Intermediate results of IMAPS: An International Multi-Centre Assessment of Prostate MR Spectroscopy

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Introduction

In order to improve the non-invasive detection of cancer in the prostate, its location, heterogeneous extent, grade and stage, currently several MR techniques are being explored. Among these proton MR spectroscopy has shown promising results. While the contrast behaviour of adenocarcinoma of the prostate compared to surrounding healthy prostate tissue appears to be ambiguous for many of the traditional diagnostic methods, analytical and clinical studies have shown significant differences if the metabolic state of the different tissue types is depicted by ^{1}H-MR spectroscopic imaging (^{1}H-MRSI). Prostate cancer tissue is characterized by reduced levels of citrate (Ci) and increased levels of choline (Cho) (1-2), which both are detectable *in vivo* with ^{1}H-MRSI. With the increasing availability of a robust MRSI pulse sequence for prostate spectroscopy at 1.5T (3), the results of different institutions are evaluated in the IMAPS trial (an International Multi-Centre Assessment of Prostate MR Spectroscopy). The primary objectives of this multi-centre trial are to prove that ^{1}H-MRSI data allows for both detecting and localizing prostate carcinoma in the two major anatomic areas of the prostate, i.e. the peripheral zone and the central gland.

Materials and methods

Data from 67 patients (of whom 4 were measured twice) with proven prostate cancer from 8 different institutions have been used in this trial up to now. All untreated patients signed an informed consent form prior to the MR exam, approved by the local ethical committee. The time between the biopsy exam (if any) and the MR exam was at least four weeks. The gold standard of reference for the presence and location of cancer in the prostate was the histopathological analysis of the complete prostate after radical prostatectomy as provided by the pathology department of the local institution.

The MRSI pulse sequence is a 3D PRESS pulse sequence with optimized 180º pulses and an echo time of 120 ms for use on 1.5T Siemens Magnetom scanners. Water and lipid signals are suppressed with two dual-frequency selective excitation pulses and crusher gradients. Nominal resolution of the spectroscopic voxels is 6x6x6 mm^3, which is enlarged by apodization of k-space for accurate localization and decreased voxel bleed. By using a short TR (650 ms) and an elliptical, weighted acquisition scheme the total acquisition time is between 10 and 12 minutes, depending on the exact number of phase encode steps and averages.

On the basis of the provided histopathology and the MRSI matrix overlaid on T2-weighted images, blinded for the spectra, an experienced spectroscopist, in consensus with an experienced radiologist, classified at least 1 to a maximum of 4 independent voxels to 4 different tissues in the prostate. An additional classification of voxels originating from locations outlined as tumor on histopathology consisted of a measure for tumor size (< 1voxel, 1 to 2 voxels, > 2 voxels) and a measure for matching accuracy (voxel possibly, probably or definitely inside tumor). The spectra from all classified healthy and tumor voxels were fitted in the time domain with model functions for the Ci, creatine (Cr) and Cho signals with the PRISMA software package (4). The supervised fit results include integral values (+ SD) for the individual signals, values for the (Cho+Cr)/Ci ratio as a marker for tumor tissue and an SNR calculation of the spectrum.

Results and discussion

The mean values (± SD) for the (Cho+Cr)/Ci ratio for healthy tissue in patients is 0.31 ± 0.14 for the healthy peripheral zone, 0.38 ± 0.15 for the healthy central gland, 0.43 ± 0.23 for the healthy (peri-) urethral zone. The median (Cho+Cr)/Ci ratio for tumor tissue is 0.77, with 25% percentile 0.54. The mean value of tumor tissue is largely determined by voxels with low or absent citrate levels leading to indefinite ratio values. For tumor tissue the largest ratio value within 5 mm of the classified voxel has been chosen to represent the tumor. At cut-off values of the (Cho+Cr)/Ci ratio of mean + 1 SD for different tissues the sensitivity and specificity are presented in table 1. In figure 1 the relation between tumor size and (Cho+Cr)/Ci ratio is plotted together with a radiological measure of confidence in matching a voxel to tumor tissue. With increasing tumor size and confidence the mean and median values of the (Cho+Cr)/Ci ratio increases. In larger tumors the partial volume effect of healthy tissue within the spectroscopic voxel identifying tumor decreases, and the confidence of accurate matching is higher, both increasing the (Cho+Cr)/Ci ratio of the voxel. In four patients measured twice, large differences were found in reproducibility of the (Cho+Cr)/Ci ratio: the mean difference between the first and second measurement varied from less than 3 to 50%. Up to now we have not found a relation between (Cho+Cr)/Ci and PSA level (Fig. 2).

Conclusions

Voxels from different prostatic tissues reveal different values for the (Cho+Cr)/Ci ratio. Therefore prostate cancer can better be detected in the peripheral zone than in the central gland, and the peri-urethral area needs to be evaluated with caution. Tumor foci exceeding the size of 1 voxel (~0.64 cc) are detected easier than smaller tumors. Altogether we conclude that also in a multi-centre setting prostate ^{1}H-MRSI is able to detect and localize prostate cancer.

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References: 1. Kurhanewicz J *et al*. Urology 1995;45:459-466. **2.**Heerschap A *et al*. Anticancer Res 1997;17:1455-1460. **3.**Scheenen T *et al*. Magn Reson Med 2004;52:80-88. **4.** Weiland E, University of Bremen and Siemens Medical Solutions. **website:** http://get.to/IMAPS

Tissue	PZ	CG	U
Threshold	0.45	0.53	0.66
Spec	0.85	0.77	0.88
Sens	0.82	0.73	0.58

Table 1. Specificity and Sensitivity for detecting cancer in different prostate tissues with corresponding (Cho+Cr)/Ci threshold values.

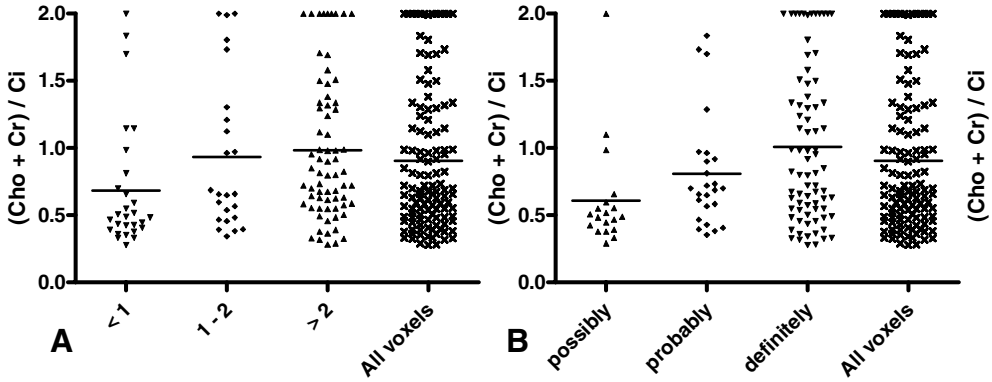

Figure 1. Breakdown of all tumor voxels into size and matching certainty classes. A. Display of three different size classes: < 1 voxel, between 1 and 2 voxels and > 2 voxels. B. Display of radiological estimate of matching a voxel to a tumor.

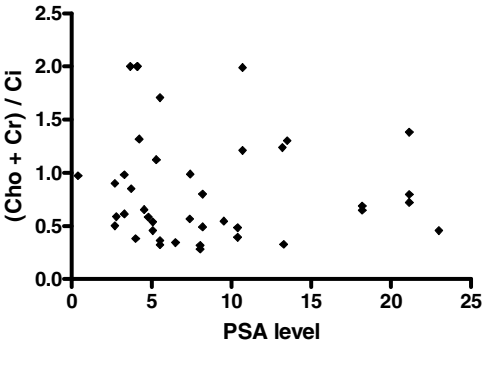

Figure 2. Plot of (Cho+Cr)/Ci ratio and PSA level. No correlation between the ratio and PSA level was found.