

# Quantification of prostate metabolites at 3 T using water as the internal reference

Jan Weis<sup>1</sup>, Francisco Ortiz-Nieto<sup>1</sup>, and Håkan Ahlström<sup>1</sup>

<sup>1</sup>Department of Radiology, Uppsala University Hospital, Uppsala, Sweden

## Introduction

The measurement of prostate metabolite concentrations holds potential promise for the monitoring of treatment efficacy associated with the effects of radiotherapy and hormone-deprivation therapy. It has been demonstrated that the intensities of MRS detectable metabolites such as, choline (Cho), polyamines (PA), creatine (Cr), and citrate (Cit) decreases with increasing exposure during therapy. Moreover, Cit resonances usually are undetectable by the end of either therapies [1, 2]. Henceforth, any quantification based on metabolite-to-Cit spectral intensity ratios becomes useless. Normalization of Cho, PA, and Cr intensities to unsuppressed water-line offers the only viable option. Notwithstanding, there still remains the additional complication of fitting overlapped Cho, PA, and Cr resonances between ca 2.9 and 3.3 ppm. Indeed, neither Cr nor PA can be reliably fitted in standard 3 T MRSI spectra [3, 4]. In light of these shortcomings, the aim of the present study was two-fold: (i) to measure the high-quality single-voxel (SV) spectra of the normal and the cancerous prostate using a surface coil, and (ii) to estimate Cho, Cit and Cr concentrations.

## Materials and Methods

Eight healthy volunteers and 16 patients with biopsy-proven prostate carcinoma were included in the study. The median age of healthy volunteers and patients was 55 (range, 52-64), and 64 years (range, 57-72), resp. The Gleason score ranged between (2+3) and (4+5). All measurements were performed with a 3 T scanner (Philips, Achieva) using a circular, two-element, receiver surface coil (loop size 20 cm). SV spectra were measured using a PRESS sequence (TR/TE 1500/140 ms; BW 2000 Hz; 1024 points; 16 phase cycle steps). 16 non-water suppressed scans were followed by 192 water-suppressed acquisitions. Net measurement time was 5 min and 15 s. Water suppression was achieved using band-selective pre-pulses followed by a BASING pulse [5]. Fat suppression was performed using a frequency-selective inversion recovery pre-pulse. The largest possible voxel size inside the prostate was chosen. Mean voxel size was  $14.9 \pm 5.7 \text{ cm}^3$ .

Metabolite-to-unsuppressed water spectral intensity ratios were determined by fitting, using LCModel v. 6.2-4 [6]. Patient spectra were classified as healthy (H), ambiguous (A), suspicious (S), and very suspicious (VS) for cancer, according to the standard deviation (SD) of mean of the (Cho+PA+Cr)/Cit ratio of healthy volunteers [7, 8]. Reference concentration 39.4 M of water in the prostate was used in the estimation of the absolute concentrations [9]. Relaxation corrections were performed using literature values:  $T_1$  1.6 s,  $T_2$  74 ms for water in healthy prostate [10], and  $T_2$  109 ms in tumor (VS spectra) [11];  $T_1$  1.1 s and  $T_2$  220 ms for Cho and Cr; and  $T_1$  470 ms and  $T_2$  170 ms for Cit [12]. Since Cr relaxation times  $T_1$  and  $T_2$  at 3 T are unknown, Cho values were used for Cr. This approximation is based on the fact that both  $T_1$  and  $T_2$  values of Cho and Cr are very close to one another at 1.5 T [13]. Baseline and phase corrected spectra were normalized by summing the squares of the intensities of each spectral point and then dividing the amplitude of each point by the square root of this sum [14]. Mean H (n = 8), and VS (n = 5) spectra were computed by averaging the values at each data point.

## Results

Cho, PA, Cit, and even Cr peaks were fitted with %SD < 40%. Figure 1a shows mean normalized spectrum, LCModel fits, and SDs of 8 healthy volunteers. Correspondent mean VS spectra of 5 patients are shown in Figure 1b. Figure 2 depicts relaxation effects uncorrected Cho-, Cr-, and Cit-to-water spectral intensity ratios. Mean absolute concentrations (mM) were estimated: healthy volunteers Cho  $1.9 \pm 0.2$ , Cr  $3.4 \pm 0.8$ , and Cit  $21.3 \pm 4.4$ ; patients with VS spectra Cho  $2.9 \pm 0.2$ , Cr  $4.2 \pm 1.1$ , Cit  $11.6 \pm 5.2$ . Figure 3 typifies patient spectra in which the water normalization approach is inevitable, as a result of the missing or unreliable Cit intensity. Figure 3a shows the spectrum of an aggressive cancer (Gleason score (4+5), and Cho 20.7 mM). Figure 3b exemplifies the spectrum of a patient after unsuccessful brachytherapy (Gleason score (4+5), Cho 1.6 mM, and Cr 2.3 mM).

## Discussion

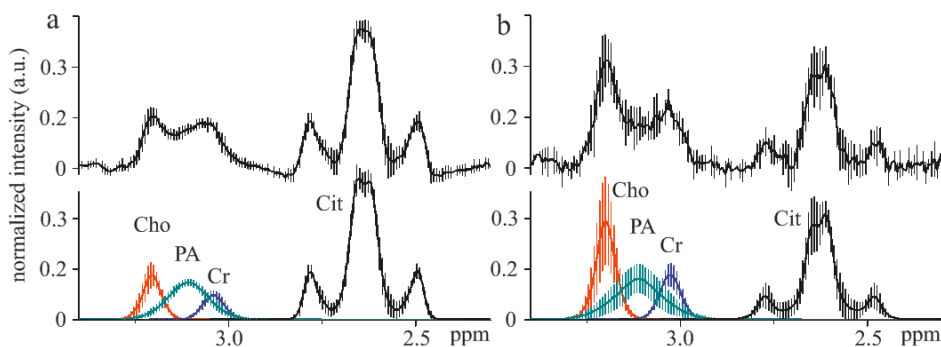
This is the first study in which prostate Cr absolute concentration was quantified. SNR ratio and spectral resolution was high enough for reliable fitting of the metabolites under question. Cho and Cit concentrations of healthy volunteers are in good agreement with the previous studies [3, 9], taken into account SDs. Though the SV approach is unable to differentiate peripheral zone from central gland, concentration estimates can serve as a reference to MRSI. The most significant source of errors lies in the concentration of the water and the unknown relaxation times in the lesions (mixture of healthy and cancerous tissue). Water concentration in tumors is increased by as much as 25% compared to normal tissues [14]. Hence, tumor metabolite concentrations can be underestimated by as much. The lower Cho/H<sub>2</sub>O and Cr/H<sub>2</sub>O ratios, when compared to the healthy prostate (Fig. 2), can be explained by the dilution of metabolites through increased water content. The main utility of the SV approach lies in its ability to globally characterize the prostate tissue, monitoring therapeutic effects, and tumor relapse detection.

## Conclusion

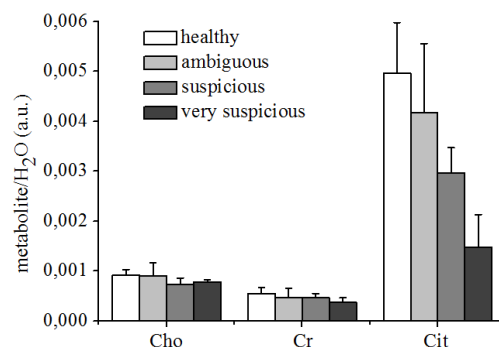
Prostate Cr absolute concentration was quantified for the first time. Single-voxel MRS of the prostate at 3 T using a surface coil is an uncomplicated and readily amenable method for estimation of metabolite concentrations.

## References

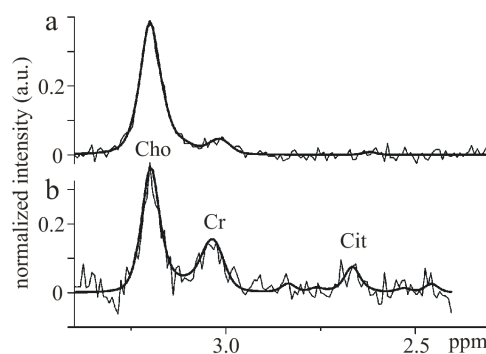
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**Fig. 1:** Mean normalized prostate spectra and LCModel fits of (a) 8 healthy volunteers and (b) 5 patients classified as very suspicious for cancer.



**Fig. 2:** Cho-, Cr-, and Cit-to-water spectral intensity ratios. Ratios were not corrected for relaxation effects.



**Fig. 3:** (a) Spectrum of aggressive prostate cancer, (b) spectrum of another patient after unsuccessful brachytherapy.