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QIN: Practical Considerations in T1 Mapping of Prostate for Dynamic Contrast Enhancement Pharmacokinetic Analyses

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Abstract

There are many challenges in developing robust imaging biomarkers that can be reliably applied in a clinical trial setting. In the case of Dynamic Contrast Enhanced (DCE) MRI, one such challenge is to obtain accurate pre-contrast T₁ maps for subsequent use in two-compartment pharmacokinetic models commonly used to fit the MR enhancement time courses. In the prostate, a convenient and common approach for this task has been to use the same 3D SPGR sequence used to collect the DCE data, but with variable flip angles (VFA's) to collect data suitable for T₁ mapping prior to contrast injection. However, inhomogeneous radiofrequency conditions within the prostate have been found to adversely affect the accuracy of this technique. Herein we demonstrate the sensitivity of DCE pharmacokinetic parameters to pre-contrast T₁ values and examine methods to improve the accuracy of T₁ mapping with flip angle corrected VFA SPGR methods, comparing T₁ maps from such methods with reference T₁ maps generated with saturation recovery experiments performed with fast spin echo (FSE) sequences.

Keywords

T1 mapping; prostate; dynamic contrast enhancement

1. Introduction

Angiogenesis can be a key feature in tumor growth, as tumors cannot grow beyond 1 cm³ without the recruitment of a vascular supply to allow for continued growth and development of metastases (1). A non-invasive method that interrogates tissue vasculature may be an important source of biomarkers, particularly in the assessment of vascular-targeted agents in cancer therapy.

Under the auspices of the Quantitative Imaging Network (QIN) (2), we are studying the utility of multiparametric MRI for the purposes of quantitative assessment of prostate cancer

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diagnosis and treatment, applied in the context of clinical trials. However, before MRI-derived quantitative metrics can be applied to study the treatment effects in this clinical application, it is prudent to investigate and quantify the sources of potential variability.

1.1 Potential merits of dynamic contrast-enhanced MRI

Dynamic contrast-enhanced (DCE) MRI has great potential due to its ability to measure properties of the microcirculation in a wide range of conditions such as cancer (3), inflammation (4), and ischemia (5). With regards to cancer imaging, it can be used in a range of applications such as tumor detection, assessment of response to therapy, and detection of tumor relapse. Pharmacokinetic (PK) modeling of DCE yields parameters related to underlying blood volume and permeability. For example, the endothelial transfer constant (K^{trans}) has been shown to be related to vascular permeability and can be affected by transient VEGF treatments (6).

However, it has become clear that for mainstream adoption and comparative DCE studies, a cross-site and cross-standardized approach to performing DCE is necessary, and the technical specifications for performing DCE must be well defined (7). Moreover, for the derived DCE parameters, such as K^{trans} , there are additional sources of variability inherent to the PK modeling approaches currently used. Such input parameters that can alter the outcome of the modeling include arterial input function and pre-contrast tissue T_1 values. In this manuscript we focus on the latter in an attempt to quantify the importance of accurate, patient-specific T_1 mapping, and to propose improved imaging techniques that would enable patient-specific T_1 measurement within the clinical constraints of image acquisition for prostate cancer patients.

1.2 Principles of DCE measurement

DCE-MR imaging is commonly performed by intra-venous administration of a low molecular weight contrast agent that readily diffuses from the blood into the extravascular-extracellular space (EES) (also termed leakage space [v_e]), at a rate determined by the permeability of the microvessels, their surface area and blood flow. Measurement of the tissue signal intensity changes can be done with fast T_1 -weighted imaging. These signal intensity changes can be interpreted quantitatively using pharmacokinetic modeling to derive physiological indices. Quantitative parameters relate to underlying physiological properties such as vessel permeability, perfusion and blood volume, and can be obtained by applying a PK model to the DCE-MRI data. This process involves converting signal-time curves into concentration-time curves that are then mathematically fit with PK models based on tracer techniques introduced by Kety and Schmidt (8). However, in order to convert the signal intensity time curves into concentration time curves, pre-contrast T_1 relaxation times of the tissue must be known, measured or assumed (9).

There are uncertainties with regard to the reliability of the quantitative parameter estimates derived from the application of tracer kinetic models to DCE-MRI data (10–13). The differences in how baseline tissue T_1 values are measured will affect the PK parameters ultimately obtained. There is no reliable clinical gold standard to confirm how kinetic parameter estimates actually compare to the underlying physiological parameter they “measure”. However, it is important to remember that these quantitative parameters can provide a non-invasive measure of important pathophysiological processes, and so optimization of input factors like pre-contrast T_1 values is necessary to allow for robust analytical approaches with clear biologically acceptable endpoints.

1.3 T₁ measurement

The simplest approach for initiating DCE PK analysis is to assign a constant value of T₁ over the prostate gland volume. T₁ quantification in the prostate has been performed at 3T on healthy young volunteers (mean age 33 years), with a mean value of 1597 milliseconds (ms) obtained (14). However, this doesn't account for changes that occur in the prostate with age, and a limitation of using a constant T₁ value is that it does not account for the inhomogeneity of the T₁ values within the gland, or for inter-patient variability. These issues motivate efforts to generate pre-contrast T₁ maps for DCE analyses. T₁ maps can be produced by a variety of methods (15). Many of the classical methods, such as multiple inversion or multiple repetition time acquisitions, typically require lengthy acquisition times that pose a problem in clinical practice. Another approach taken in the context of the prostate has been to employ spoiled gradient-echo (SPGR) sequences where it is possible to obtain T₁ estimates in relatively short acquisition times by varying the RF flip angle (α). An important benefit of the variable flip angle (VFA) SPGR method is that it provides T₁ maps using the same 3D SPGR sequences that are commonly used for DCE acquisitions, so that identical spatial resolution and coverage is obtained. However, difficulties have been encountered as a consequence of B₁ inhomogeneities particularly at the higher field strengths. These inhomogeneities lead to discrepancies between the flip angle imposed by the MRI scanner (α_{applied}) and the flip angle actually seen by the tissue (α_{actual}) where we define $K = (\alpha_{\text{actual}}/\alpha_{\text{applied}})$ as the magnitude of this discrepancy. Several methods have been proposed to provide accurate T₁ mapping by estimating K (16–22), which are generally time consuming, and are not yet widely available.

In this work, we first demonstrate the sensitivity of PK parameters to pre-contrast prostate T₁ values and determine the effect of variations in T₁ estimation on tumor and normal tissue PK values. We also determine inter-patient variability in T₁ values within the prostate gland using a reference saturation recovery T₁ measurement method based on FSE acquisitions using 6 TR values, in addition to T₁ estimates derived from an optimized subset of 3 TR's culled from the full 6 TR data set. We also investigated the feasibility of using a simple method for improved T₁ mapping from VFA imaging by estimating K from an assumed reference T₁ in pelvic muscle adjacent to the prostate. Specifically, we corrected the flip angles using an assumed T₁ of peri-prostatic muscle and then applied the K- corrected α values to prostate data to evaluate the flip angle corrected VFA SPGR approach for T₁ measurement in the prostate.

2. Methods

Digital phantom experiments—To determine the effect of variability on PK values obtained, we used a custom research software tool (Cinetool, GE Global Research) to perform PK analysis using a fixed prostate T₁ value of 1597 ms (14) in areas of pathology-proven tumor (T) and in areas of normal tissue (N). We then varied the T₁ value by $\pm 20\%$, and determined the effect of this variability on PK results obtained.

In vivo T₁ measurements—Eleven patients underwent multiparametric 3T MRI prostate cancer exams as part of routine clinical examination. All patients had suspected prostate cancer with elevated Prostate Specific Antigen (PSA) level, and most already had a known prostate cancer diagnosis from prior prostate biopsy. Endorectal prostate MR was performed for tumor detection, characterization and staging, or in some cases, for identification of suspicious lesions for MR targeted biopsy.

The imaging exam included 3-plane single-shot fast spin-echo localizers, 3-plane T2-weighted imaging, diffusion-weighted imaging, and DCE, in addition to the T₁ mapping

sequences described below. All patient data for this study were acquired with institutional IRB approval including informed consent. Studies were performed with a 3.0 T General Electric (Waukesha, WI) Twin-speed system, utilizing software version 15X (HDx) and employing the 8-channel abdominal array coil along with the Medrad Endorectal coil (Warrendale, PA).

2.1 The Variable Flip Angle Spoiled Gradient Echo (VFA) Sequence

In order to provide T_1 maps at the same spatial positions as the DCE sequence, a 3D SPGR with SPECIAL spectral fat suppression was employed where the applied flip angle was varied: $TR/TE = 8.8-9.1/2.7\text{ms}$, $\alpha_{\text{applied}} = 18, 15, 12, 9, 6, 3^\circ$, $BW \pm 30\text{ kHz}$, $FOV 26 \times 26\text{ cm}^2$, Matrix 256×128 , 16–18 slices/slab, slice thickness 6 mm, 20 dummy cycles, no phase wrap, 1 average, total acquisition time 270 seconds. Here, α_{applied} is the RF flip angle applied by the scanner's RF amplifier (which may not be equal to the actual flip angle as seen at the voxel), BW is the receiver bandwidth and FOV is the Field of View. The following standard equation for the signal intensity (SI) expected from the SPGR sequence (neglecting T_2^* effects) was employed for T_1 analyses:

$$SI(\alpha_{\text{actual}}) = M_0 \sin \alpha_{\text{actual}} (1 - \exp(-TR/T_1)) / (1 - \cos \alpha_{\text{actual}} \exp(-TR/T_1)) \quad \text{Equation 1}$$

In this equation, $\alpha_{\text{actual}}(x, y, z)$ is the actual radio frequency (RF) flip angle seen by the tissue at a given x, y, z spatial position, TR is the repetition time and M_0 the equilibrium magnetization.

2.2 The flip-angle-corrected 3D VFA T_1 analysis

The SI (α_{applied}) images acquired by the 3D SPGR sequence were processed on a General Electric Advantage Windows (Waukesha, WI) workstation using prototype software, Cinetool (GE Global Research, Niskayuna, NY). Initially, the user placed a Region of Interest (ROI) on the right obturator internus muscle in a central slice of the series, as shown in Figure 1. The software then assumed a T_1 value for the muscle of 1420ms at 3T (23), and fit the muscle data with free parameters K and M_0 , essentially scaling the applied flip angles in equation 1 above (using $\alpha_{\text{actual}} = K * \alpha_{\text{applied}}$). We solved this for the flip angle correction factor K in the muscle ROI. We then assumed that the K value so obtained also applies to the prostate region, and therefore yields the actual flip angles for the prostate gland. We substituted these values into Eq 1 and applied Eq 1 to the prostate VFA data, with M_0 (the equilibrium magnetization) and T_1 as the free parameters. The variation of K values between slices in a small number of patients was determined using individual slice ROIs placed on the pelvic muscle.

2.3 The Variable Repetition Time Fast Spin Echo (VTR) Sequence

For purposes of comparing the VFA results to a reference standard, we acquired images with 2D FSE sequences at multiple TR values and assumed signal intensities of the form:

$$SI = M_0 (\exp(-TE/T_2)) (1 - \exp(-TR/T_1)) \quad \text{Equation 2}$$

Sequence parameters were: $TE = 42\text{ ms}$, $TR = 500, 1000, 1500, 2000, 3000, 6000\text{ms}$, $BW \pm 16\text{ kHz}$, $ETL = 3$, $FOV 24 \times 24\text{ cm}$, Matrix 256×128 , slice thickness 3 mm, 1 average, 3 interleaved slices, total acquisition time ~ 10 minutes.

Because of the long acquisition time (~10 minutes) in performing a 6TR VTR sequence, we also considered T_1 estimates derived from an optimized subset of 3 TR culled from the full 6 TR data set, for fewer point measurements of target T_1 values. (The optimization process for

selecting this optimized subset of 3 TR's from the 6 TR data set is provided in the appendix).

2.4 Image post-processing

Post-processing was performed in 3D Slicer (<http://slicer.org>) using its standard functionality and in-house developed analysis modules. The prostate region was manually contoured in each of the 3 slices covered by the VTR sequence. Approximate alignment of the VFA and VTR maps was checked visually by overlaying TR=6000 ms data from the VTR sequence over the VFA map. VFA maps were then reformatted to the slices covered by VTR sequence. T_1 values were estimated using all 6 TRs and also a subset of 3 TRs (500, 1500 and 6000) from the VTR image sequence by monoexponential fit at each pixel in the prostate ROI. Comparison was done over the contoured prostate gland voxels in the VTR-covered slices. T_1 values outside the [500,3000] range were considered invalid and discarded from both the VTR- and VFA-derived T_1 maps. Considering that the T_1 prostate values estimated from the 6TR method was used as the reference standard, relative errors were calculated for the maps derived using 3 TRs and using the VFA-based approach.

2.5 Summary analysis

Summary reports were generated to show the VTR color-coded T_1 maps, the flip-angle-corrected VFA color-coded T_1 map, as well as the percentage difference between both the T_1 values estimated using VFA and 3TR VTR method to the relative the reference 6TR VTR method within each slice as follows:

$$\% \text{Difference} = (T_{1, 6\text{TR}} - T_1) / \text{mean}(T_{1, 6\text{TR}}) 100\%, \quad \text{Equation 3}$$

where $\text{mean}(T_{1, 6\text{TR}})$ is the mean of T_1 values in prostate in that specific slice using the 6TR VTR method.

In addition, left-right (L-R) and anterior-posterior (A-P) mid-gland profiles for the estimated T_1 maps were reported to demonstrate the inhomogeneity of T_1 values within a slice.

3. Results

3.1 Sensitivity of pharmacokinetic parameters to inherent tissue T_1 values

As seen in Figure 2, PK-derived indices (K^{trans} and v_e) were different in areas of T and N at specific T_1 values. However, there was overlap in PK results between T and N when T_1 was changed in the $\pm 20\%$ range, underscoring the importance of accurate T_1 estimation for DCE analysis, especially for longitudinal clinical studies.

3.2 Inter-patient variability in prostate T_1 values obtained

The variability in T_1 maps obtained within 3 slices of the prostate gland in all individual patients, and between patients using our reference VTR method, are outlined in Figure 3(A). The overall mean $\pm$ SD prostate T_1 values obtained using this method were 1434 $\pm$ 295 ms.

3.3 Comparison of flip-angle-corrected 3D VFA-based and 6TR VTR-based T_1 estimation

VTR and flip-angle-corrected VFA T_1 estimation methods were both applied in 11 prostate cancer patients. As outlined in Table 1, the dynamic range of K in 10 slices of the prostate gland in 5 patients was 0.6–1.4, demonstrating the large variability of effective flip angles at 3T. The overall mean $\pm$ SD prostate T_1 values obtained using the flip-angle-corrected VFA method were 1530 $\pm$ 498 ms. As can be seen in Figure 3, there were large differences in the mean and standard deviation of T_1 values using the VFA method (Figure 3C) compared to the VTR (Figure 3A), in all slices of all 11 cases. We observed that the relative error

between the flip-angle corrected VFA and VTR in some cases exceeded as much as 50% (the relative error was thresholded at 50%), as demonstrated in two case examples in Figure 4. This figure also demonstrates how the T_1 profiles for the left-right and anterior-posterior mid-gland line differed between the flip-angle corrected VFA and VTR methods.

3.4 Comparison of 6 TR VTR-based and 3 TR VTR-based T_1 estimation

The prostate T_1 values obtained using the VTR method (using the full complement of 6 TR's) (Figure 3A) was compared to those obtained using just 3 TRs (Figure 3B), with an optimized "two-point" TR approach for prostate targeted T_1 values as described in the appendix. It can be seen from these graphs that there was only a small change in the prostate T_1 values between the 2 methodologies. The overall mean $\pm$ SD prostate T_1 values obtained using the 6TR VTR method was 1434 $\pm$ 295 ms, and 1400 $\pm$ 278 ms for the 3TR VTR method. Qualitatively, the topography of the internal architecture within the prostate appears to be maintained, as demonstrated in Figure 5.

3.5 Effect of different T_1 mapping methods on estimated K^{trans} values

In a small number of cases (not possible in all cases as FOV for VTR-based T_1 mapping only covers select slices which does not always cover areas of tumor), we determined the variability in estimated K^{trans} values obtained in areas of tumor and normal tissue (Figure 6) when different T_1 mapping methods are used by the model. An example of the variability of K^{trans} values in one such case is outlined in Table 2.

4. Discussion

DCE MR imaging studies of the prostate require pre-contrast T_1 maps in order to convert signal intensity vs. time curves into contrast agent concentration vs. time curves for subsequent PK analyses. In this study, we have demonstrated the importance of reliable, robust T_1 mapping in the prostate as variations in T_1 measurement by $\pm 20\%$ can have the effect of changing the PK analysis of tissue from a benign to a malignant range. Using a pre-set T_1 value is a suboptimal solution to this problem, as if the true T_1 prostate value is 20% greater than or less than this pre-determined number, erroneous PK values will be obtained. In addition, this study demonstrates that the heterogeneous prostate gland in fact does have much variability in its T_1 values, both within the gland on a single slice, between slices, and of course between patients. Utilization of more patient-specific T_1 values may prove to be very important in longitudinal clinical studies, where patients are being monitored for response to therapy. Specific (currently non-commercial) acquisition sequences may be available in the future for definitive T_1 mapping, many of which may require significant acquisition times and not be ready for adaption into a clinical environment for some time. In the meantime, we are in need of a relatively reliable method of determining prostate T_1 values that can be utilized for quantitative analysis of prostate cancer, amenable to a busy clinical environment.

The main benefit of using the VFA sequence is that it is relatively fast and provides identical spatial resolution and coverage to that obtained with DCE imaging. It is therefore the optimal sequence for use in the clinic and for quicker post-processing workflow. Initial studies using the VFA SPGR approach performed in our laboratory indicated that use of the prescribed flip angles in the signal intensity modeling equation was not appropriate. A potential simple solution to this problem using VFA SPGR was to assume known T_1 values for a control tissue (such as adjacent muscle) close to the prostate, and scaling the flip angles linearly to achieve this control T_1 value. To further explore how well such approaches might work we also generated T_1 maps for 3 central prostate slices of each patient with conventional saturation recovery methods using FSE readouts and 6 TR values from 500 ms

to 6000 ms, the VTR method. The results from our reference 6 TR VTR method yielded T_1 values that are in close agreement with previous literature values (14) (acknowledging the limitation that these literature values are from a different patient population to those in our study), allowing us to feel confident in our reference method for T_1 prostate estimation. Despite a major improvement in the mean VFA values prior to flip angle correction (data not shown), there is far greater variation in T_1 values obtained with flip-angle-corrected VFA compared to VTR. Assuming our reference method is correct, this greater variation in the T_1 value using the VFA may be partly explained by the fact that that flip angle correction derived from that of obturator internus muscle on one slice only (a mid-section slice) within the prostate is not sufficient to correct for the discrepancies between the flip angle imposed by the MRI scanner and the flip angle seen by the tissue on all slices. This variability in flip angles is likely not only a result of the variation in tissue T_1 values, but also secondary to the change in flip angle seen between middle and edge slices within the field of view, as shown in Table 1.

However, there are drawbacks to using a 6TR VTR sequence in a busy clinical practice, primarily the long acquisitions times. If the number of TRs necessary to produce these T_1 maps could be reduced, however, full prostate gland coverage for T_1 mapping could be achieved in more reasonable scan times. This motivated our investigation of the 3TR VTR analyses in comparison with the 6TR analyses where a long TR (6000 ms) is assumed to yield full magnetization and the second TR was selected to optimize measurement of T_1 values expected for the prostate (see appendix). The shortest TR (500 ms) in this 3 TR approach is used to add accuracy and to allow for assessment of shorter T_1 's expected for hemorrhagic areas secondary to prostate biopsy often encountered in our patient population. The 3 TR T_1 maps obtained were indeed very similar to the 6 TR T_1 maps, suggesting that it is possible to replace the 6TR with the 3TR method, and also reduce the imaging time substantially.

Considering the B_1 variations outlined in Table 1, it is possible that B_1 inhomogeneity has an impact on the estimation of contrast agent concentration, and subsequent quantitative DCE analysis. This is an area that requires future work. Also, as both VTR and VFA are saturation techniques, it could also be argued that the VTR method can also be affected by B_1 inhomogeneities, including imperfect slice profiles. However, such effects are likely secondary, as our T_1 measurements with the VTR method are in agreement with literature values measured with more precise inversion recovery experiments. With regards to the flip-angle-corrected VFA, a limitation of this study is that we did not look at a larger muscle reference region, or use multiple slices to improve through-slice B_1 correction for flip-angle-corrected VFA, which may indeed allow for more precise T_1 estimates. In this contribution we attempt to provide patient-specific prostate T_1 values, recognizing the heterogeneity of T_1 values within the gland, and the range of T_1 values obtained in individual patients. While both the VTR and muscle-adjusted VFA sequences have definite limitations, T_1 values obtained using these methods offer more definitive patient-specific information regarding the underlying tissue T_1 value that is obtained. This is especially true when compared to using non-adjusted VFA (where known discrepancies between the flip angle imposed by the MRI scanner and the flip angle seen by the tissue caused definitively large errors in T_1 values to be obtained) or using a pre-determined set T_1 value (not tissue or patient specific enough, and may give rise to completely erroneous PK values). In future work, comparison of consistency of PK parameters in a larger patient cohort, as well as determining the impact of T_1 mapping on the characterization of parameter changes in longitudinal studies, will be necessary. Until new methodology for estimating α_{actual} becomes readily available (24) and is applicable in routine clinical practice, we recommend either a flip angle corrected VFA method or a VTR FSE approach with judiciously chosen TR values that can minimize scan time, while retaining reasonable accuracy for T_1 values expected in the prostate.

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Appendix

Optimizing “two-point” T_1 measurements with variable TR method.

Let $x = \exp(-R_1 TR)$ and S_0 be the signal intensity at infinite TR as estimated from a long TR acquisition such as our 6000 ms TR data. If we know the target relaxation rate $R_1 = 1/T_1$ of the tissue of interest (0.65 s^{-1} for prostate), then the question is posed as to what would be the single, optimal TR to deploy with the long TR measurement that would maximize the accuracy of such a “two-point” T_1 measurement? Let S be the signal generated at this optimal TR and let us further assume that S and S_0 have similar noise variations ΔS_0 . The following relation for calculating R_1 , based on standard monexponential saturation recovery of the relaxation, is assumed:

$$R_1 = (-1/TR) \ln(1 - S/S_0). \quad [A1]$$

We first consider the variance of R_1 given by

$$\sigma_{R_1}^2 = (dR_1/dS_0 \Delta S_0)^2 + (dR_1/dS \Delta S)^2 \quad [A2]$$

where, again, we have assumed that the noise in both images, ΔS_0 and ΔS , is the same. We then form the coefficient of variation (COV) as the ratio σ_{R_1}/R_1 and take the derivative of the COV with respect to x , set this to 0 to find the minimum for x along the interval 0 to 1 on the real line. Following some algebraic manipulation we arrive at the following transcendental relation

$$(2x - x - 2) \ln x - x^2 + 2x - 2 = 0 \quad [A3]$$

which is satisfied for $x \approx 0.43 = \exp(-TR/T_1)$ or $TR = 0.84 T_1$. Thus the optimal TR value is approximately $0.84 T_1$ where T_1 is the target value T_1 of the tissue of interest. This result demonstrates perhaps why the subset of TR values (6000, 1500 and 500 ms) yielded results very similar to the larger data set consisting of 6 TR values.

Figure 1.

Example of the user interface utilized in Cinetool for using the pelvic muscle to correct the VFA-based T_1 map. (A) ROI (large circle) placed on a VFA slice indicating region to be fit and T1RF (small ellipse) region indicating the obturator internus pelvic muscle, used for calculation of K . (B) T_1 map before correction and (C) T_1 map after correction. Note that mean T_1 values increase by approximately 100% in this slice between (B) and (C), since $K=0.8$.

Figure 2.

Graph demonstrating the effect of changing T_1 value on K^{trans} and v_e values in areas of tumor (red) and normal tissue (black). The dot corresponds to a fixed T_1 value of 1600, and the error bars are $\pm 20\%$. This graph shows that there is the possibility of some overlap between PK results (K^{trans} expressed as min^{-1}) in regions of tumor and normal tissue when T_1 of prostate is varied by 40%, indicating the need for reliable T_1 measurement.

Figure 3.

Box and whisker plot outlining the distribution of T_1 prostate values in 11 patients using (A) gold standard VTR (with 6 TRs: 500, 1500, 2000, 3000, 4000, 6000ms), (B) at the same locations using 3 TRs (500, 1500, 6000ms), and (C) using flip-angle-corrected 3D VFA (C). There are 3 box plots for each patient, representing the mean and standard deviation of T_1 values in 3 individual slices for each patient. It can be seen from this graph that there is a lot of variation between patients, and indeed between slices in an individual patient. There was only slight change in T_1 values obtained using the 3TR (B) compared to 6TR (A) gold standard VTR methodology. However, comparing the flip-angle-corrected VFA T_1 technique (C) to the VTR technique (A), far greater variation in values was noted using the VFA. (Blue line represents a T_1 value of 1597 ms (21); green line represents 1597 ms $\pm$ 10%, and red line represents 1597 ms $\pm$ 20%).

Figure 4.

Two separate cases [case 7 (A) and case 8 (B)] demonstrate examples of color-coded T_1 maps obtained using 6TR VTR (column 1) and flip-angle-corrected 3D VFA T_1 (column 2), across 3 different slices (3 separate rows) in the prostate. The third column is a color-coded map of the relative error between 6TR VTR and VFA. The fourth column demonstrates the T_1 profiles for the left-right (continuous line) and anterior-posterior (broken line) mid-gland line for VTR (red lines) and flip-angle-corrected VFA (blue lines), demonstrating differences in T_1 profiles between the two T_1 mapping methodologies. (Of note, there is likely inductive coupling between the receiving endorectal coil and the transmitting body coil, which manifests itself more on the more sensitive VFA images).

Figure 5.

Spatially overlapping series from 2 different slices (one slice = A–D; second slice = E–H) within the prostate from Case 9. A and E are T2WI's, B and F are 6TR VTR T_1 maps, C and G are 3TR VTR T_1 maps, and D and H are flip-angle-corrected VFA maps. The visible topographical features of the prostate remain visible on all T_1 mapping sequences.

Figure 6.

Single slice through the prostate demonstrating tumor (outlined in red) and normal tissue (outlined in yellow) as defined by both T2 WI (top row, left) and ADC map (bottom row, left). K^{trans} values were estimated in these outlined areas of tumor and normal tissue, using T1 maps obtained by 6 VTR (top row, middle); muscle-adjusted VFA (top row, right); 3VTR (bottom row, middle) and using a set T1 value of 1597ms. K^{trans} values obtained are outlined in Table 2.

Table 1

Variation of K values per slice (SI) for slices from the base of the prostate gland (SI1) to the apex of the gland (SI9) in 5 patients, as computed using individual slice ROIs on the pelvic muscle. The dynamic range of K in the 5 subjects is from 0.6–1.4, demonstrating the large variability of effective flip angles at 3T. Variability at the edges can also be due to reduced flip angles due to the 3D SPGR slab profile.

	SI1	SI2	SI3	SI4	SI5	SI6	SI7	SI8	SI9
Patient 1	0.875	0.833	0.854	0.875	0.917	0.958	1	0.979	0.979
Patient 2	0.854	0.792	0.812	0.792	0.813	0.792	0.792	0.771	0.854
Patient 3	0.645	0.687	0.729	0.708	0.666	0.708	0.771	0.75	0.646
Patient 4	0.75	0.791	0.771	0.792	0.792	0.792	0.771	0.75	0.729
Patient 5	1.229	1.333	1.42	1.375	1.312	1.292	1.333	1.396	1.333

Table 2

Variation in K^{trans} values (min^{-1}) obtained using different T1 mapping methods. Results are expressed as mean ($\pm$ SD).

	Tumor PZ	Normal PZ
T1 map from 6 VTR	0.38 ($\pm$ 0.13)	0.14 ($\pm$ 0.04)
T1 map from 3 VTR	0.41 ($\pm$ 0.14)	0.15 ($\pm$ 0.04)
T1 map from FA-corrected VFA	0.27 ($\pm$ 0.08)	0.09 ($\pm$ 0.02)
T1 map from 6 VTR	0.34 ($\pm$ 0.11)	0.13 ($\pm$ 0.03)