Hormone Ablation of Localized Prostate Cancer: Effects of Duration of Therapy on Prostate Metabolism Demonstrated by 3D 1H MR Spectroscopy

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Purpose
The goals of this study were to assess the rates of metabolic atrophy in healthy and cancer-bearing tissue with 3D 1H MR spectroscopy (MRSI) and to determine metabolite ratio cutoff levels for the differentiation of healthy and cancer-bearing tissue for different durations of hormone ablation therapy for localized prostate cancer.

Introduction
Hormone ablation of localized prostate cancer has become an important neoadjuvant therapy which precedes either radical prostatectomy or radiation therapy (1,2). Due to the availability of different types of therapy for localized prostate cancer, staging information becomes necessary not only prior to, but also after the commencement of neoadjuvant hormone ablation. Precise information on tumor presence, tumor extent, and tumor location can be obtained from MRI and MRSI of the prostate with a combined endorectal and pelvic phased-array coil system in patients with prostate cancer who have not undergone hormone ablation (3,4). While cutoff levels have been determined for the (choline+creatine)/citrate ratio in the differentiation of healthy and cancer-bearing tissue in the peripheral zone of the prostate in previously untreated patients (5), it is unclear if the same cutoff values apply to patients under neoadjuvant hormone ablation therapy.

Methods
This retrospective, cross-sectional study is based on data gathered during combined endorectal/phased array coil MRI and 3D 1H MRSI examinations performed between March, 1996, and June, 1998, in 88 patients with localized prostate cancer proven by transrectal ultrasound-guided biopsy. Twenty patients (controls; n=54) for various durations (0--6 weeks, 18 patients, n=332 weeks and >16 weeks of hormone ablation therapy for localized prostate cancer. Since citrate production is under hormone control, it is more severely affected by hormone ablation than choline and creatine. Cutoff levels for (choline+creatine)/citrate in healthy prostate tissue, 2SD above average, do not differ between untreated patients and patients with <6 weeks of hormone ablation. Cutoff levels increased for 7--16 weeks (0.41f0.32 from 72% of patients) and >16 weeks (0.40f0.21 from 36% of patients) of hormone ablation, mainly due to decreased citrate peak areas. In patients without detectable citrate (17% <6 weeks, 28% 7--16 weeks, 64% >16 weeks), detectable choline [(choline+creatine)/mean noise >5] implied cancer. The overlap between metabolite ratios for healthy and cancer tissues increased with duration of hormone therapy due to increased variance of metabolite ratios in both groups.

Conclusion
Metabolic atrophy is a duration-dependent feature of hormone ablation therapy for localized prostate cancer. Since citrate production is under hormone control, it is more severely affected by hormone ablation than choline and creatine. Cutoff levels for (choline+creatine)/citrate in healthy prostate tissue, 2SD above average, do not differ between untreated patients and patients with <6 weeks of hormone ablation. Cutoff levels increased for 7--16 weeks and >16 weeks of hormone ablation. For patients who demonstrate total loss of citrate, the existence of detectable choline levels may be used to infer the presence of cancer tissue.

References