Correlation between cancer and altered proton MR spectroscopic imaging in the prostate's central gland

A. Moreno-Torres[1], A. Blanch[2], C. Arribas[3], J-M. Gil-Vernet Sedò[4], and I. Bonet-Palau[5]
[1]Research Department, Cetir Grup Medic, Esplugues de Llobregat, Spain, [2]Unitat Clinica El Pilar, Cetir Grup Medic, Barcelona, [3]Unitat Clinica El Pilar, Cetir Grup Medic, Barcelona, Spain, [4]Centro Gil-Vernet de Urología, Centro Médico Teknon, Barcelona, Spain, [5]Barcelona, Spain

Background and goals

During the last decade, proton MR spectroscopic imaging has shown high sensitivity and specificity for detecting prostate tumors of the Peripheral Zone (PZ) based on the elevation of choline-containing compounds (Cho) and the reduction of citrate (Cit) in cancerous tissue in areas with low signal intensity in T2-weighted MR imaging. Although most prostate cancers arise in the PZ, up to 30% of them may be found in the central gland. Cancer detection in such a location is difficult as the elevation of Cho and the reduction of Cit in cancerous tissue shows a broad range (1), and the area has low signal intensity similar to that of cancer and often contains benign prostatic hyperplasia (BHP), which may have a heterogeneous appearance. Moreover, in our experience, in some examinations the only voxels with altered spectra are found in the central gland. In this ongoing and retrospective work, our goal was to study the correlation between the observed alterations and the presence of cancer in the central gland. Such information is highly valuable in a clinical setting for the interpretation of the MRS findings.

Methods

To date, a subset of 23 subjects have been selected from patients referred to our institution for clinical examination between 2005-2007. The group included 12 subjects (age: 65.5 ± 9.9 years) with altered MRS in the central gland reported at the time of examination (reduced citrate and elevated choline) and 11 controls (age: 58.7 ± 7.6 years) with no alterations in the central or peripheral glands. Diagnosis was carried out by means of biopsy or step-section histology and, in all cases, follow-up was available. Three subjects of the altered MRS group were diagnosed with cancer (Adenocarcinoma, Gleason scores 2+2, 2 subjects, and 3+3, 1 subject). No cancer was diagnosed in the non-altered group, and a variable degree of BPH was seen to be present in all the prostates studied. MR imaging and spectroscopic imaging were acquired on a Signa 1.5 Tesla LX. system with Excite II (GE Healthcare, Milwaukee, WI) using the body coil for RF transmission and a combination of a pelvic phased-array coil (Torso PA; GE Medical Systems) with a commercially available balloon-covered endorectal coil (Endo ATD; Medrad, Pittsburgh, Pa) for signal reception. Proton spectra were collected throughout the prostate's entire volume using the manufacturer supplied PROSE sequence (PRESS volume selection with fat and water saturation; 1000/130 ms; studied volume, 110 x 55 x 55 mm; matrix, 16 x 8 x 8 resulting in 1024 voxels with a spatial resolution of 0.32 cm3; scan time, 17 minutes). Spectral data were aligned with axial T2-weighted multiple spin echo images (4740/82.3 ms; echo train length, 16; field of view, 14 cm; section thickness, 3 mm; no section gap; number of acquisitions, 4) using Functool-2 (GE Healthcare, Waukesha, WI) and spectra automatically post-processed, reconstructed and quantified with such commercial software. Spectra from voxels including the urethra, ejaculatory ducts or the veru montanum were excluded from the subsequent analysis. Within the altered MRS group, data analysis included the comparison of the altered Cho+Cr/Cit ratios between the cancer and non-cancer subgroups (Mann-Whitney U test) and the evaluation of the presence of spectral patterns suggesting malignancy (Figure 1) and correlation with the presence of cancer (Chi-square test).

Results

Analysis of the 1621 quantifiable spectra of controls produced a Cho+Cr/Cit ratio of 0.49 ± 0.14 (mean ± SD), range 0.164-1.58, and 19 outliers with a ratio value higher than 0.91 (mean + 3 SD) but with spectral patterns showing no elevated choline. Taking 0.91 as a reference, spectra showing higher values were defined as altered. From the 2729 central gland quantifiable spectra within the altered MRS group, a 10.8% (296 spectra) showed ratios higher than 0.91. At an individual level, this supposed alterations in 1-74 spectra per prostate, corresponding to 0.9-42.3 % of total central gland spectra. Within the altered MRS group, although the comparison of the Cho+Cr/Cit ratio between the cancer and non-cancer subgroups showed statistically higher values in the cancer subgroup, there was too much overlap to differentiate cancer and non-cancer prostates (Figure 2). Nor did the proposed MRS malignancy patterns allow such differentiation as no preferred distribution between the cancer and non-cancer subgroups was observed (Table 1). Consequently, the Chi-square test correlation analysis showed no relationship between the presence of cancer and spectra with patterns suggesting malignancy in any of the MRS malignancy patterns studied.

Conclusions

Prostates with Cho+Cr/Cit ratio values higher than 0.91, in our experimental setup, and/or MRS malignancy patterns in the prostate's central gland included both cancer and non-cancer prostates, which could not be differentiated by the ratio values or a preferred distribution of MRS malignancy patterns. In our opinion, such data, together with the real percentages of cancer true and false positives, and the pathologies behind the false positives, is highly relevant information when interpreting and reporting MR spectroscopic alterations in the central gland and merits the analysis of a larger number of cases.

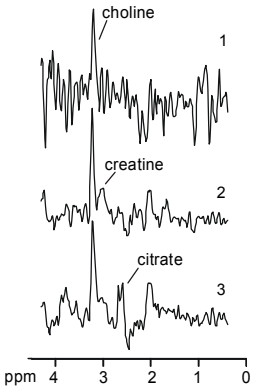

Figure 1. Examples of spectral patterns suggesting malignancy in the prostate central gland. 1, only choline and no citrate as suggested by Zakian et al (1); 2, high choline, little creatine, no citrate; 3, high choline, little creatine, little citrate (< ½ choline).

	pattern 1	patterns 1+2	patterns 1+2+3
Cancer (n=3)	1 (16.2)	1 (35.1)	3 (0.3-59.5)
non-Cancer (n=9)	4 (2.2-34.5)	5 (6.7-39.7)	7 (8.3-42.4)

Table 1. Distribution of MRS malignancy patterns in cancer and non-cancer subgroups with altered MRS. Data refer to number of patients and, in brackets, the percentage of spectra showing patterns from the total altered spectra.

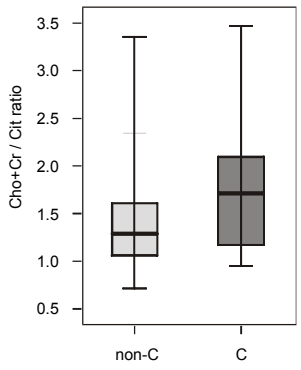

Figure 2. Comparison of Cho+Cr/Cit ratios in subjects with altered proton MR spectroscopic imaging. "C", cancer subgroup (63 spectra); "non-C", non-cancer subgroup (145 spectra). Box-and-whisker plots are shown for each group. Statistically significant differences were present (Mann-Whitney U test, Z = -3.612, p=0.0003).

References: 1. Zakian KL et al. Transition Zone Prostate Cancer: Metabolic Characteristics at ^{1}H MR Spectroscopic Imaging-Initial Results. Radiology 229: 241–247, 2003.