Encoding Directions	3, orthogonal	3, orthogonal	3, orthogonal
Number of b-Factors	2	2	11
b-Factors (Excitations)	0 (1) and 500 (8) s/mm ²	0 (1) and 1400 (16) s/mm ²	12.5 (4), 25 (1), 50 (1), 75 (1), 100 (1), 150 (1), 200 (1), 300 (1), 400 (1), 500 (4) and 1400 (8) s/mm ²
Diffusion timing, δ , τ , $-\delta/3$	13.6 / 27.8 / 23.2	20.7 / 34.9 / 28.0	18.3 / 31.6 / 25.4
TE / TR	64 ms / 6350 ms	79 ms / 7550 ms	78 ms / 5050 ms
Scan Time	2 min 45 s	6 min 18 s	6 min 04 s

Table 2:

Average conventional single-shot (ADC_C), accelerated segmented (ADC_S) ADC values obtained at $b_{max}=500$ s/mm² and $b_{max}=1400$ s/mm², as well as perfusion-free diffusion coefficient and corresponding perfusion fraction obtained from multi-b IVIM analysis. The last two columns provide AUC values for the ability of each parameter to differentiate normal from suspected lesion and low from high Gleason score, respectively. Mean and standard deviations are shown across all patients. The level of significance for the difference between normal PZ and TZ ROI values is indicated with stars. For PZ and TZ lesions, when compared to respective normal tissue values, the significance of the observed differences was $P<0.0001$ for all diffusion measurements. For the corresponding perfusion fraction comparison, significance was not reached. Statistical significance of the AUC (normal vs lesion) difference between conventional vs segmented acquisition was $P=0.0001$ for $b_{max}=500$ s/mm² and $P<0.05$ for $b_{max}=1400$ s/mm².

	Normal PZ (n=24)	Normal TZ (n=23)	PZ Lesion (n=15)	TZ Lesion (n=4)	All Lesions (n=19)	AUC	AUC Gleason 6 vs 7 (n ₆ =7, n ₇ =15)
ADC_C ($\mu m^2/ms$) ($b_{max}=500$ s/mm ²)	1.82 +/- 0.29	1.56 +/- 0.20 **	1.04 +/- 0.29	0.88 +/- 0.04	1.00 +/- 0.27	0.96+/-0.03	0.81+/-0.11
ADC_S ($\mu m^2/ms$) ($b_{max}=500$ s/mm ²)	2.11 +/- 0.31	1.89 +/- 0.20 *	1.21 +/- 0.27	1.14 +/- 0.23	1.19 +/- 0.25	0.99+/-0.01	0.79+/-0.11
ADC_C ($\mu m^2/ms$) ($b_{max}=1400$ s/mm ²)	1.54 +/- 0.25	1.29 +/- 0.14 **	0.84 +/- 0.21	0.75 +/- 0.05	0.82 +/- 0.19	0.99+/-0.02	0.83+/-0.11
ADC_S ($\mu m^2/ms$) ($b_{max}=1400$ s/mm ²)	1.65 +/- 0.27	1.46 +/- 0.18 *	0.92 +/- 0.20	0.93 +/- 0.10	0.93 +/- 0.18	1.00+/-0.01	0.89+/-0.09
Perfusion-Free Diffusion Coefficient ($\mu m^2/ms$)	2.01 +/- 0.31	1.74 +/- 0.19 **	1.12 +/- 0.28	1.06 +/- 0.18	1.11 +/- 0.26	0.99+/-0.02	0.81+/-0.11
Perfusion Fraction (%)	4.0 +/- 2.7	6.6 +/- 3.6 *	4.3 +/- 2.8	4.8 +/- 3.7	4.4 +/- 2.9	0.57+/-0.08	0.66+/-0.13

* $P<0.01$,

** $P<0.001$ (comparison normal PZ vs normal TZ)