Preliminary 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 adeno-carcinoma 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

In this trial data is included of male patients with proven prostate cancer who were treated with a radical prostatectomy. They signed an informed consent form before the MR exam, approved by the local ethical committee; they did not have contra-indications to the MR exam; they did not receive hormone deprivation therapy prior to the MR exam and 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 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 (see Fig.3). The spectra from these 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 (CC/C ratio) as a marker for tumor tissue and an SNR calculation of the spectrum.

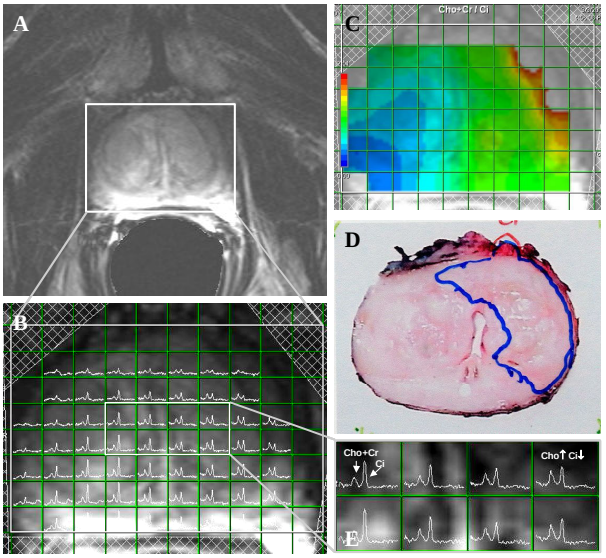

Figure 1. Example of IMAPS data. The axial T2-weighted image (A) is used for matching voxel locations to histopathological specimens (D). One of the spectral maps (B), partially expanded in (E), reflects the quality of the MRSI data throughout the slice. Deviations in the CC/C metabolite ratio map in (C) largely correspond to the tumor location indicated with the blue line in (D).

Results and discussion

An example of one slice of a 3D data-set of one patient of the IMAPS trial is shown in figure 1. Voxel classification is done with the T2-weighted images (Fig.1A), the MRSI matrix grid (Fig.1b but **without** the actual spectra) and the histopathology (Fig.1D). The PRISMA fit to two of these spectra is shown in Figure 2. Figure 3 comprises the CC/C ratio for all classified voxels with a successful fit for the first 34 patients of 5 different institutions. The mean values (± SD) for the CC/C ratio for healthy tissue in patients is 0.36 ± 0.15, which can be separated into the different tissues: 0.30 ± 0.14 for the healthy peripheral zone, 0.38 ± 0.14 for the healthy central gland, 0.41 ± 0.17 for the healthy (peri-) urethral zone. The mean CC/C ratio for tumor tissue is 0.92 ± 0.54. For tumor tissue the largest ratio value within 5 mm of the classified voxel has been chosen to represent the tumor. A cut-off or threshold CC/C ratio for the distinction between healthy and tumour tissue can now be chosen at e.g. the mean value + 2x SD, either for separate tissues or the whole gland.

Conclusions

The first preliminary results of this multi-center trial on prostate spectroscopic imaging reveal different values for the CC/C ratio for different tissues. The peripheral zone of the prostate has the lowest CC/C ratio and the smallest spread in ratio values, whereas the central gland and (peri-)urethral zone have slightly larger CC/C ratios and spread. Although CC/C ratios of tumor voxels overlap with healthy tissues, these values can be used to detect and localize prostate cancer. On the basis of further patient data, additional aged-matched volunteer data and a refined analysis the prediction of the exact sensitivity and specificity of ^{1}H-MRSI for detecting and localizing prostate cancer is in reach.

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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 *et al.* Towards an Automatic Assessment of Quantification Results of in vivo Prostate MRS Data, this conference.

website: http://get.to/IMAPS

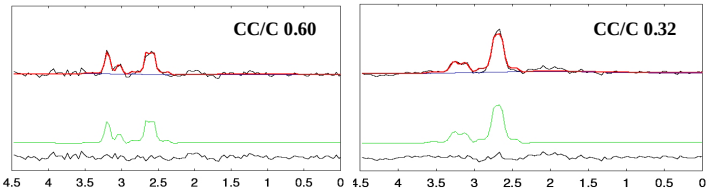

Figure 2. Spectral fit with PRISMA. From top to bottom: measured spectrum (black) overlaid with the fit (red) and baseline (blue), metabolite fit (green), residual between data and fit (black).

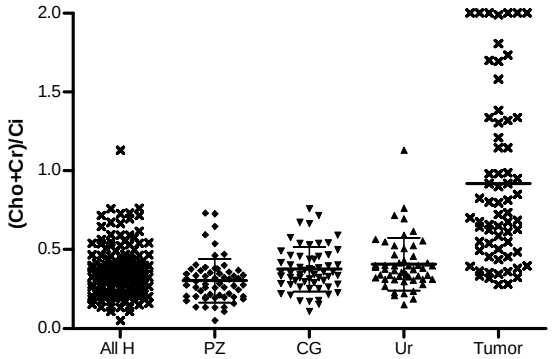

Figure 3. Results of the first 34 patients with prostate cancer of the IMAPS trial. The CC/C ratio of healthy tissues in the different anatomical regions of the prostate are shown together with tumor tissue: All H All healthy tissues together, PZ peripheral zone, CG central gland, Ur (peri-)urethral zone. Values for the CC/C ratio above 2 have been set to 2 for display purposes