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CLINICAL INVESTIGATION **Prostate**

TUMOR VOLUME AND METABOLISM OF PROSTATE CANCER DETERMINED BY PROTON MAGNETIC RESONANCE SPECTROSCOPIC IMAGING AT 3T WITHOUT ENDORECTAL COIL REVEAL POTENTIAL CLINICAL IMPLICATIONS IN THE CONTEXT OF RADIATION ONCOLOGY

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Purpose: To determine whether a relationship exists between the tumor volume (TV) or relative choline content determined using magnetic resonance spectroscopy imaging (MRSI) at 3T and the clinical prognostic parameters for patients with localized prostate cancer (PCa).

Methods and Materials: A total of 72 men (mean age, 67.8 ± 6.2 years) were stratified as having low-risk (n = 26), intermediate-risk (n = 24), or high-risk (n = 22) PCa. MRSI was performed at 3T using a phased-array coil. Spectra are expressed as the total choline/citrate, total choline plus creatine/citrate, and total choline plus polyamines plus creatine/citrate ratios. The mean ratio of the most pathologic voxels and the MRSI-based TV were also determined.

Results: The mean values of the total choline/citrate, total choline plus creatine/citrate, and total choline plus polyamine plus creatine/citrate ratios were greater for Stage T2b or greater tumors vs. Stage T2a or less tumors: 7.53 ± 13.60 vs. 2.31 ± 5.65 (p = .018), 8.98 ± 14.58 vs. 2.56 ± 5.70 (p = .016), and 10.32 ± 15.47 vs. 3.55 ± 6.16 (p = .014), respectively. The mean MRSI-based TV for Stage T2b or greater and Stage T2a or less tumors was significantly different (2.23 ± 2.62 cm^3 vs. 1.26 ± 2.06 cm^3, respectively; p = .030). This TV correlated with increased prostate-specific antigen levels (odds ratio, 1.293; p = .012). Patients with high-risk PCa had a larger TV than did the patients with intermediate-risk PCa. A similar result was found for the intermediate-risk group compared with the low-risk group (odds ratio, 1.225; p = .041).

Conclusion: Biomarkers expressing the relative choline content and TV were significant parameters for the localization of PCa and could be helpful for determining the prognosis more accurately.

Prostate cancer, Magnetic resonance spectroscopic imaging, Radiation oncology, Tumor volume, Biomarkers.

INTRODUCTION

Prostate cancer (PCa) is the most common noncutaneous cancer and the second most common cause of cancer-related deaths in European and North American men (1, 2). Although endorectal magnetic resonance imaging (MRI) has widely been used for the detection and localization of PCa, even this modality has been found to be limited because of unsatisfactory sensitivity and specificity (3–7). However, the introduction of proton magnetic resonance spectroscopic imaging (MRSI) has shown great potential as an addition to conventional MRI in the localization of PCa (8–13).

Magnetic resonance spectroscopic imaging allows the assessment of tumor metabolism by displaying the relative concentrations of total choline, creatine, polyamine, and citrate. Differences in the concentrations of these metabolites could allow for better tumor localization, thereby decreasing inter-observer variability (10, 11).

Although the use of an endorectal coil is indispensable at 1.5T, endorectal coils have several disadvantages, especially

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when preceding radiation oncology applications and when several follow-up examinations are planned. More importantly, the presence of an endorectal coil will significantly deform the prostate gland, thereby making co-registration of images with other imaging and therapeutic modalities difficult (14).

At higher fields, it has been suggested that external phased-array coils might provide sufficient signal/noise ratio and adequate spectral and spatial resolution to alleviate the need for endorectal coils for both MRI and MRSI (15–17). The addition of MRSI/MRI to clinical models for predicting pathologically cancerous tissues has resulted in significant improvement compared with models using clinical parameters alone (18). In this context, we hypothesized that MRSI at 3T without an endorectal coil could provide greater patient compliance and more useful complementary information to clinicians on the extent or the aggressiveness of tumors in patients with PCa selected for radiotherapy or brachytherapy.

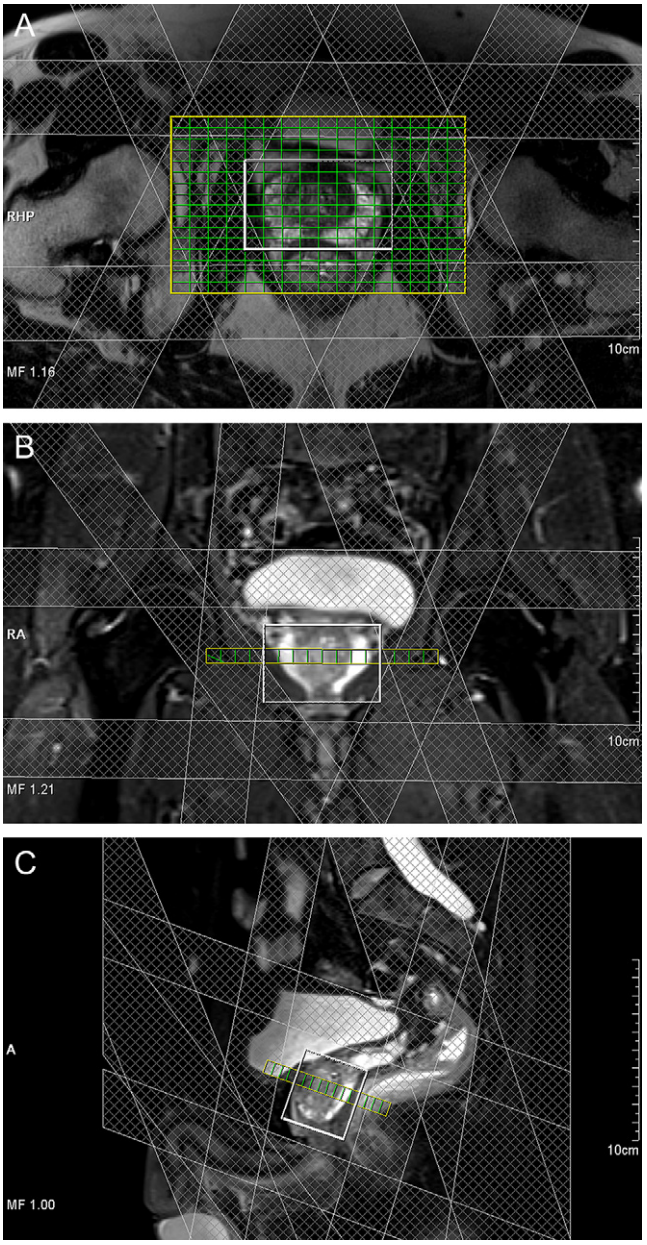

Fig. 1. Position of spectroscopic grid with respect to prostate form and orientation. (a) Axial, (b) coronal, and (c) sagittal T_2-weighted magnetic resonance images showing placement of water- and lipid-suppressed double-spin-echo point-resolved spectroscopic sequence box (box around prostate) and outer volume saturation bands (crosshatched bands). Partition of three-dimensional interpolated 1H-magnetic resonance spectroscopic imaging matrix (yellow box) was superimposed. Outer volume saturation labs extend into water- and lipid-suppressed double-spin-echo point-resolved spectroscopic sequence selected volume of interest (white box).

METHODS AND MATERIALS

Study subjects

Between December 2006 and November 2008, 323 men underwent combined MRI/MRSI of the prostate. From this population, we retrospectively identified 82 men with biopsy-proven untreated PCa with complete clinical data (TNM stage, pretreatment prostate-specific antigen (PSA) level, and Gleason score). The International Union Against Cancer (2002) classification was used to grade tumors from T1a to T1c for tumor in ≤5% of resected tissue, >5% of tumor in resected tissue, and needle biopsy-proven cancer, respectively. Stage T2a to T2c indicates tumor involving one-half of a lobe, one lobe, and both lobes, respectively. Stage T3 indicates tumor that has infiltrated the capsule. The MRI/MRSI examinations were performed ≥8 weeks after the most recent biopsy. Ten patients out of the 82 patients were excluded from the study because the MRSI data were deemed to be of insufficient quality. The prostate volume was determined using MRI and a simple manual planimetric method on axial three-dimensional (3D) T_2-weighted images. Our institutional committee on human research approved the study, with a waiver for the requirement for written consent, because MRSI was included in the workup procedure for all patients referred for brachytherapy or radiotherapy. The mean age of the 72 men was 67.8 years (range, 55–79.6). Before imaging, a Microlax enema was administered to the patients to assist bowel emptying. Peristalsis was also suppressed with an intravenous injection of phloroglucinol. The tumor stage was Stage T1b in 4 patients, T1c in 28 patients, T2a in 14 patients, T2b in 11 patients, T2c in 4 patients, T3a in 10 patients, and T3b in 1 patient. Pathologic extracapsular extension was identified in the biopsy specimens in 7 patients. The median tumor Gleason score was 6 (range, 5–8). The mean serum PSA level before hormonal therapy or radiotherapy was 12.9 ng/mL (range, 2.8–68 ng/mL). The percentage of positive biopsy cores was defined with respect to the total number of cores obtained in each patient and was available for 62 patients. The average percentage of positive biopsy cores was 35% (range, 2–100%). The average prostate volume was 42.4 cm^3 (range, 17–108). Using the prognostic classification described by D'Amico *et al.* (19), the patients were assigned to a risk group (Table 1), as commonly performed in radiation oncology. The patient and tumor characteristics classified by group risks are summarized in Table 1.

Pathologic evaluation after prostatectomy and image correlation

A separate subgroup of 12 patients, who had undergone radical prostatectomy as a part of their treatment, was used solely with the aim of defining a 5-point classification scheme for use with the principal study population. Therefore, we matched the anatomic and pathologic data to MRI and MRSI from this subgroup. The specimens were step sectioned and stained with hemalun-eosin-saffron. The slice thickness was about 4–5 mm. The cancer foci were outlined in ink on whole-mount step-section pathologic slices