Introduction: Proton MRS [e.g.,2] and dynamic Gd-MRI [3] can each provide useful information for the diagnosis of prostate cancer. Combined use of these techniques may help improve characterisation of prostate cancer. The aim of this study was to compare, in the same patient, the ratio of the citrate and choline signals as obtained from MRSI with contrast agent uptake in the healthy peripheral zone (PZ) and in regions with histologically proven prostate carcinoma (PCa), or benign prostatic hyperplasia (BPH).

Methods: In an ongoing study, MR data were evaluated from 7 patients with histologically confirmed PCa and 1 patient with bladder cancer. Water and fat signals were suppressed using frequency-selective 180° pulses surrounded by dephasing gradients. Spectra from individual MRSI voxels were acquired using a 1.5T Magnetom Vision system. The ratio of the citrate and choline amplitudes was calculated after correction for different T1 weighting.

Multi-slice proton density (PD) weighted MR images (TR/TE: 2000/4 ms; α: 8°; FOV: 320 mm) and dynamic contrast-enhanced images, using a T1-weighted TurboFLASH sequence (TR/TE of 504/4 ms, α: 60°; FOV of 320 mm), covering the whole prostate were recorded. Both series included the same slice as was used for spectroscopic imaging. The dynamic contrast-enhanced MR images were recorded with a temporal resolution of one image every 2 s, following intravenous bolus injection (0.5 mM, 2.5 ml/s) of gadopentetate dimeglumine (Gd-DTPA), Magnevist, Schering). Postprocessing of the contrast-enhanced images to analyze the uptake kinetics of the contrast agent was done on a pixel-by-pixel basis using home-built software. The citrate-to-choline ratios, as obtained by MRSI, were compared to kinetic parameters that describe the contrast agent uptake in homotopic regions of the prostate. A quantitative pixelwise analysis of Gd uptake curves [4] yielded values for (1) Ve, which is proportional to the fractional volume of the extravascular extracellular space (EES), (2) kep, which is the rate constant between EES and blood plasma, and (3) t0 which is the time of onset of enhancement [5]. To allow a pairwise comparison of the MR techniques, these kinetic parameters, were averaged for ten pixels randomly distributed across the corresponding SI voxel.

Figure 1: dynamic MRI (left) indicated a possible tumour site in the central gland (CG), but rapid enhancement in the CG is often caused by BPH. BPH was excluded by MRSI (right), which showed increased choline/citrate ratio, indicating prostate cancer.

Results and Discussion

1H MRSI yielded well-resolved 1H spectra from voxels of 0.8 cm3 nominal volume, covering the peripheral zone and central gland of the prostate. Figure 1 shows for a single patient a contrast-enhanced MR image (left) and the MRSI metabolite map displaying altered citrate/choline ratios (right).

From eight patients, 38 MRSI voxels were selected that contained largely uncontaminated signal from either PCa (n=9), BPH (n=19) or normal PZ (n=10), as confirmed by histopathological examination of whole mount sections. Table I compares mean values for Cit/Cho ratios with mean kinetic parameters for Gd uptake for PCa, BPH and PZ voxels.

Table 1: Metabolite ratio’s and Gd-uptake parameters in tumour (PCa), benign prostatic hyperplasia (BPH) and peripheral zone (PZ)

<table>
<thead>
<tr>
<th></th>
<th>Cit/Cho</th>
<th>Vc (a.u.)</th>
<th>KeP (min⁻¹)</th>
<th>t0 (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCa</td>
<td>0.47±0.3</td>
<td>1159±216</td>
<td>5.6±2.6</td>
<td>5.5±2.3</td>
</tr>
<tr>
<td>BPH</td>
<td>4.0±1.5</td>
<td>1080±231</td>
<td>3.5±1.0</td>
<td>5.4±2.1</td>
</tr>
<tr>
<td>PZ</td>
<td>3.8±1.9</td>
<td>812±213</td>
<td>3.8±1.5</td>
<td>5.3±2.3</td>
</tr>
</tbody>
</table>

The average citrate-to-choline ratio was significantly lower in PCa (P<0.05) than in BPH or normal PZ. This is consistent with earlier data [1,2], showing reduced citrate and elevated choline levels in prostate tumours. Ve was significantly higher (P<0.01) in PCa and in BPH than in PZ. This suggests a larger interstitial volume in tumour regions. Tumour regions showed more rapid enhancement, as indicated by a higher KeP, in PCa than in BPH (P<0.01) or PZ (P<0.01). This may reflect the high density of newly formed capillaries in tumour tissue. The time of onset of enhancement, t0, was similar in all tissue types. Liney et al. [6] recently reported qualitatively similar results, but these authors used single voxel MRS and dynamic MRI with lower temporal resolution. MRSI allowed a relatively good separation of PCa voxels from BPH or PZ voxels, using a cut-off Cit/Cho ratio of about 1.5. However, when examining the data for individual voxels, neither of the parameters obtained from the dynamic Gd-uptake curves appeared very efficient in discriminating PCa from BPH and PZ. This can partly be ascribed to the large variability in the Gd-uptake kinetic parameters between different patients and heterogeneity across the relatively large (SI) voxels. It should be noted that, contrast enhanced MRI has proven useful for single patient diagnosis, particularly in case of poorly differentiated tumours [3]. Future work will be directed towards improvement of analysis routines and proper scaling of results from different patients. This may add to the potential of combined dynamic contrast-enhanced MRI and MR spectroscopic imaging for characterisation of prostate cancer.

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References: