Reproducibility of 3D 1H MR spectroscopic imaging of the prostate at 1.5T.

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Introduction

The promising results of single institution studies of using proton MR spectroscopic imaging (^{1}H-MRSI) to improve the non-invasive detection and localization of cancer in the prostate have not yet led to a widespread application of the technique. One of the prerequisites for this is proof that the technique produces homogeneous and reproducible results in comparable patient groups of different institutions. 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 expand the status from site-specific expertise by validating its possibilities in a multi-centre setting. With ^{1}H-MRSI, prostate cancer tissue is characterized by reduced levels of citrate and increased levels of choline-containing compounds, summarized in the (choline+creatine)/citrate ratio (CC/C). Apart from evaluating results from single measurements of patients of different institutions, one of the objectives of this study was to estimate the reproducibility of the technique. Here we present an analysis of 10 subjects that were measured twice to report the robustness of the measurement technique itself.

Materials and methods

After signing an informed consent form, seven patients with prostate cancer and three young healthy volunteers were asked to undergo two MR imaging and spectroscopy examinations with an endorectal coil at 1.5T on two separate days (mean time between measurements: 9 days, range 1 to 58 days). After T2-weighted MRI in three orientations to delineate anatomy, 3D ^{1}H-MRSI with a PRESS pulse sequence with optimized 180º pulses was performed at an echo time of 120 ms for use on 1.5T Siemens Magnetom systems [1]. 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.

In these 10 subjects, based on axial T2-weighted images and an overlay of the MRSI matrix (but blinded for the spectra), an experienced spectroscopist allocated between 8 and 20 independent voxels to the same location in two measurements of the same subject. The spectra from all classified voxels were fitted in the time domain with model functions for the citrate, creatine and choline signals with the PRISMA software package [2]. A visual quality check consisted of inspection of the original spectrum together with the curve fit and residual plot. 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. The calculated values for the (Cho+Cr)/Ci ratio (CC/C) of the two separate measurements were used as input for a Bland Altman analysis, reporting the bias and standard deviation as a measure for the difference between two calculated CC/C values of one location in a repeated measurement.

Results and discussion

Seventy-seven voxels out of 136 initially assigned locations had spectra passing the quality check from both measurements. As the locations originate from both patients and healthy volunteers the full range of CC/C values was covered, with all values above 1 set to 1 for display purposes. In the Bland Altman analysis (fig. 1) the bias between the two repeated measurements was -0.01, whereas the standard deviation of the bias was 0.13 (95% Confidence interval of bias -0.27 to 0.25). The small bias indicates that there is no significant difference between the first and the second measurement in the subjects, as could be expected. The standard deviation of the bias is as small as the standard deviation of the mean value for the (Cho+Cr)/Ci ratio for healthy peripheral zone tissue in patients with prostate cancer (table 1, from the IMAPS study). Therefore, the difference in a repeated measure of the CC/C will generally be smaller
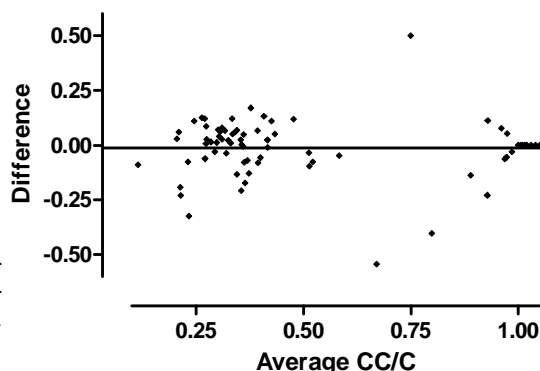

Figure 1. Bland Altman plot of the difference between two measurements in the CC/C ratio of 7 patients and 3 healthy volunteers. The bias in CC/C is -0.01 with a standard deviation of 0.13. CC/C values >1 are set to 1.

Tissue	PZ	CG	U
Mean CC/C	0.31	0.38	0.44
SD	0.13	0.15	0.21

Table 1. CC/C of non-cancer peripheral zone (PZ), central gland (CG) and peri-urethral area (U) in 99 patients with prostate cancer, taken from the IMAPS study.

(or the same for PZ) than the naturally occurring variation in non-cancer tissues of the prostate. By using the mean and standard deviation for healthy PZ to define thresholds for the CC/C using a 5-step standardized scoring system [3] ranging from definitely benign to definitely malignant, it was possible to visualize the repeated measurements according to their radiological score (figure 2). Most voxels reclassify with the same score (83%), or shift by only one class (13%).

Conclusions

3D ^{1}H-MRSI of the prostate is a reproducible technique. In repeated measurements the difference in CC/C ratio of the same locations is smaller than the naturally occurring differences in non-cancer tissues in the prostates of patients with prostate cancer. Differences in CC/C between different tissues or cancer can therefore indeed be attributed to the different metabolite concentrations in these tissues, rather than variation in the acquisition technique.
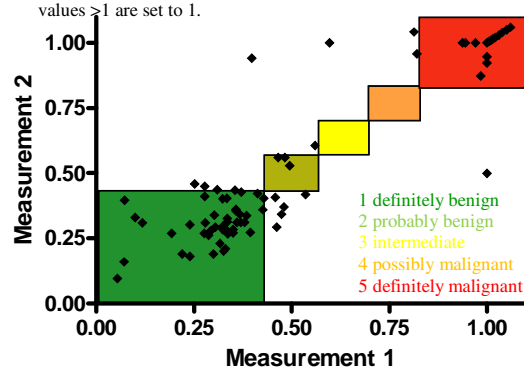

Figure 2. CC/C of the same location of the first measurement versus the second from voxels of 10 subjects. Green to red boxes indicate classification according to a standardized scoring system: green, definitely benign → towards red, definitely malignant.

References: 1. Scheenen T *et al*. Magn Reson Med 2004;52:80-88. **2.** Weiland E, University of Bremen and Siemens Medical Solutions. **3.** Futterer JJ, *et al*. Invest Radiol. 2007;42:116-22.