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

T. W. Scheenen[1], J. J. Fütterer[1], E. Weiland[2], P. van Hecke[3], M. Lemort[4], C. M. Zechmann[5], H-P. Schlemmer[6], D. R. Broome[7], G. M. Villeirs[8], J. Lu[9], J. O. Barentsz[1], S. O. Roell[2], and A. Heerschap[1]

[1]Radiology (667), Radboud University Nijmegen Medical Center, Nijmegen, Netherlands, [2]Siemens Healthcare, [3]University Hospital, Katholieke Universiteit Leuven, Belgium, [4]the Bordet Institute, Belgium, [5]German Cancer Research Center DKFZ, Germany, [6]University of Tuebingen, Germany, [7]Loma Linda University Medical Centre, United States, [8]Ghent University Hospital, Belgium, [9]Shanghai Changhai Hospital, China, People's Republic of

Introduction

In order to improve the non-invasive detection of cancer in the prostate, its location, heterogeneous extent, grade and stage, several MR techniques have been and are being explored. Among these proton MR spectroscopic imaging (^{1}H-MRSI) has shown promising results. Multiple studies showed significant differences in the metabolic state of different tissue types as depicted by ^{1}H-MRSI. Prostate cancer tissue is characterized by reduced levels of citrate (Ci) and increased levels of choline-containing compounds (Cho), which both are detectable *in vivo* with ^{1}H-MRSI. In the IMAPS (International Multi-Centre Assessment of Prostate MR Spectroscopy) study, the first steps are taken for ^{1}H-MRSI of the prostate to move beyond the status of site-specific expertise by validating its possibilities in a multi-centre setting. The primary objective of this study was to prove that ^{1}H-MRSI data allows for localizing prostate carcinoma in the two major anatomic areas of the prostate, i.e. the peripheral zone and the central gland.

Materials and methods

Ninety-nine patients with proven prostate cancer from 8 different institutions underwent T2-weighted MR imaging and 3D ^{1}H-MRSI with an endorectal coil at 1.5T. 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. After the MR exam, patients were treated with a prostatectomy, and the histopathological analysis of the resected prostates as provided by the pathology department of the local institution was the gold standard for the presence and location of cancer. Extensive details on the 3D ^{1}H-MRSI PRESS pulse sequence are described elsewhere (TR 650 ms, TE 120 ms, voxel size 0.64 cc, measurement time 10 to 12 minutes, [1]).

Based on the gold standard and the MRSI matrix overlaid on T2-weighted images, blinded to the spectra, two experienced radiologists independently classified at least 1 to a maximum of 4 independent voxels to 4 different tissues in the prostate; peripheral zone (PZ), central gland (CG), (peri-)urethral area (U), and cancer (PCa). Voxels assigned to PCa were additionally classified with a measure for tumor size (< 1voxel, 1 to 2 voxels, > 2 voxels) and for matching certainty (voxel possibly, probably or definitely inside tumor). The spectra from the selected assigned voxels were fitted in the time domain with model functions for the Ci, creatine (Cr) and Cho signals with the PRISMA software package [2]. The original spectrum together with the curve fit and residual plot were visually inspected by two spectroscopists. Spectra with a correct automatic frequency alignment of the resonances, without lipid signal contamination and baseline distortions around the resonances of interest, and minimal intensity in the residual plots, passed this quality check, and values for the (Cho+Cr)/Ci ratio (CC/C) were calculated as a marker for tumor tissue. In an ROC analysis the accuracy for distinguishing cancer from non-cancer tissue was calculated for the peripheral zone and the combined centra gland and peri-urethral area.

Results and discussion

The two radiologists classified 805 voxels to the different tissues in 99 patients. 70% of voxels in non-cancer tissue passed the quality check. As for PCa, the largest CC/C value within 5 mm of the classified voxel had been chosen to represent the tumor, 90% of voxels in cancer tissue had a representing voxel passing the quality check. The CC/C values for the selected voxels after the quality check are plotted in figure 1A, and summarized with median values for the

Tissue	PZ	CG	U	Pca
median CC/C	0.28	0.36	0.4	0.82

Table 1. Median (Cho+Cr)/Ci values for different tissues in patients with prostate cancer.

CC/C ratio in table 1. Median values for PZ, CG and PCa were significantly different (P<0.001, Dunn's multiple comparison test). Median CC/C values for CG and U did not differ significantly. Evaluating only PCa voxels across all participating institutions showed a statistically significant non-zero slope after linear regression of the CC/C value with radiological classification certainty (Fig. 1B) and cancer focus size (data not shown). Within non-cancer tissues, but between patients of different institutions, no statistically significant differences were found (Fig. 1C for the peripheral zone). The area under the ROC curve, discriminating between cancer and non-cancer tissue was 0.88 for PZ and 0.76 for the combined CG & U.

Conclusions

3D ^{1}H-MRSI of the prostate has outgrown the status of site-specific expertise: in patients with prostate cancer, recruited from different institutions, it is demonstrated to be a robust and quantitative technique, producing significantly different CC/C values for cancer compared to non-cancer tissue for both the central gland and the peripheral zone.
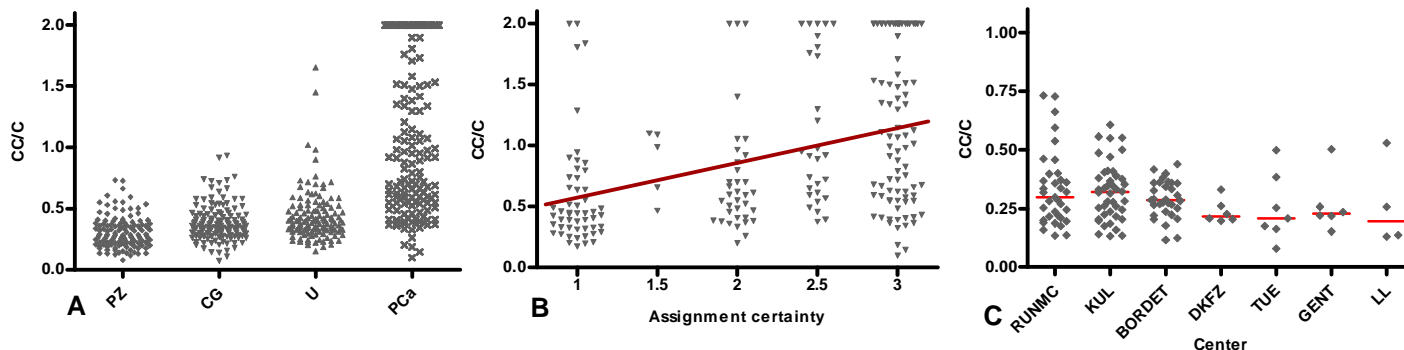
Figure 1. Distribution of CC/C values for three non-cancer tissues and PCa (classes 2 to 3) of selected voxels in patients with prostate cancer (A). Breakdown of all tumor voxels into assignment certainty classes, including a linear regression line (B). Distribution of CC/C values in non-cancer peripheral zone of patients contributed by different institutions (C). For display purposes the largest CC/C values in (A) and (B) are set to 2.0.