MR Spectroscopy of the Prostate at 3T: Measurements of Relaxation Times and Quantification of Prostate Metabolites using Water as an Internal Reference

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Purpose: We performed single-voxel magnetic resonance spectroscopy (MRS) of the human prostate at 3 tesla using a surface coil to measure prostate water, choline (Cho), creatine (Cr), and citrate (Cit) relaxation times $T_1$, $T_2$, and to estimate concentrations of Cho, Cr, and Cit in healthy volunteers.

Methods: In nine of 17 healthy volunteers, we performed experiments to estimate relaxation time, and we used the spectra of the other eight to compute metabolite concentrations. Spectra were processed by LCModel and AMARES (advanced method for accurate, robust, and efficient spectral fitting) algorithms. $T_1$ and $T_2$ values were obtained by mono-exponential fitting of the spectral intensities. Metabolite concentrations were estimated using prostate tissue water as an internal concentration reference.

Results: Relaxation times are reported for prostate water ($T_1$, 2163 ± 166 ms; $T_2$, 110 ± 18 ms), Cho ($T_1$, 987 ± 71 ms; $T_2$, 239 ± 24 ms), Cr ($T_1$, 1128 ± 149 ms; $T_2$, 188 ± 20 ms), and Cit ($T_1$, 476 ± 70 ms; $T_2$, 228 ± 42 ms). Mean concentrations in healthy prostate were Cho, 2.6 ± 0.3 mM, Cr, 5.8 ± 1.3 mM, and Cit, 26.9 ± 5.5 mM.

Conclusion: We observed metabolite relaxation times and concentrations consistent with published values of healthy volunteers at 1.5 and 3T. $T_1$ values increased and $T_2$ slightly decreased with magnetic field strength. Our preliminary patient results indicate that water-referenced quantitative MRS of the human prostate is a promising tool for monitoring therapeutic effects and detecting tumor relapse, i.e., in situations when Cit intensity is small or undetectable.

Keywords: absolute quantitation, prostate, relaxation times, water reference, $^1$H-MRS, 3 tesla

Introduction

Proton single-voxel magnetic resonance spectroscopy ($^1$H-MRS) and MRS imaging (MRSI) have been used to assess prostate metabolites levels in vivo since the 1990s. An aim of the examinations was to detect, localize, grade, and stage prostate cancer. Increased levels of choline compounds (Cho) and decreased levels of citrate (Cit) and polyamines (PA) compared with those levels in healthy tissue were recognized as biomarkers for malignancy. Because overlapped Cho, PA, and creatine (Cr) spectral lines cannot be fitted accurately in 1.5-tesla spectra, a robust ratio of the spectral intensity of (Cho + PA + Cr) to that of Cit has become a widely used indicator of prostate cancer despite a theoretical more sensitive ratio of Cho to Cit or Cho to (PA + Cit). However, citrate is not an ideal quantification reference. The spectral shape of a J-modulated Cit quadruplet depends on such factors as echo time (TE), shape and timing of excitation impulses, and off-resonance effects. The metabolite-to-citrate ratio tends to be extremely large if Cit is low, such as in tumors or as a consequence of radio- or hormone-deprivation therapy. A decrease in spectral intensities with increasing exposure during therapy has been demonstrated. Moreover, Cit resonances usually become undetectable by the end of therapies. In such cases, any quantification based on
metabolite-to-citrate spectral intensity ratios is useless. Normalization of Cho, PA, and Cr intensities to unsuppressed water line offers the only viable option.

Unsuppressed water line is almost exclusively used as the concentration reference in spectroscopy of soft tissues, such as the brain, liver, heart, and skeletal muscle, but the prostate is an exception. Exclusion of the water reference in prostate spectroscopy can be explained by the fact that most studies have been performed using water-suppressed 3-dimensional (3D) MRSI, and time constraints precluded 3D MRSI acquisition of the water lines. To our knowledge, only 4 spectroscopic studies have reported quantification of prostate metabolites relative to water. In vivo concentration of Cit was estimated by single-voxel MRS at 1.5T by Liney and Lowry et al in 1990s.2,3,6 In addition and more recently, Cho and Cit have been quantified by 2D MRSI using 3T scanner.9

Relaxation time corrections of spectral intensities are inevitable in quantifying prostate metabolites because of the relatively long TEs (140 to 145 ms) and short time repetitions (TR, 750 to 1500 ms) used in prostate spectroscopy. The T1 relaxation times of Cho, Cr, and water are comparable or larger than TR. The T2 value of water is shorter than TE and that of metabolites of interest.3,10–12 Few measurements of prostate relaxation time have been performed at 3T. Two studies measured water T2 by imaging techniques,10,11 and only de Bazelaire et al report T1,10 Relaxation times T1, T2 of Cho, and Cit of a mixture of normal and malignant prostate tissue have only been estimated by Scheenen et al12 by 2D MRSI using an endorectal receiver coil. The relaxation times of prostate Cr were not estimated in this study because of the unreliable separation of Cho and Cr line from J-modulated PA intensities as a consequence of low signal-to-noise ratio (SNR). Surprisingly, single-voxel MRS, the natural first step in estimating prostate metabolite relaxations times and concentrations at 3T, has not been carried out.

We report single-voxel spectroscopy of healthy and malignant prostate tissue using a receiver surface coil. We chose to combine single-voxel MRS with a surface coil because standard MRSI techniques require an endorectal coil and/or long measurement time. In addition, most healthy volunteers refuse the unpleasant and often painful insertion of the coil into the rectum.

Our primary goal was to measure prostate water, Cho, Cr, and Cit T1 and T2 relaxation times of healthy volunteers (for the first time). Knowledge of the relaxation times enabled us to estimate the mean concentrations of prostate metabolites, a secondary but equally important aim of this study.

Materials and Methods

Study population

Because of the long duration of measurements, we divided 17 healthy volunteers into 2 groups. The first group of 9 volunteers (median age 57 years, range 27 to 67 years) was used for measurement the relaxation times of prostate metabolites. We used the spectra of the second group of 8 volunteers (median age 55.4 years, range 52 to 64 years) to quantify metabolite concentrations and compute the mean spectrum. The levels of prostate specific antigen (PSA) in volunteers ranged between 0.4 and 2.7 ng/mL. No abnormalities were observed on either routine T2- or diffusion-weighted images (b = 1000 s/mm2) or on apparent diffusion coefficient (ADC) maps (b = 0, 100, 200, 400, 500 s/mm2).

To demonstrate the water normalization approach as a result of missing or low Cit intensity, we used the spectra of a 72-year-old patient with aggressive prostate cancer (Gleason score 4 + 5) and a 62-year-old patient who underwent brachytherapy.

Our local ethics committee approved the study protocol, and we obtained informed consent from all participants.

Data acquisition

Patients and healthy volunteers underwent scanning on a 3T clinical system (Philips Achieva, Best, The Netherlands) using a whole body coil for excitation. Uniformity of the radiofrequency (RF) field (B1) was improved by the parallel use of multicore RF transmission with multiple RF transmit chains and coil elements.13 A 6-element receiver coil (cardiac coil) was used in MR imaging of patients. However, only 2 coil elements placed anterior and posterior with respect to the prostate were used for signal reception in spectroscopy. Relaxation times of healthy volunteers were measured with a circular 2-element receiver coil (diameter 20 cm) placed in the front and back of the pelvis. T2-weighted turbo spin echo images were used to guide the positioning of the spectroscopic volume of interest. Single-voxel spectra were acquired using the manufacturer’s default point-resolved spectroscopy (PRESS) sequence (spectral bandwidth, 2000 Hz; 1024 points; TR/TE, 1400/140 ms; delay time between 90° and the first 180° pulse, 18.3 ms). Iterative first-order shimming was used to correct magnetic field homogeneity. The spectra were measured with 16 phase cycle steps. Sixteen non-water-suppressed and 192...
water-suppressed scans were performed in consecutive experiments in 5 minutes. Water suppression was achieved using band-selective prepulses and band-selective inversion with gradient dephasing (BASING) pulse. Fat suppression was achieved by a frequency-selective inversion recovery prepulse. Chemical shift displacement between Cit and Cho PRESS boxes was 1.5, 0.8, and 1.3 mm in anterior-posterior, left-right, and feet-head directions, respectively. The largest possible voxel was placed inside the prostate. Representative volume of interest position was shown elsewhere.

Single-voxel spectra of healthy volunteers were used to estimate T1 and T2 relaxation times. Measurements were performed in 3 sessions: (i) water T1 and T2; (ii) Cho, Cr, Cit T1, and Cit T2; and (iii) Cho, Cr, and Cit T2.

We estimated the relaxation times of water using spectra acquired with 9 TRs (0.7, 0.85, 1.0, 1.4, 1.8, 2.2, 3, 4, 5 seconds; TE 140 ms; and number of scans (NS) (NS 16), and 7 TEs (125, 150, 175, 200, 225, 250, 275 ms; TR 1500 ms; and NS 16).

T2 values of the Cho and Cr were quantified using the spectra measured at 5 TEs (120, 140, 175, 250, 260 ms; TR 1500 ms; NS 192) (Fig. 1).

We estimated the T2 values of Cit from the 2 spectra measured at TEs of 140 and 260 ms (TR 1500; NS 256).

The T1 values of Cho, Cr, and Cit were estimated from the spectra measured at TE 140 ms and TRs 0.825, 0.9, 1, 1.25, 1.5, and 1.75 s (NS 192). Use of BASING pulse rather than inversion recovery prepulse to suppress fat signal enabled lowering of the minimum TR to 825 ms.

Spectrum and data processing

We did not use apodization of the free induction decay (FID) to improve SNR. We estimated the spectral intensity ratios of Cho, Cr, and Cit to the unsuppressed water line using LCModel v. 6.2–4 software. Only reliable spectra were considered. Inclusion criteria were SNR greater than or equal to four and standard deviation (SD) of LCModel fits less than 40%. We normalized the baseline and phase-corrected spectra and the fits by summing the squares of the intensities of the spectral points in each spectrum and then dividing the amplitude of each point by the square root of this sum. Mean normalized spectra were computed by averaging the values at each data point. These spectra were used exclusively for presentation purposes. To convert the individual metabolite-to-water spectral intensity ratio, R_{MET}, to metabolite absolute concentration, C_{MET}, expressed as mmol/liter (mM), we used the equation (Provencher SW, LCMModel user’s manual, 2011, http://s-provencher.com):

\[
C_{\text{MET}} = R_{\text{MET}} \times \frac{2}{N_{\text{MET}}} \times \frac{\text{attH}_{2}\text{O}}{\text{attMET}} \times W_{\text{H}_{2}\text{O}},
\]

where \(N_{\text{MET}}\) is the number of metabolite equivalent protons contributing to the spectral line intensity (\(N_{\text{Cho}} = 9, N_{\text{Cr}} = 3, N_{\text{Cit}} = 4\)), and \(W_{\text{H}_{2}\text{O}} = 39,400\) mmol/kg is the water content of the prostate, which corresponds to 40 188 mM taking into account prostate density of 1.02 g/cm³. AttH₂O and attMET are PRESS relaxation attenuation factors:

\[
\text{att}(\text{TE}, \text{TR}, T_1, T_2) = \exp\left(-\frac{\text{TE}}{T_2}\right) \times \left[1 - \exp\left(-\frac{\text{TR}}{T_1}\right)\right].
\]

We processed spectra used to estimate the relaxation times of water, Cho, and Cr using magnetic resonance user interface (MRUI) software package version 4.2. It should be noted that the LCModel basis set customized by the manufacturer was con-
Fig. 2. Prostate spectrum (echo time [TE] 140 ms) of a healthy volunteer (bottom), fits and residue (top). The spectrum was processed utilizing advanced method for accurate, robust, and efficient spectral fitting (AMARES) as implemented in magnetic resonance user interface (MRUI) software package. Struc-
tured for TE 140 ms. LCModel was, therefore, unable to fit Cho, PA, and Cr spectral lines reliable at other TEs due to the complicated J-modulation of PA (spermine) lines. Spectral lines were fitted by Gaussians in the time domain using a nonlinear least-squares algorithm AMARES (advanced method for accurate, robust, and efficient spectral fitting) (Fig. 2). The fit of Cit inner lines at TE 140 ms was simplified to a single Gaussian. The prior knowledge utilized the mean chemical shift differences between spectral lines and line widths determined from the spectra of healthy volunteers by LCModel. The following data were used: mean position and line width 3.2 and 0.06 ppm for Cho; 3.11 and 0.13 ppm for PA; 3.04 and 0.07 ppm for Cr; and 2.64 and 0.08 ppm for Cit inner lines fitted by single Gaussian (Fig. 2). The distance between Cit outer lines and central Gaussian was 0.14 ppm, line widths 0.05 ppm. The positions, line widths, and spectral intensities of Cho and Cit inner lines (TE 140 ms) were estimated by AMARES. The positions and line widths of PA and Cr intensities were defined using fixed values with respect to Cho or Cit line. The positions and line widths of Cit outer lines at TE 140 ms were defined using fixed values with respect to the central Gaussian. Baseline correction was performed in 2 steps. The first step applied a Henkel Lanczos singular values decomposition (HLSVD) filter to remove the underlying tails from the residual water and lipid resonances between 1.5 and 0.8 ppm, and the second step truncated the first 2 points of the FID. The phases of all peaks were set to zero relative to the estimated zero- phase. We used AMARES to estimate the zero- and first-order phase correction and LCModel to fit the spectral intensities of Cit at echo times 140 and 260 ms (Fig. 1) used to estimate relaxation times. $T_1$ and $T_2$ relaxation times were determined by monoexponential fitting of the spectral intensities by a Levenberg-Marquardt algorithm using ORIGIN v. 8.6 commercial software (OriginLab, Northampton, MA, USA). Spectral intensities ($y$) vs. TE or TR times ($x$) were fitted according to Equation (2) by functions $y = A \times \exp(-x/T_2)$, and $y = B - B_0 \times \exp(-x/T_1)$, where $A$, $B$ are constants. Citrate $T_2$ values were estimated from the spectral intensities measured at TEs of 140 and 260 ms using equation $\ln(y) = \ln(A) - x/T_2$.

Statistics

Quantitative results are presented as means ± one standard deviation (SD). An adjusted coefficient of determination $R^2$ (adj. $R^2$) was used to express goodness of nonlinear fits.

Results

Not all measurements of relaxation times were successful because of insufficient SNR or artifacts caused by the movement of volunteers. Spectral intensities of 5 volunteers were fitted to estimate $T_1$ and $T_2$ relaxation times of water (Fig. 3). Levenberg-Marquardt algorithm provided an excellent match of peak intensities to monoexponential relaxation curves (adjusted $R^2$ ≥ 0.994). Spectra of 5 volunteers were used to estimate the $T_1$ of Cho (0.758 ± adj. $R^2$ ≤ 0.998), Cr (0.538 ± adj. $R^2$ ≤ 0.988), and Cit (0.701 ± adj. $R^2$ ≤ 0.983). Spectral intensities of 6 volunteers were used to compute the $T_2$ values of Cit. The most difficult step was estimating the $T_2$ relaxation times of Cho and Cr. The Cho and Cr line could only be reliably separated from J-modulated PA intensities in the spectra with SNR ≥ 4 for Cho. This SNR was achieved in the spectra of 3 older volunteers (60, 62, 67 years) as a result of increased voxel size (21 to 28 cm$^3$). Increased prostate volume was caused by benign prostatic hyperplasia, a normal physiologic state of healthy men over age 50. Figure 1 shows the spectra of a 60-year-old volunteer collected at increasing TEs. The spectra reveal changes caused by the
Fig. 3. Monoexponential fit of the spectral line intensities of water versus (a) repetition time (TR) and (b) echo time (TE).

Table 1. Average $T_1$ and $T_2$ relaxation times (ms) of healthy prostate at 3 tesla

<table>
<thead>
<tr>
<th></th>
<th>Water</th>
<th>Choline</th>
<th>Creatine</th>
<th>Citrate</th>
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<tbody>
<tr>
<td>$T_1$</td>
<td>2163 ± 166</td>
<td>987 ± 71</td>
<td>1128 ± 149</td>
<td>476 ± 70</td>
</tr>
<tr>
<td>$T_2$</td>
<td>110 ± 18</td>
<td>239 ± 24</td>
<td>188 ± 20</td>
<td>228 ± 42</td>
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combined effects of the $T_2$ decay and J-modulation of PA and Cit. The $T_2$ values of Cho and Cr were fitted with adj. $R^2$ between 0.821 and 0.992. Table 1 summarizes relaxation times.

Figure 4a-c shows the mean normalized single-voxel spectra and corresponding LCModel fits of 8 healthy volunteers. The mean voxel size was 13.1 ± 2 cm$^3$ (range 11.3 to 17.7), and mean SNR was 11.1 ± 2.6 (range 8 to 16). Table 2 shows mean absolute concentrations. The SD of LCModel fits were 17.1 ± 7.2% (range 9 to 33) for Cho, 27.3 ± 6.4% (range 18 to 36) for Cr, and 2.8 ± 0.7% (range 2 to 4) for Cit. Figure 5 illustrates patient spectra in which the water normalization approach was inevitable because of missing or low Cit intensity. Figure 5a shows the spectrum of an aggressive prostate cancer (Gleason score 4+5, Cho 15.9 mM, Cr 6.1 mM). Figure 5b exemplifies the spectrum of a patient after unsuccessful brachytherapy (Cho 1.2 mM, Cr 2.1 mM). The SD of Cr LCModel fit was 16 in Fig. 5a and 18% in Fig. 5b.

Discussion

This is the first 3T study to estimate the $T_1$ and $T_2$ relaxation times of prostate water by spectroscopic method. de Bazelaire and colleagues$^{10}$ performed the single previous measurement of water $T_1$ using inversion recovery, single-shot, fast spin-echo imaging sequence with 6 inversion times (TI) between 100 and 1000 ms. Their $T_1$ value, 1597 ± 42 ms, is lower than our result, 2163 ± 166 ms. The disagreement could be explained by a relatively short maximum TI compared to $T_1$ and by limitations of the single-shot method, such as imperfections of 180° pulses and relaxation effects during the spin echo train. In contrast, our water $T_2$ value, 110 ± 18 ms, lies between the published values of 74 ± 9 ms for the whole prostate$^{10}$ and 142 ± 24 ms for the periph-

Fig. 4. Normalized prostate spectra (echo time [TE] 140 ms). Mean spectra (thick line) and standard deviation (SD) (vertical lines). (a) Mean spectrum of 8 healthy volunteers and (b, c) corresponding mean LCModel fits.
Fig. 5. (a) Normalized spectrum of aggressive prostate cancer (Gleason score 4 + 5). (b) Normalized spectrum of another patient after unsuccessful brachytherapy.

eral zone.\textsuperscript{11} Whereas de Bazelaire’s group\textsuperscript{10} used a variable 90° to 180° delay before single-shot fast spin-echo imaging sequence, Gibbs et al\textsuperscript{11} applied dual-echo fast spin-echo with echo times of 30, 60, 90, and 120 ms. Note that somewhat lower water T\textsubscript{2} was reported in the central gland (71 ± 10 ms) than the peripheral zone (114 ± 30 ms) at 1.5T.\textsuperscript{3} Differences in T\textsubscript{2} values could, therefore, be explained by differences in experimental methods and by various mixtures of tissues of the peripheral zone and central gland in the voxels. The relaxation time estimations of Cho and Cit (Table 1) can only be compared with the 2D MRSI results of the study by Scheenen et al\textsuperscript{12} (Cho T\textsubscript{1} 1100 ± 400 ms, T\textsubscript{2} 220 ± 90 ms; Cit T\textsubscript{1} 470 ± 140 ms, T\textsubscript{2} 170 ± 50 ms). However, these published results should be taken with caution. Measurements were performed in patients with cancer, and the authors could not discriminate between tumor and non-tumor voxels because of large voxel size. Relaxation times were roughly estimated either by a fit of 3 points or by calculation when only 2 points were available. In contrast, the Cho (T\textsubscript{1}, T\textsubscript{2}), Cr (T\textsubscript{1}, T\textsubscript{2}), and Cit (T\textsubscript{1}) relaxation times of our normal volunteers were obtained by fitting of 5 (T\textsubscript{2}) or 6 (T\textsubscript{1}) points. However, relaxation times of Cho and Cit estimated by Scheenen et al\textsuperscript{12} are in good agreement with our values taking into account the large SDs of Scheenen’s results.\textsuperscript{12} To our knowledge, there are no previous estimates of Cr relaxation times at 3T that can be compared with our values. As expected, our creatine T\textsubscript{1} value, 1128 ± 149 ms, is larger than the T\textsubscript{1}, 864 ± 98 ms, estimated at 1.5T, and our T\textsubscript{2} value, 188 ± 20 ms, is somewhat shorter than the 209 ± 97 ms reported at 1.5T.\textsuperscript{19}

Scheenen and colleagues\textsuperscript{12} estimated Cit T\textsubscript{2} using 2 or 3 spectra acquired in relatively short echo times of 75, 100, and 145 ms. We could not achieve echo time shorter than 115 ms without omitting BASING components. Taking into account the positive influence of the selective BASING pulse on the spectrum quality, we chose to use a longer TE.\textsuperscript{16} Cit T\textsubscript{2} values were computed from the spectral intensities measured at TE 140 and 260 ms. It should be noted that Cit signal oscillates between the inner and outer lines, and the spectrum shape depends on TE and on the time delay between 90° and the first 180° PRESS pulse.\textsuperscript{12,16} The PRESS sequence used in this study produced Cit spectra with a predominantly absorptive line shape at TE of 140 and 260 ms (Fig. 1). The amplitudes of Cit outer lines tend toward zero at echo time of 260 ms, and total signal intensity is focused in the inner lines, which appeared to be in-phase.\textsuperscript{16} The accuracy of Cit T\textsubscript{2} can be improved by using spectra measured at more than 2 TEs and comparing them with numerical simulations,\textsuperscript{12,16} such as by including simulated Cit spectra in the LCModel basis set\textsuperscript{24} or in the prior knowledge of AMARES. A significant limitation of such an approach is the relatively coarse theoretical simulations.\textsuperscript{16} In present, they cannot reflect chemical shift evolution during the RF pulses, pulse imperfections, interference with BASING pulses, and off-resonance effects.

To the best of our knowledge, the present work is the first 3T study in which absolute concentrations of the prostate metabolites have been estimated by single-voxel spectroscopy. The advantage of a single-voxel approach lies in its superior spectral quality and higher SNR to those of spectroscopic imaging. Its use leads to a more reliable fitting of the spectral lines (SD of LCModel fits were <40% for Cho and Cr). Though the single-voxel approach cannot differentiate the peripheral zone from the central gland, concentration estimates can serve as an orientation reference for future 2D or 3D MRSI measurements. This is the first 3T study in which prostate Cr concentrations have been quantified. The concentrations for Cho and Cr in the healthy
Table 2. Metabolite concentrations (mM) and metabolite-to-citrate spectral intensity ratio (arbitrary units) in healthy prostate

<table>
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<tr>
<th></th>
<th>(Cho)line</th>
<th>(Cr)eatine</th>
<th>(Cit)rate</th>
<th>Cho/Cit</th>
<th>(Cho + polyamines [PA] + Cr)/Cit</th>
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<tbody>
<tr>
<td><strong>Mean</strong></td>
<td>2.6 ± 0.3</td>
<td>5.8 ± 1.3</td>
<td>26.9 ± 5.5</td>
<td>0.17 ± 0.05</td>
<td>0.59 ± 0.06</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td>2.2 to 2.9</td>
<td>4.0 to 7.4</td>
<td>17.3 to 32.4</td>
<td>0.10 to 0.24</td>
<td>0.47 to 0.64</td>
</tr>
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</table>

prostate estimated by single-voxel technique (Table 2) are in good agreement with those determined by the same method at 1.5T (Cho 3.1 ± 0.7 mM, Cr 4.4 ± 0.8 mM). However, our Cho concentration (2.6 ± 0.3 mM) is somewhat lower than the concentration estimated by 2D MRSI at 3T for a normal-appearing peripheral zone (4.2 ± 2 mM). Comparison of Cit concentration is not so straightforward. Cit concentration was found higher in the peripheral zone (46 ± 20 mM) than in the central gland (21 ± 6 mM). Whereas Cit concentration of the peripheral zone increases significantly with advancing age, concentration in the central gland does not change. The Cit concentration, 26.9 ± 5.5 mM, of our older healthy volunteers represents a mixture of tissues of the peripheral zone and central gland and lies between the peripheral zone and central gland concentrations estimated by Lowry et al.

Metabolite concentrations of illustrative patients with cancer (Fig. 5) must be taken with caution. The most significant source of quantification errors lies in the unknown concentration of water and relaxation times in the lesions. Both are subject to individual change because each voxel contains a different mixture of normal and cancerous tissues. Because we have used relaxation time corrections valid for healthy tissue, the metabolite concentrations of the lesions should be viewed as institutional estimates.

In most cases, standard radiotherapy and hormone-deprivation therapy affect the entire prostate. Therefore, single-voxel MRS utilizing the largest possible voxel size inside the prostate is a suitable tool for monitoring the global changes of the prostate tissue. Because Cit is at the level of noise (Fig. 5b) or undetectable by the end of therapies, normalization of Cho, PA, and Cr intensities to the unsuppressed water line offers the only available option for quantifying therapeutic effects or detecting tumor relapse.

**Conclusion**

We have shown single-voxel MRS at 3T using a surface coil to be an uncomplicated and easily available method for estimating Cho, Cr, and Cit relaxation times and concentrations. The information value of the water-referenced examination increases at the cost of a relatively small prolongation (a few seconds) of the measurement time needed for acquisition of unsuppressed water lines. Our preliminary patient results indicate that water-referenced quantitative MRS of the human prostate is a promising tool for monitoring therapeutic effects and tumor relapse detection, such as in situations when Cit intensity is small or undetectable.

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