Published in final edited form as:

Magn Reson Med. 2018 March ; 79(3): 1586–1594. doi:10.1002/mrm.26816.

Performance of a fast and high resolution multi-echo spin echo sequence for prostate T_2 mapping across multiple systems

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Abstract

Purpose—To evaluate the performance of a multi-echo spin echo sequence with k-t undersampling scheme (k-t T_2) in prostate cancer.

Methods—Phantom experiments were performed at five systems to estimate the bias, short-term repeatability, and reproducibility across all systems expressed with the within-subject coefficient of variation (wCV). Monthly measurements were performed on two systems for long-term repeatability estimation. To evaluate clinical repeatability, two T_2 maps (voxel size $0.8 \times 0.8 \times 3$ mm³; 5 min) were acquired at separate visits on one system for thirteen prostate cancer patients. Repeatability was assessed per patient in relation to spatial resolution. T_2 values were compared for tumor, peripheral zone, and transition zone.

Results—Phantom measurements showed a small bias (median = -0.9 ms) and short-term repeatability (median wCV = 0.5%). Long-term repeatability was 0.9% and 1.1% and reproducibility between systems was 1.7%. The median bias observed in patients was -1.1 ms. At voxel-level the median wCV was 15%, dropping to 4% for structures of 0.5 cm³. The median tumor T_2 values (79 ms) were significantly lower ($p < 0.001$) than in the peripheral zone (149 ms), but overlapped with the transition zone (91 ms).

Conclusion—Reproducible T_2 mapping of the prostate is feasible with good spatial resolution in a clinically reasonable scan time, allowing reliable measurement of T_2 in structures as small as 0.5 cm³.

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Keywords

T₂ mapping; prostate cancer imaging; quantitative; repeatability; multi-center; k-space undersampling

Introduction

T₂-weighted (T_{2w}) MRI is an important image modality for detection and staging of prostate cancer (1–3). However, the images are less suitable for quantitative analysis, since the grey value intensities of these images can only be interpreted at a qualitative level. The values depend on the exact protocol settings and the platform and coils being used. For example, changes in acquisition parameters result in changes in contrast in T_{2w} images. A quantitative approach, like T₂ mapping, is needed if multiple scans of a patient are to be compared, such as during active surveillance or treatment response monitoring, or in multi-center clinical trials. So far, the added value of T₂ mapping for prostate imaging has been shown for tumor detection (4–8) and treatment monitoring (9).

Until recently, the application of T₂ mapping has been limited by the long acquisition time necessary for accurate measurement of T₂ values. This usually resulted in limited spatial coverage and resolution. In the last years, T₂ acquisition schemes have been improved making T₂ mapping feasible in clinical practice (6,10–12). For example, the standard multi-echo spin echo (ME-SE) sequence can be accelerated with a reduced field-of-view method using tilted angles (6) or a k-t undersampling scheme in which acceleration is obtained by skipping lines in k-space interleaved across multiple echoes (13). Previous studies have shown that the latter yields accurate and artifact free prostate T₂ maps with voxel sizes close to the standard T_{2w} images (11,14).

A key requirement for a T₂ mapping sequence to be applicable in a longitudinal or multi-center setting is reliable performance across multiple visits and systems. For the k-t T₂ technique the repeatability in patients was found to be a few percent by acquiring two T₂ maps within the same MRI exam on a single system (11). Bias, short-term and long-term repeatability as well as the reproducibility across multiple were not investigated. Therefore, the purpose of this study is to assess the performance of k-t T₂ maps for in prostate cancer. An important aspect of repeatability is its close relation to the size of the regions of interest (ROIs) that are being investigated. Typically, repeatability increases for increasing ROI size, because averaging values over a larger region reduces the effect of image noise (15). Therefore, it is important to estimate repeatability in relation to the smallest ROI size for which changes in T₂ values can be detected with the desired reliability. We investigated these aspects with multi-system phantom experiments as well as test-retest data of prostate cancer patients on a single system.

Methods

Study Design

To evaluate the performance of the k-t T₂ sequence, for multi-center and longitudinal trials we investigated the following aspects:

1. Bias with respect to reference sequence to determine whether the acceleration of the k-t T_2 sequence affected the estimation of T_2 values ($T_{2,k-t}$). To this end, we compared the values to those of a ME-SE sequence without any acceleration ($T_{2,ref}$). Since we allowed for system specific optimizations in the sequence, we estimated the bias on five different systems. For this question phantom measurements were appropriate, as it allowed us to investigate the effect of the sequence itself.
2. Short-term repeatability measurements were done to verify if the bias was stable. In case variations within one exam without changing the set-up would be large, this would limit the reliability of the measurements. Therefore, we repeated the k-t T_2 measurements ten times within one scanning session. Measurements were performed with phantoms to prevent influence of motion and changes in tissue. Short-term repeatability was also assessed on multiple systems to verify if stability of the measurements was dependent on protocol differences.
3. Reproducibility of the k-t T_2 sequence over multiple systems to investigate the variations between systems and optimized sequences. This aspect is especially important for multi-center studies. For this purpose, we used k-t T_2 measurements mentioned in (1) and (2) on five systems.
4. Long-term repeatability: we assessed the stability of T_2 measurements at multiple visits. By using a phantom we investigated the effects of the sequence, scanner variations, minor software upgrades, and phantom set-up, excluding any tissue variations that might happen in patients.
5. Clinical repeatability. The phantom measurements do not inform on the spatial detail for which T_2 values can be measured reliably in a clinical setting. That is influenced by a combination of image noise, day-to-day variations in patient set-up in the scanner, and day to day variations in prostate tissue. Also registration errors between exams may reduce the observed reproducibility. The most realistic method to obtain an estimate for the combination of these factors, that determine the usefulness in clinical practice, is a test-retest study in patients.

Phantom Experiments

Phantom experiments were performed on five different systems from a single vendor (Philips Healthcare, Best, the Netherlands). We used the Eurospin TO5 phantom (Diagnostic Sonar, Livingston, Scotland), which consists of a Perspex cylinder with twelve openings to insert gel samples. Eighteen agarose gel samples doped with different amounts of Gadolinium are available. Twelve samples were chosen including the expected range of T_2 values of healthy and tumorous prostate tissue (49 – 212 ms at 296 K for 3T). The same copy of the phantom was used for systems A, B, D, and E, whereas a different copy was used for system C.

The k-t T_2 sequence as proposed in (14) was optimized for each system separately. The k-t T_2 technique uses undersampling of k-space for each echo except for the center of k-space for calibration purposes. The undersampling strategy is based on the assumption that k-space

information between consecutive echoes in a ME-SE sequence is highly correlated through an exponential decay (13). The position of the acquired k-lines is shifted between consecutive echoes to get better coverage of k-space over multiple echoes. The missing k-lines are then interpolated from neighboring echoes taking a mono-exponential decay for the signal intensity into account. This undersampling scheme is combined with partial-Fourier acquisition and parallel imaging to further reduce the scan time (14). Criteria for system specific optimizations were a similar dynamic range (~ 200 ms) and the use of same type of slice selective refocusing pulses. For a minimal echo time (TE) the system uses a truncated sinc pulse without side lobes. For longer TE values sinc pulses with two side lobes are used. Preliminary experiments on system A showed a substantial difference ($6.4 \pm 1.1\%$) between T_2 values estimated from ME-SE scans between those two types of refocusing pulses. The minimal echo time (TE) that results in a sinc pulse with side lobes, varies between systems depending on the gradient performance. Based on these criteria, we chose the settings for repetition time, echo spacing, number of echoes, and maximum allowed B_1 transmit field (Table 1). Other settings were identical: field of view = $256 \times 256 \times 2$ mm³, voxel size = $2 \times 2 \times 2$ mm³, partial-Fourier factor = 0.625, parallel imaging factor = 2, k-t T_2 reduction factor = 4. Furthermore, the first echo was discarded during the acquisition since the signal intensity tends to be lower than for subsequent echoes, as, in contrast to later echoes, it is unaffected by stimulated echoes (8,16).

T_2 values were determined for ROIs centered in each tube (diameter 1.2 cm) by fitting a monoexponential decay function to the average decay curve with a nonlinear least-squares method. The temperature was measured before and after each scan to correct estimated T_2 values to a reference of 296 K using the manufacturer's phantom specifications indicating an average change of 2 ms in T_2 value per degree Celsius. The k-t T_2 measurements were repeated ten times without repositioning the phantom, whereas the reference sequence was repeated three times. Long-term repeatability was determined by repeating k-t T_2 scans monthly for one year on two systems (A and B).

Patient Study

Thirteen patients with biopsy-proven prostate cancer (median 67, range 59 – 72 years) underwent a multi-parametric (mp-) MRI exam twice (average time interval 21 ± 9 days) prior to prostatectomy. Time of biopsy taken prior to MRI and the first MRI session was 4 to 9 weeks. Time between the first MRI and surgery was 5 to 13 weeks. Patient 4 received additional biopsies between the two MRI sessions. All patients gave written informed consent for participation in this trial approved by the institutional review board (Oct 2014 – March 2016).

Ten patients were scanned at system A with a 6-channel cardiac coil in combination with an endorectal coil, whereas three patients were scanned at system E with a 16-channel anterior and 12-channel posterior coil. The imaging protocol included T_{2w} MRI in three directions, a fat-saturated 3D T_{1w} sequence, diffusion weighted imaging, and dynamic contrast-enhanced MRI, consistent with the current ESUR guidelines (2). Additionally, a T_2 map was acquired with the k-t T_2 technique. Similar settings were used as for phantom measurements. Field-of-view and voxel size were adapted such that whole prostate T_2 maps with good signal to

noise were obtained within 6 minutes. T_2 values were estimated per voxel with a monoexponential decay function with maximum likelihood estimation to account for Rician noise characteristics as implemented in the scanner software (17). Acquisition details of the T_{2w} , T_{1w} , and k-t T_2 mapping sequences are presented in Table 2.

To correct deformations caused by different endorectal coil positions between the scan sessions, deformable registration of the transversal T_{2w} images was done with in-house developed software (18). A rigid registration based on correlation ratio was applied for a region around the prostate, followed by a deformable registration with b-spline deformations using correlation ratio as cost function. These transformations were then applied to the k-t T_2 maps. Additional intra-session rigid registration was performed between the k-t T_2 maps and T_{2w} images when a displacement was visible between the scans.

To relate the repeatability results to the differences that can be expected in prostate, we assessed T_2 values from different tissue types in the prostate. For this purpose ROIs were delineated on the grid of the transversal T_{2w} image of the first scan session. ROIs inside tumor regions (T) were delineated based on the mp-MRI data according to the PIRADS-2 guidelines using the T_{2w} images, diffusion weighted images including apparent diffusion coefficient maps, and dynamic contrast-enhanced MRI (1). Tumor presence was visually verified with corresponding hematoxylin and eosin stained pathology slices. Multiple tumor ROIs within one patient were delineated in case multiple lesions were visible. Pathology data was also used to delineate ROIs for uninvolved peripheral zone (PZ) and transition zone (TZ). For all ROIs T_{1w} image was used to exclude post-biopsy hemorrhage from the delineations. The delineated ROIs were propagated to the k-t T_2 map to estimate T_2 values in healthy and tumorous prostate tissue. Since post-biopsy hemorrhage can reduce the T_2 value, we delineated an ROI (H) in hemorrhage areas visible on the T_{1w} image. This ROI was propagated to the T_2 map of the second scan session to determine if the T_2 values changed in between the scan sessions due to a reduction of the hemorrhage effect.

Statistical Analysis

All statistical tests were performed with Matlab (The Mathworks, Inc., R2013a) using the statistics toolbox. A Kruskal-Wallis test at 5% significance level was used to test for significant differences between the medians of four ROIs (T, PZ, TZ, H). A multiple comparison test was performed to establish which groups are significantly different from each other.

For the phantom measurements we performed a linear regression analysis per **system** to estimate whether the relationship between $T_{2,k-t}$ and $T_{2,ref}$ values was proportional (19). For this purpose, we compared the mean of the ten repeated k-t T_2 measurements with the mean of the three reference measurements. When the slope is close to one, the intercept is a measure for the bias (19). Next, short-term repeatability was estimated for each system with the within-subject coefficient of variation (wCV) for the ten repeated measurements. We chose this metric to account for the differences being proportional to the mean T_2 values (19). wCV was calculated after log transformation of the data (20). Analysis of variance was used to estimate the within-subject variance from which the wCV and the 95% confidence interval (CI) were determined for all gel samples and measurements (19). Reproducibility

was assessed by calculating wCV and CI across systems. For this we compared the means of the ten repeated k-t T_2 measurements per system. In this case, we chose to use the same metric as for repeatability for easier comparison. This is valid if we can assume that the condition of the phantom was similar for all reproducibility measurements (19). In our case, this assumption holds for the measurements on systems A, B, D, and E since we used the same copy of the phantom and used temperature normalization afterwards. However, on system C a different copy of the phantom was used, so we excluded it from this part of the analysis. Finally, long-term repeatability of system A and B was assessed in a similar way by determining wCV and CI for all monthly measurements ($n = 12$) of all gel samples.

Patient test-retest data was used to estimate repeatability in relation to spatial resolution to identify the repeatability for ROIs of different sizes. This was assessed at voxel-level by creating difference maps of the two T_2 maps for each patient. Voxels suspected of hemorrhage on the T_{1w} images of one of the scan sessions were excluded. The bias per patient was defined as the mean of the differences for all prostate voxels. Outliers were identified by a bias either smaller than $Q1 - 1.5 \cdot IQR$ or larger than $Q3 + 1.5 \cdot IQR$, where IQR is the interquartile range between lower quartile (Q1) and upper quartile (Q3) of the biases across all patients (19). Like in the phantom data analysis, repeatability was assessed from log-transformed data by the wCV (20). The relation between repeatability and spatial resolution was investigated by applying smoothing block filters with increasing kernel size to the T_2 maps. We used a simple block filter to smooth the data, calculating an average value over that area, because this is typically what happens when ROI values are being reported. The kernel size was specified by the number of voxels. A smaller kernel size was applied in the slice direction to accommodate the difference between in-plane resolution and slice thickness. The maximum kernel volume was 0.6 cm^3 . wCV was calculated for every smoothing level and for every patient. The median wCV over all patients was calculated. This value was used to calculate the minimum detectable difference, which we defined as 2.77 times wCV analogous to the definition of the repeatability coefficient (19,23).

Results

Phantom Experiments

Fig. 1a shows the accuracy of the k-t T_2 sequence compared to the reference ME-SE sequence for the five different systems with the phantom experiments. The temperature ranged between 293 and 296 K for all experiments. The relation between the $T_{2,k-t}$ values and the $T_{2,ref}$ values could be approximated by a line for all five systems. The slope of this line was estimated with linear regression analysis and was close to 1 for all five platforms (range 0.99 – 1.02). This suggests that the bias is constant and can be estimated by the intercept. The bias was small and comparable across all five platforms (median -0.9 ms , range $-1.3 - 0.9 \text{ ms}$, Table 3). wCV for the repeated measurements within one scan session (i.e. short-term repeatability) was on average 0.5% (range 0.3 – 0.6%) for all five systems, suggesting a good short-term repeatability (Table 3). The reproducibility across systems was lower than the short-term repeatability: wCV is 1.7% (CI 1.3 – 2.1%). Long-term repeatability for the monthly repeated measurements was lower than short-term repeatability

but better than reproducibility: wCV is 0.9% for system A and 1.1% for system B (Fig. 1b). Trends were not visible in the variations in T_2 values over time for both systems.

Patient Study

Fig. 2 shows two examples of repeated T_2 maps with the standard transversal T_{2w} and T_{1w} images as a comparison. Fig. 2a shows an example of a patient in whom the T_2 maps of the two scan sessions have clear visual resemblance. Fig. 2b shows an example in which the hemorrhage area reduced between the two scan sessions (see bright area on left side of prostate in T_{1w} images). In total, nineteen tumor areas were delineated in twelve patients. For patient 1, the tumor area was overlapping with post-biopsy hemorrhage areas, so a tumor ROI could not be identified on MRI. The Gleason score was 3+3 for ten tumor areas, 3+4 for five, and 4+4 for four. For two patients (patient 1 and 13) the PZ ROI could not be delineated due to presence of tumor and hemorrhage. The median tumor T_2 values (78 ms, range 67 – 105 ms) were significantly lower than median T_2 values in PZ (149 ms, range 111 – 223 ms) ($P < 0.001$, Fig. 3). The median T_2 values in the TZ (91 ms, range 70 – 109 ms) overlapped partially with the tumor T_2 values. The tumor T_2 values were also significantly lower than the median T_2 values in the hemorrhage areas (103 ms, range 74 – 160 ms). In general, the T_2 values in the hemorrhage region did not change between the two scan sessions (median difference = 1 ms). However, in four patients the T_2 increased with more than 10 ms in the second scan session with a maximum of 52 ms (patient 2, Fig. 2b). In these patients also a clear reduction of the hemorrhage area was visible in the T_{1w} image of the second scan session.

The median bias between the T_2 maps across all ten patients was –1 ms (range –14 – 0 ms; Fig. 4a). Two patients, patient 3 and 4, were identified as outliers: the bias was –14 ms for both cases. The mp-MRI images of these patients are shown in Fig. 5. For patient 3 an increase in signal intensity in the prostate was also visible in other imaging sequences for which we could not find an explanation. For patient 4, an additional set of biopsies was taken between the two MRI examinations. Therefore, patient 4 was excluded from further repeatability analysis. The repeatability results for the remaining twelve patients are plotted in relation to spatial resolution in Fig. 4b: at voxel-level the median wCV is 15% (range 12 – 20%), while the differences between the two T_2 maps decrease for increasing kernel size. More specifically, for ROIs of 0.5 cm^3 or larger, the median wCV is 4% (range 2 – 9%). Based on these results the minimum detectable difference is 42% at voxel-level and 11% for ROIs of 0.5 cm^3 .

Discussion

The goal of this study was to assess the performance of the k-t T_2 mapping sequence for the use in multi-center and longitudinal trials. For this purpose we used phantom measurements on five systems to assess the accuracy and repeatability within a certain system and reproducibility across different systems. Patient test-retest data were used to assess the clinical repeatability in relation to spatial resolution. Our results show that it is possible to acquire reproducible T_2 maps with the k-t T_2 technique in a clinically reasonable scan time (~5 min). The T_2 values obtained with this technique for ROIs in tumor, PZ, and TZ are

consistent with other studies (4,8,10,12,24): reported tumor T_2 values range between 72 – 100 ms, healthy PZ between 113 – 193 ms, and central gland between 83 – 88 ms.

From test-retest data of multiple visits we assessed the repeatability of the k-t T_2 mapping sequence in relation to the spatial resolution. At voxel-level wCV is on average 15% and is influenced by a combination of image noise, remaining registration errors, day-to-day variations in prostate tissue, and day-to-day scanner variations. By applying a smoothing kernel of increasing size (i.e. lowering the spatial resolution) the effects of noise and registration errors are reduced and repeatability is only influenced by day-to-day variations in prostate tissue (e.g. (25)) and scanner variations. The wCV was on average 4% for ROIs of 0.5 cm³. This value is comparable to other reported reproducibility values for ROIs in prostate: Kershaw et al. reported a wCV of 3% for PZ and TZ (26), whereas Foltz et al. (9) reported an average standard deviation of 3% for PZ and 4% for TZ.

With Fig. 3b we can determine the smallest size of ROIs for which we can reliably detect relevant differences or changes in T_2 values. To illustrate this we determined T_2 values in healthy and tumorous tissue to investigate if a distinction between these areas is possible. The difference between tumor and healthy PZ (about 70 ms based on our results) appears to be large enough to be detected for ROIs of 0.001 cm³ with the k-t T_2 technique. However, the required repeatability depends on the questions asked. Little is currently known about the changes in T_2 values that we can expect in follow-up measurements such as for active surveillance or monitoring of the effect of hormonal treatment or radiotherapy. Foltz et al. have demonstrated a decrease in T_2 of 26% in the peripheral zone after eight weeks of radiotherapy (9). With the current k-t T_2 technique we are able to detect these differences in ROIs of 0.01 cm³.

The dependence of repeatability on ROI size has also been acknowledged in a recent review about reproducibility of the apparent diffusion coefficient, where they show that the reproducibility in larger ROIs is usually better compared to smaller ROIs (27). The study by Korporaal et al. illustrated a similar behavior for dynamic contrast-enhanced CT data (15). In order to relate the repeatability to image noise, we used spatial smoothing of the acquired T_2 maps. By applying a smoothing filter we do the same as calculating an average value for a ROI. In this way we could investigate how the repeatability is related to the size of the ROI. Since the spatial resolution of the k-t T_2 mapping sequence is still lower than that of clinical T_{2w} images, T_2 mapping cannot replace T_{2w} images yet.

One patient was excluded from the repeatability analysis, because our assumption that we performed a test-retest experiment did not hold anymore for this patient. Although the hemorrhage areas were excluded from the analysis, the additional biopsies may have caused inflammation affecting other areas of the prostate as well. Patient 3 was also identified as an outlier, but we could not find evidence explaining the change in signal intensity in the imaging sequences. Therefore, this patient was still included in the repeatability analysis.

From the phantom results we conclude that the bias in k-t T_2 values for different systems is very small and the short-term repeatability high. We assessed the bias by comparing the k-t T_2 values to those of an unaccelerated T_2 technique. In both measurements we did not

correct for influencing factors related to ME-SE sequences in general, such as B_1 inhomogeneities (28, 29). This implies that with ME-SE sequences, including k-t T_2 , apparent T_2 values are measured rather than the *true* T_2 values. The variations across systems were larger than the short-term or long-term variations within the systems. Note that we did not use identical protocols, but optimized for each system. We did not observe significant differences between the results of 1.5T and 3T scanners. For reproducibility assessment we did not include system C in the analysis, because the T_2 values were on average 10% higher than on system A. This was most likely because a different copy of the phantom was used. Thus the requirement that the conditions for measurements were identical, was not met. This was not anticipated when setting up the study. For the bias and short-term repeatability it was not relevant that the data were acquired with a different copy of the phantom, because we compared the T_2 values within the same system and within the same phantom. The long-term repeatability with less than 2% variation over one year showed that the k-t T_2 technique can be used for longitudinal measurements such as active surveillance. During this period we did not observe a trend over time in the longitudinal measurements. Therefore, instability of the gels was not an issue during the period of our measurements (23). Since bias and short-term repeatability were small on all systems, the long-term measurements were only performed on two systems. The phantom measurements indicated that the variations between scanners are small compared to the observed clinical repeatability. This justifies our choice to carry out the test-retest study on a single scanner.

The k-t T_2 undersampling technique is not the only recent development for clinical prostate T_2 mapping, illustrating the increased interest in faster T_2 mapping sequences. For example, the tilted angle approach makes it possible to scan with a reduced field-of-view and a shorter acquisition time (6). Since this method is also a ME-SE sequence, it might be possible to combine this with the k-t T_2 approach to even further reduce the scan time. Another promising approach is the three-dimensional dual echo steady state sequence (30) that has recently been applied to the prostate (12). With this method the acquisition time is about 1 minute for voxels of $1.1 \times 1.1 \times 3.5 \text{ mm}^3$. Acquisition times of k-t T_2 and their approach become similar if the same voxel sizes are used. The T_2 values of tumor and healthy prostate tissue are comparable between our studies.

One of the limitations of this study is that deformable registration was necessary for repeatability analysis at voxel-level. The accuracy of the deformable registration is difficult to validate. We visually inspected the results of the registration algorithm. In this study, we performed all registration steps on the T_{2w} images, because they were independently acquired from the T_2 maps, although both imaging modalities are based on the same contrast information. However, the registration accuracy mainly affects the reproducibility results at voxel-level. When applying smoothing kernels to the data, the effect of registration inaccuracy is reduced. Another limitation is the small number of patients used in this study. The inclusion of more patients or more measurements per patient will provide a more precise estimation of the minimum detectable difference threshold for different voxel sizes (19). Finally, in this study we used ROI analysis to appreciate the repeatability results. We drew ROIs inside the tumor area instead of the entire tumor area. With this approach we most likely underestimated the tumor heterogeneity. However, to be more accurate about the

spread in T_2 values in the different regions, more accurate registration and analysis between MRI and the pathology slices is necessary.

In conclusion, accurate and reproducible T_2 mapping of the prostate is feasible in a clinically reasonable scan time (< 6 min). We have shown that changes larger than 11% can reliably be detected for ROIs of 0.5 cm³ or larger. Therefore, this technique is promising in patients who will be imaged frequently, for instance in patients that are on active surveillance. Longitudinal trials are necessary to investigate the changes that can be expected due to treatment effects.

Acknowledgments

This study was part of the DR THERAPAT project (FP7-ICT-2011-9, Project No. 600852). The authors would like to thank Erik van Muilekom, Corinne Tillier, and Tineke Vijlbrief-Bosman for their help with patient inclusion.

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Fig. 1.

Bias and repeatability results for phantom measurements. (a) shows the difference between $T_{2,k-t}$ and $T_{2,ref}$ for the five different systems. Each marker represents a gel sample. The error bars indicate the standard deviation for the repeated measurements ($n = 10$) and represent the short-term repeatability. (b) shows the results for long-term repeatability measurements on system A and B. Each marker represents a gel sample, whereas the error bars indicate the standard deviation for the monthly repeated measurements ($n = 12$).

Fig. 2.

Two examples of test-retest T_2 maps for patient 9 (a) and 2 (b). Shown are the standard transversal T_{2w} image, a T_{2w} image from the k-t T_2 sequence with a TE close to the standard T_{2w} image (TE = 128 ms), the k-t T_2 map, and the transversal T_{1w} image. The white arrows in the T_{2w} image point towards the location of the tumor. The black arrow in the T_{1w} image in (b) points towards the large post-biopsy area that is present in the first scan and was reduced in the second scan.

Fig. 3. Boxplot of the median T_2 values in tumor (T), uninvolved peripheral zone (PZ), uninvolved transition zone (TZ), and hemorrhage (H) ROIs.

Fig. 4. Bias (a) and reproducibility (b) results for all patients. Each gray line in (b) represents a patient; solid lines are patients scanned on system A, whereas dashed lines are patients scanned on system E. The thick black line represents the median across all patients. The results are shown for increasing kernel volumes.

Fig. 5.

MRI data of patient 3 (a) and patient 4 (b) showing differences between the two scan sessions. Shown are the standard transversal T_{2w} image, the k-t T_2 map, and the transversal T_{1w} image. The arrows in the T_{2w} image point towards the location of the tumor.

Table 1

System specific settings for k-t T₂ sequence of phantom measurements.

	System A	System B	System C	System D	System E
System	3T Achieva	1.5T Achieva	3T Achieva	1.5 T Ingenia	3T Achieva dStream
Coils	6-ch cardiac	Torso XL	32-ch cardiac	Anterior-posterior coil	Anterior-posterior coil
Repetition time (ms)	2459	2693	2273	2360	2459
No. of echoes	12	16	12	16	12
First echo time/Echo spacing (ms)	32/16	22/11	32/16	22/11	32/16
Max B₁ field (μT)	9.5	max	9.5	max	9.5

Table 2

MR imaging acquisition parameters of the transversal T_{2w}, k-t T₂ map, and T_{1w} images. The first value is for scans on system A, second value for system E. In case only one value is mentioned they were the same for both systems.

Parameter	Transversal T _{2w}	k-t T ₂	T _{1w}
Field of view (mm ³)	140×140×75/200×281×75	170×170×60	280×400×80/280×448×70
Acquired voxel size (mm ³)	0.46×0.58×3/0.7×0.7×3	0.8×0.8×3/1×1×3	1×1×1
Reconstructed voxel size (mm ³)	0.27×0.27×3 / 0.4×0.4×3	0.4×0.4×3 0.6×0.6×3	1×1×1/0.85×0.85×3
Fold-over suppression	Yes	Yes	Yes
Turbo spin/field echo factor	24/30	12	88
Repetition time (ms)	3143/3685	2459	3.6
First echo time/echo spacing (ms)	120	32/16	1.8
No. of echoes	1	12	1
Flip angle (degrees)	90	90	10
Parallel imaging factor	1	2	1
Partial-Fourier factor	no	0.625	0.7/0.625
Max B1 field (μT)	9.5/default	9.5	default
Acquisition time (mm:ss)	3:14/3:26	5:00/4:16	1:47/2:18

Table 3

Bias and repeatability results for phantom measurements on five systems

	Bias	Short-term repeatability	Long-term repeatability
	Intercept (ms)	wCV (%) [CI]	wCV (%) [CI]
System A	−1.3	0.4 [0.4 – 0.5]	0.9 [0.8 – 1.0]
System B	−0.9	0.6 [0.5 – 0.6]	1.1 [1.0 – 1.3]
System C	−0.7	0.3 [0.2 – 0.3]	-
System D	−0.9	0.5 [0.4 – 0.5]	-
System E	0.9	0.5 [0.5 – 0.6]	-