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Prostate 1H-MRS spectroscopy: comparison of 1.5T endorectal three dimensional MRS vs. 3T MRS using a surface coil

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Summary

Background: The aim of this study was to compare prostate 1H-MRS spectrum obtained with a surface coil at 3T and at 1,5T system with an endorectal coil. Chemical shift and possibility of metabolite characterization present in the prostate gland were taken into consideration.

Material/Methods: Our study comprised 15 randomly chosen patients (age 51-77 years, mean 66.2±7.7). 1HMRS examination was performed using an endorectal coil (Medrad) with 1,5T (Siemens Avanto) scanning unit. Our study additionally included 15 patients (age 52-77 years, mean 66.3±7.7) whose examination was performed with a 6-channel surface coil at 3T (Philips Avanto) system.

Evaluated factors: 1. resolution – understood as the possibility to resolve Cho (3.2 ppm) and Cr (3 ppm) peaks; 2. character of Cit peak (2.6 ppm); 3. spermine detection (3.1 ppm).

Results: Among spectrums obtained at 1,5T using an endorectal coil in 54/150 (36%) Cho (3.2 ppm) and Cr (3 ppm) peaks were clearly separated. In 94/150 (64%) Cho (3.2 ppm) and Cr (3 ppm) peaks were not resolved – visible as overlapping peaks. In all Cit (2.6 ppm) spectrums, the peak was visible as a singlet or as a nonsymmetrical shape singlet. The spermine peak (3.1 ppm) was not detected in any spectrum.

In all 150/150 (100%) spectrums obtained at 3T using a 6-channel surface coil, Cho (3.2 ppm) and Cr (3ppm) peaks were clearly resolved, visible as separated peaks. In 137/150 (91%) Cit (2.6 ppm) resonance was visible as a triplet or as a triplet with a nonsymmetrical central peak. In 10/150 (6,6%) spectrums, a spermine peak (3.1 ppm) was detected.

Conclusions: 1. Prostate examination using a surface coil at 3T allows to obtain a spectrum of the same or better quality in comparison with a spectrum obtained at 1,5T using an endorectal coil. 2. Cho and Cr peaks separation is statistically significantly more possible at 3T than at 1,5T; 3. Cit peak was always visible as a multiplet at 3T and never at 1,5T; 4. Spermine peak was detected in 10/150 spectrums (6.6%).

Key words: 1H-MRS of prostate • endorectal coil • Cho • Cr peaks separation

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Background

During the recent years, 1H-MRS spectroscopy came out of the laboratory and became a valuable tool in clinical diagnostics – especially in brain pathologies [1]. There is an increasing interest in 1H-MRS prostate spectroscopy [2], MRS of the liver and breast applications [3]. 1H-MRS allows, in a non-invasive way, to detect molecules, which are fingerprints of prostate metabolism.

CSI method (Chemical Shift Imaging), which is used in prostate more often than SVS, covers the whole prostate gland.

In 1H-MRS examination one can observe a resonance of citrate (Cit 2,6 ppm), choline-containing compounds (Cho 3,2 ppm) and creatine-phosphocreatine complex (Cr 3 ppm). In a healthy prostate, within each voxel, citrate (2.6 ppm) peak dominates. In prostate cancer, increased signal intensities of Cho compared to Cit can be observed. Cho is thought to be a marker for increased membrane turnover or higher cellular density [4] and Cr is a marker for energy metabolism.

Based on this characteristic metabolic feature of cancer tissue, clinical studies have shown that combined MRI/MRSI enables improved tumor detection and localization [5]. Diagnostic MRSI as an adjunct to conventional MRI can improve specificity of peripheral zone tumors detection [6]: from 46%-61% up to 91% reported by Scheidler [7], from 58.3% up to 82.1% reported by Yuen [8] and from 56% up to 81% reported by Casciani [9].

Prostate 1H-MRS can be indicated in evaluation of patients with suspicious PSA levels but negative biopsy, providing improved tumor localization and support for following targeted biopsy [10]. 1H-MRS was found helpful also in evaluation of patients with rising PSA levels during follow-up after therapy: improved detection and localization of local recurrence [11].

In prostate spectroscopy examination the main application is CSI_3D, which covers the whole prostate gland in time similar or a little bit longer than single voxel acquisition.

The aim of this study was to compare prostate 1H-MRS spectrum obtained with a surface coil at 3T and at 1.5T system with an endorectal coil. Chemical shift and possibility of characterization of the metabolites present in the prostate gland were taken into consideration.

Materials and methods

Our study consisted of 15 randomly chosen patients (age 51-77 years, mean 66.2±7.7). 1H-MRS examination was performed by using an endorectal coil (Medrad) with a 1.5T (Siemens Avanto) scanning unit. Our study additionally included 15 patients (age 52-77 years, mean 66.3±7.7) whose examination was performed with a 6-channel surface coil at 3T (Philips Avanto) system. Among the patients examined at 1.5T 12 were healthy subjects not treated in any way, and 3 receiving external beam radiotherapy. None of 15 patients examined at the 3T system were treated for a prostate tumor before MR examination.

The acquisition was performed with the following parameters (according to [12, 13]) depicted in tab. 1:

Quantification analysis and post processing were performed with software provided by the manufacturer.

Our analysis included only spectrums recognized as diagnostic. The following criteria were taken into account: SNR (signal-to-noise ratio) above 5, flat baseline within the spectrum range 2-4 ppm, no visible artifacts. Our study consisted of 10 voxels from 1 slice from CSI_3D acquisition – 300 spectrums altogether: 150 obtained at 1.5T and 150 obtained at 3T system.

Evaluated factors:
4. resolution – understood as possibility to resolve Cho (3.2 ppm) and Cr (3 ppm) peaks;
5. character of Cit pear (2.6 ppm);
6. spermine detection (3.1 ppm).

Results

Among spectrums obtained at 1.5T using an endorectal coil, in 54/150 (36%) Cho (3.2 ppm) and Cr (3 ppm) peaks were clearly identified [Fig. 1]. In 94/150 (64%) Cho (3.2 ppm) and Cr (3 ppm) peaks were not resolved – visible as overlapping peaks. In all Cit spectrums (2.6 ppm), the peak was visible as a singlet or as a nonsymmetrical shape singlet [Fig. 2]. Spermine peak (3.1 ppm) was not detected in any spectrum.

In all 150/150 (100%) spectrums obtained at 3T using a surface 6-channel coil, Cho (3.2 ppm) and Cr (3 ppm) peaks were

Table 1. Acquisition parameters.

Parameter	3T *	1.5T
TE/TR [ms]	140/1500	120/690
Acquisition voxel /reconstruction voxel [mm]	10x10x12/ 5x5x12	6,7x6,7x6,7/6,7x6,7x6,7
Bandwidth [Hz]	2000	1300
Sequence	SE PRESS CSI_3D	SE PRESS CSI_3D
NSA	1	6
Water suppression/FAT suppression	Yes/Yes	Yes/Yes
Coil type	SENSE_Cardiac_6	Endorectal
Rest slabs	No	Yes
Buscopan injection	Yes	Yes
Acquisition time	6:30-8min (depending on the resolution)	6-8 min

SE – Spin Echo, PRESS – Point Resolved Spectroscopy

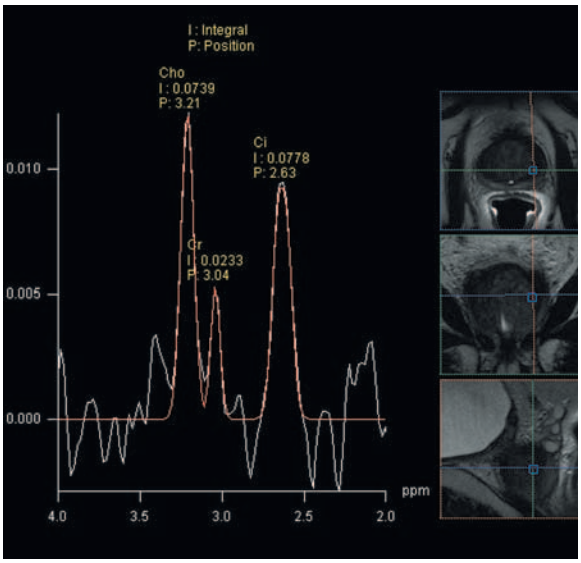


Figure 1. Good quality spectrum. No artifacts found. Cho Ci and Cr are well separated. Endorectal coil, 1,5T.

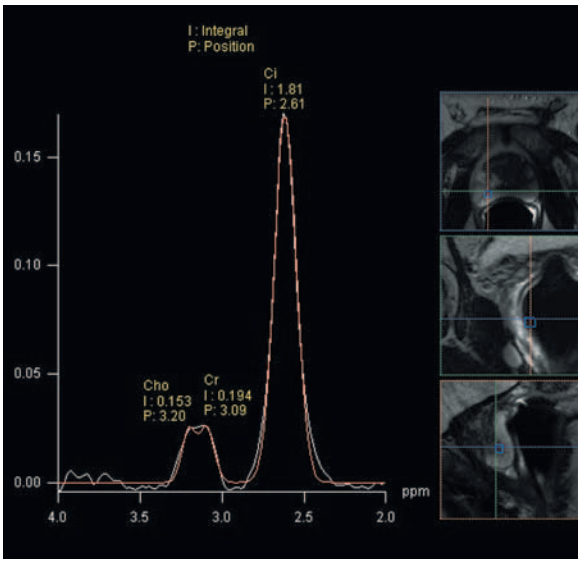


Figure 2. Cit (2.6 ppm) peak visible as a singlet or as a nonsymmetrical shape singlet. Typical spectrum from a healthy patent at 1.,5T. Cit peak dominates. Cr and Cho impossible to resolve. Endorectal coil, 1.5T.

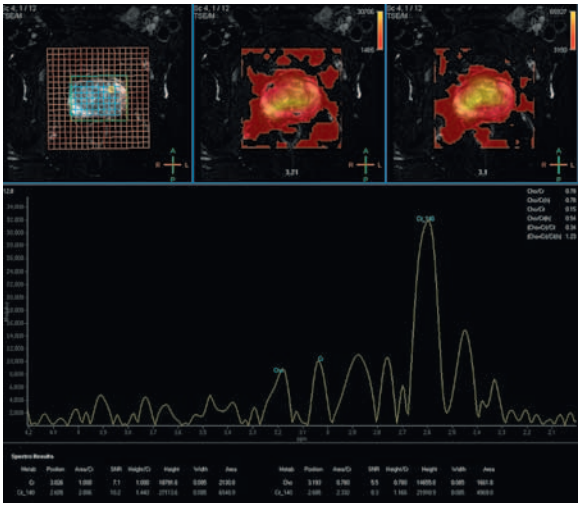


Figure 3. An example of a spectrum obtained at 3T,with a surface coil. Citrate visible as a triplet with an asymmetric central peak - probably including two overlapping peaks.

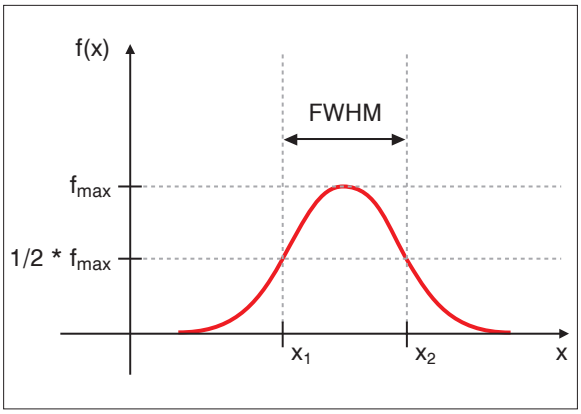


Figure 4. FWHM - Full Width at Half Maximum - in Hz or ppm. The higher FWHM value, the wider the peak is.

clearly resolved, visible as separated peaks. In 137/150 (91%) Cit (2.6 ppm) resonance was visible as a triplet or as a triplet with a nonsymmetrical central peak [Fig. 3]. In 10/150 (6,6%) spectrums, spermine peak (3.1 ppm) was detected.

Statistical analysis, carried out with Statistica 7 software, showed that with p=0,000002 it can be stated that spectrums obtained at 3T using a surface coil provide better chance to resolve Cho (3.2 ppm) and Cr (3 ppm) peaks than spectrums obtained using an endorectal coil at 1.5T.

This advantage enables calculation of integral under the specific metabolite peak.

Visualization of complex nature of Cit (2.6 ppm) as a multiplet and spermine detection are also significantly (p<0.001) more possible using a surface coil at 3T as compared to results obtained with an endorectal coil at 1.5T.

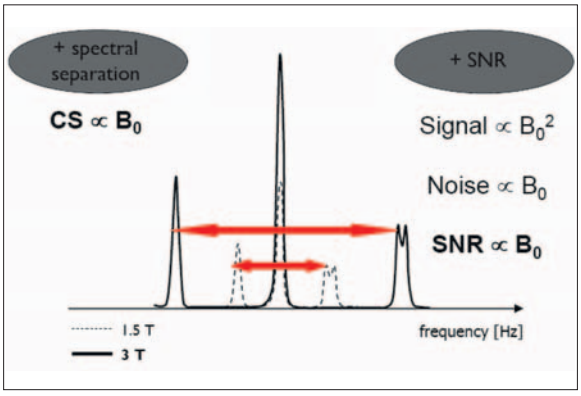


Figure 5. Comparison of spectrums obtained at 3T (solid line) and 1.5T (dashed line). The distance between peaks is doubled for 3T compared to 1.5T. That means better resolution is achievable.

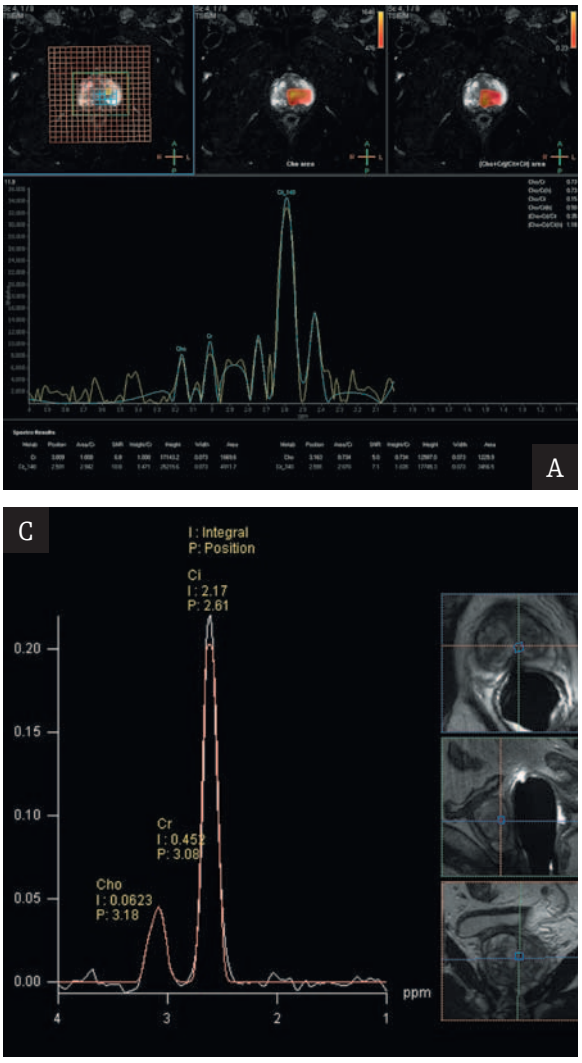


Figure 6. Comparison of spatial resolution a) spectrum obtained at 3T in ppm, b) spectrum obtained at 3T in Hz, c) spectrum obtained at 1,5T in ppm d) spectrum obtained at 1,5T in Hz. Spectrums a) and b) are wider than spectrums c) and d), respectively. a) spectrum range 1-4ppm (3T); b) spectrum range ~140Hz- ~500Hz (3T); c) spectrum range 1-4ppm (1.5T); d) spectrum range ~50Hz-~250Hz.

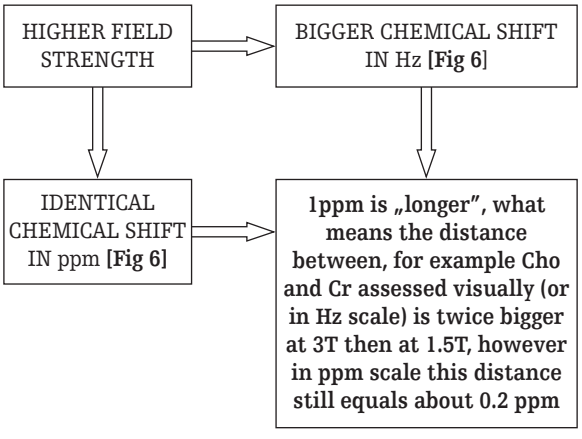
Discussion

Spectrum resolution, understood as the distance between neighboring peaks, depends on magnetic field strength. Spectrum resolution is better at higher field strength because of direct proportional dependence of chemical shift and field strength.

Nevertheless, peak width slightly increases with field strength, which can cause some problems with resolving closely located peaks. The peak width visible at MRS examination is depicted as Full Width at Half Maximum (FWHM) [Fig. 4]. FWHM is a function of T2 time and field homogeneity. Shorter T2 time at 3T compared to field strength of 1.5T means faster signal decay. The final result of Fourier transformation (a mathematical tool that converts data from time domain to frequency domain, for example spectrum, image) of faster decaying signal is a wider peak, which can cause troubles with resolving closely located peaks like Cho (3.2 ppm) and Cr (3 ppm). FWHM (the higher value of FWHM, the wider the peak) is also a function of field homogeneity. In a very homogenous field peaks become narrower. Improving field homogeneity is called shimming. In SVS acquisition, FWHM is in the order of few Hz and in CSI in the order of several Hz (5-15Hz).

To summarize:
Field strength [T]↑=T2 time ↓= FWHM ↑= wider peak
"better" shimming= ↓FWHM=narrower peak
field strength [T] ↑= crucial shimming

Peaks localization is depicted on X axis with Hz or ppm (part per million) units.



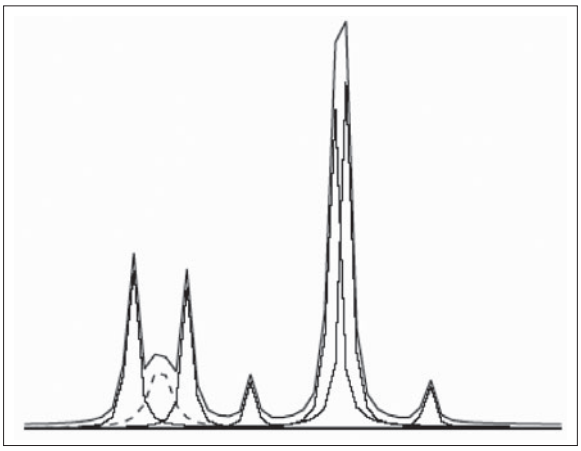


Figure 7. A simulated normal tissue spectrum shown in detail: the upper thick line represents the total spectrum, the individual resonances are drawn in thin lines. The resonance of the polyamines, which has a larger line width than the other resonances, is drawn dashed. The overlap between choline, creatine and polyamines can be seen clearly. Figure taken from P. Pels.

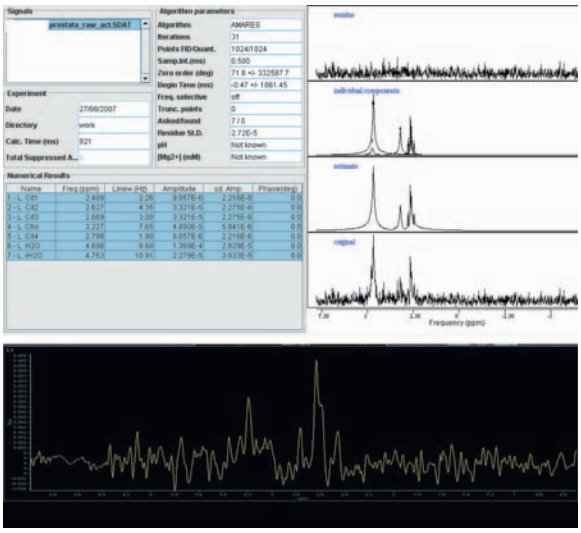


Figure 8. Example of prostate spectrum analysis obtained at 3T with jMRUI software. Residual water signal, choline (Cho) and a Cit quartet of 1:3:3:1 intensity are visible.

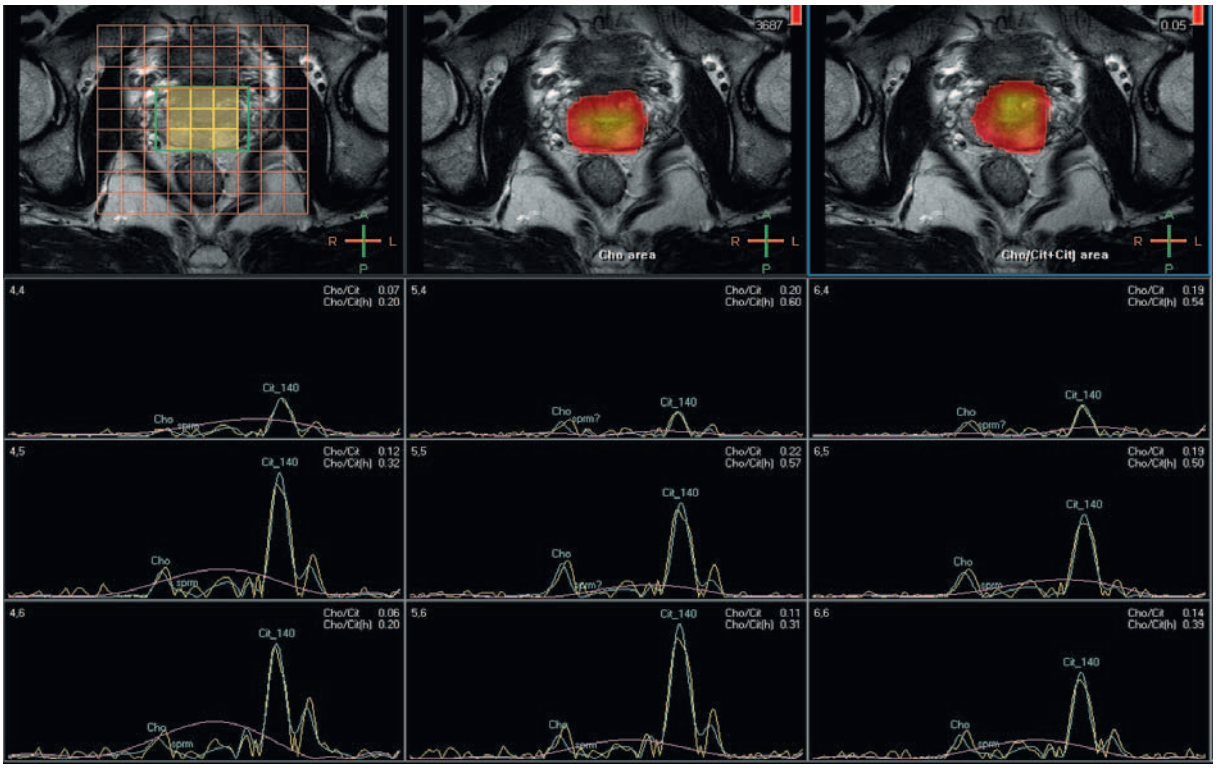


Figure 9. Prostate spectroscopy, additional Cho and (Cho+Cr)/Cit maps generated. High quality, good peak separation, high SNR, lack of artifacts, flat baseline - using surface coil at 3T. No rest slabs.

The scale in ppm is independent on magnetic field strength; however, the Hz scale depends on field strength. That means that localization of the peak in ppm is always the same irrespectively of field strength. For 1.5T, 1 ppm equals about 64Hz and for 3T 1 ppm= about 127Hz. For example, despite the fact that the distance between Cho and Cr peaks is always equal to 0.2 ppm, at 1.5T 1 ppm equals 12.8Hz and at 3T it equals 25.55Hz.

The observation described above means in practice better resolution, and, as a consequence, easier and more reliable spectrum analysis. The aforementioned bigger distance between peaks exceeds the influence of shorter T2 time.

At 1.5T Cho and Cr peaks separation is usually impossible. In the presented material, we succeeded in 36% spectrums what corresponds to results of other authors [14, 15, 16]. Calculation of integrals under the curve of Cho and Cr and

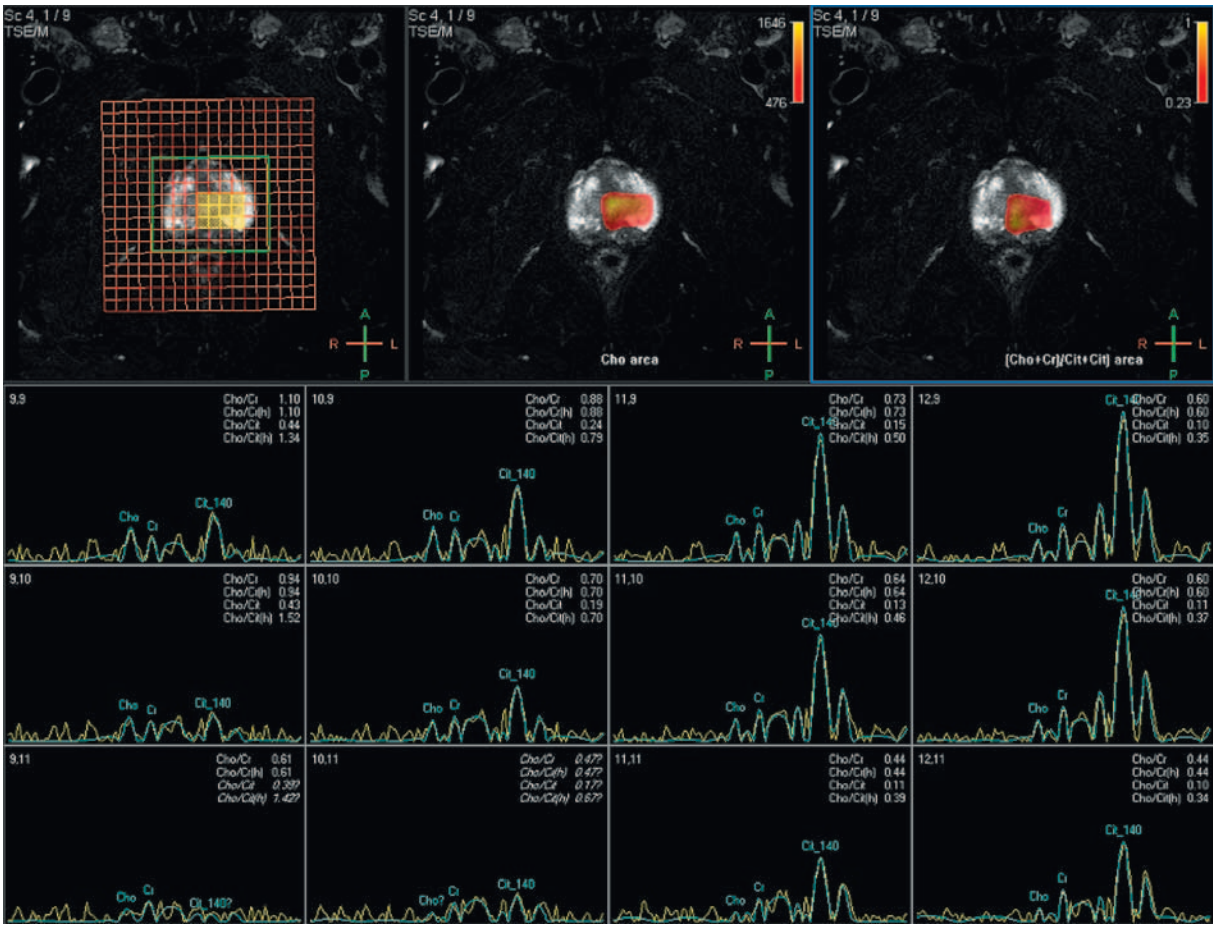


Figure 10. The result of CSI_3D prostate spectroscopy. Citrates visible as a triplet. 3T, surface coil.

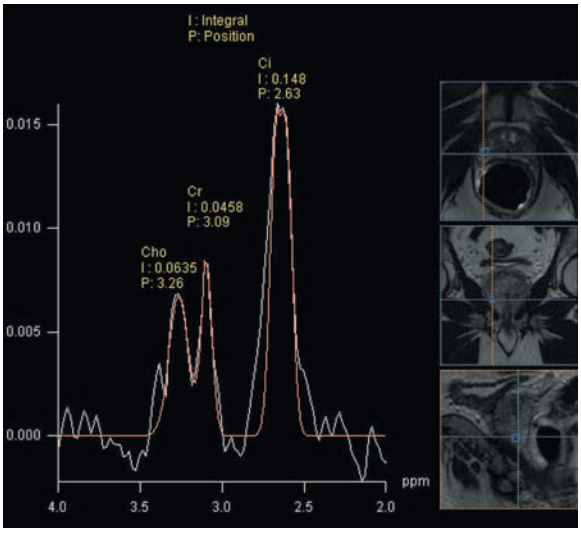


Figure 11. Spectrum obtained at 1,5T. Cho and Cr peaks visible. Cit as overlapping peaks. Endorectal coil.

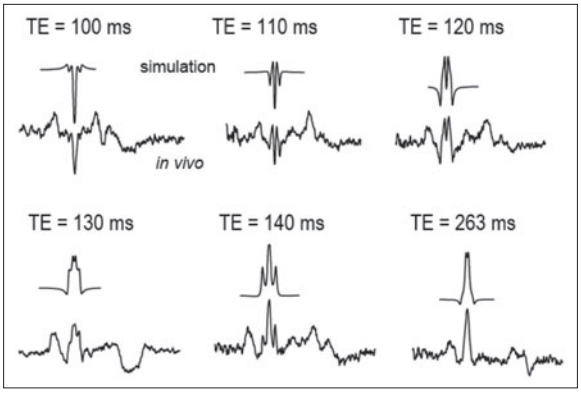


Figure 12. Citrate signal evolution at 3T depends on TE. Coupling evolution. Simulation (upper row) and in vivo results. Course materials, Spectroscopy Application Course ETH Zurich.

common ratio (Cho+Cr)/Cit is a consequence. It is impossible to calculate Cho/Cr ratio, or for example Cho/Cit ratio in a reliable way.

Separation of Cho (3.2 ppm) and Cr (3 ppm) makes calculation of Cho/Cr, Cho/Cit ratios possible, allows more precise evaluation of metabolic state of the prostate gland and may increase sensitivity and specificity in recognition and evaluation of prostate cancer extent.

Better resolution allows also to search for metabolites previously invisible, for example spermine, whose chemical shift approximates 3.1 ppm and is localized between Cho (3.2 ppm) and Cr (3 ppm). Swindle et al. [17] suggests that spermine (3.1 ppm) may have very significant meaning in

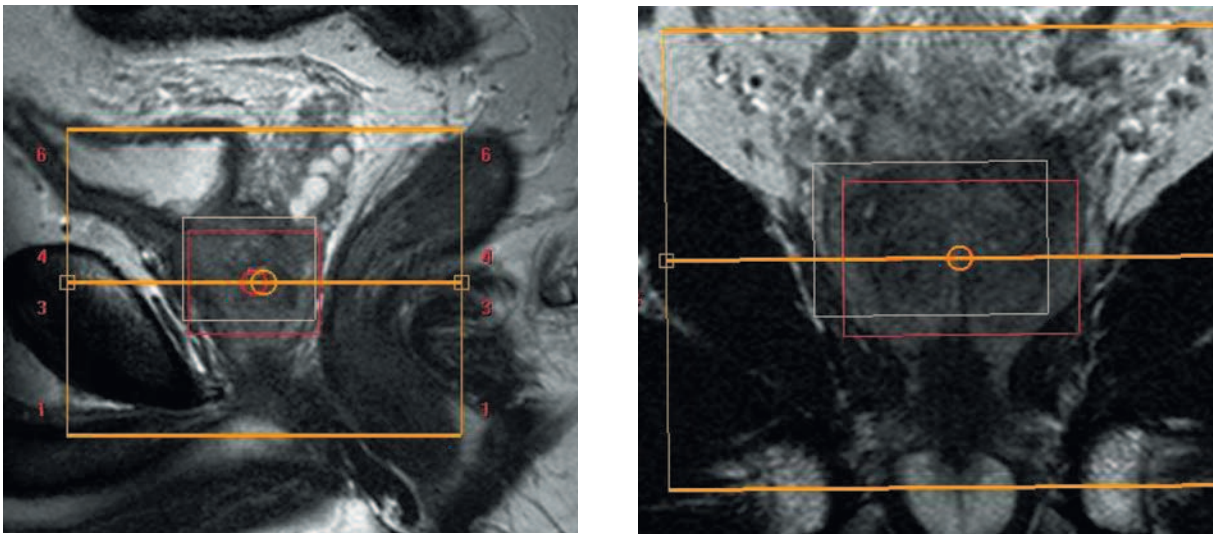


Figure 13. Chemical shift during planning the CSI in prostate. The red box represents the area where the Cit signal comes from, the grey box represents the area where the lipids and lactates signal comes from. 3T surface coil.

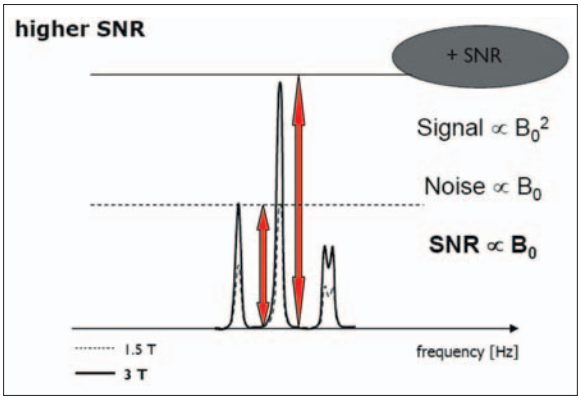


Figure 14. Theoretical comparison of SNR for 1,5T (dash line) and 3T (solid line).

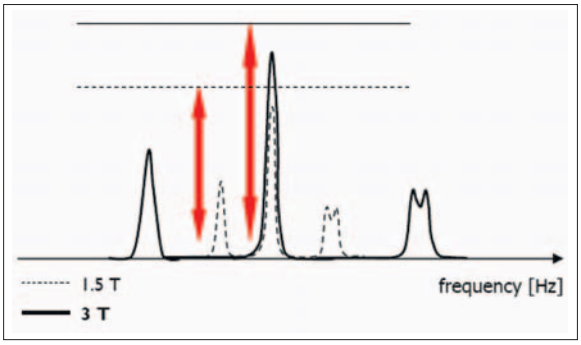


Figure 15. Actual increase of SNR is lower than theoretical prediction.

differentiation of prostate pathologies and links spermine peak presence (3.1 ppm) with benign prostate hypertrophy. Spermine, spermidine, and other polyamines [18, 19] are also listed as diagnostic. Citrate and choline allow localization of prostate cancer [20, 5] and prediction of extracapsular extension [21] with the sensitivity and specificity required for clinical use.

In our material, spermine was manifested in none out of 150 spectrums obtained at 1.5T. However, we found spermine peaks in about 7% of spectrums obtained at 3T. Pels et al. [22] in doctoral thesis takes notice of Cho, Cr and spermine peaks overlap at 1.5T field strength [Fig. 7].

A huge advantage of high fields (3T) in prostate spectroscopy is better manifestation of complex chemical nature of metabolites. The shape of the spectrum depends strongly on field strength and sequence time parameters setup. In 1H-MRS at high field, Cit (2.6 ppm) should be visible as a multiplet (triplet or even quartet [Fig. 8, 9, 10]), wchich means that its resonance consists of 3 or 4 peaks because the signal is a result of strong spin coupling in a magnetic field.

In our study, Cit (2.6 ppm) peak was always demonstrated as a multiplet at 3T and always as a singlet or a nonsymmetrical singlet at 1.5T. Other authors (among others Pels [22]) confirm this sort of overlap and nonsymmetrical shape [Fig. 11].

As a consequence of spin evolution and strong coupling effects, the optimal echo time (TE) to visualize Cit (2.6 ppm) as a multiplet at 3T equals 140 ms [Fig. 12].

Chemical shift is twice bigger at 3T compared to 1.5T and it has an influence upon planning strategies [Fig. 13]. Even if VOI (Volume of Interest) perfectly covers the whole prostate gland, the contamination of lipids signal from outside the VOI is still possible. That is why precise planning becomes crucial.

SNR

SNR of the metabolites at 3T demonstrates an increase. Theoretically, SNR improvement should reach factor of 2 when increasing field strength from 0.5T up to 1T or from 1.5T up to 3T [Fig. 14]. Signal intensity is directly proportional to square of field strength (SI – signal intensity~B_0^2). Noise is directly proportional to field strength (N~B_0).

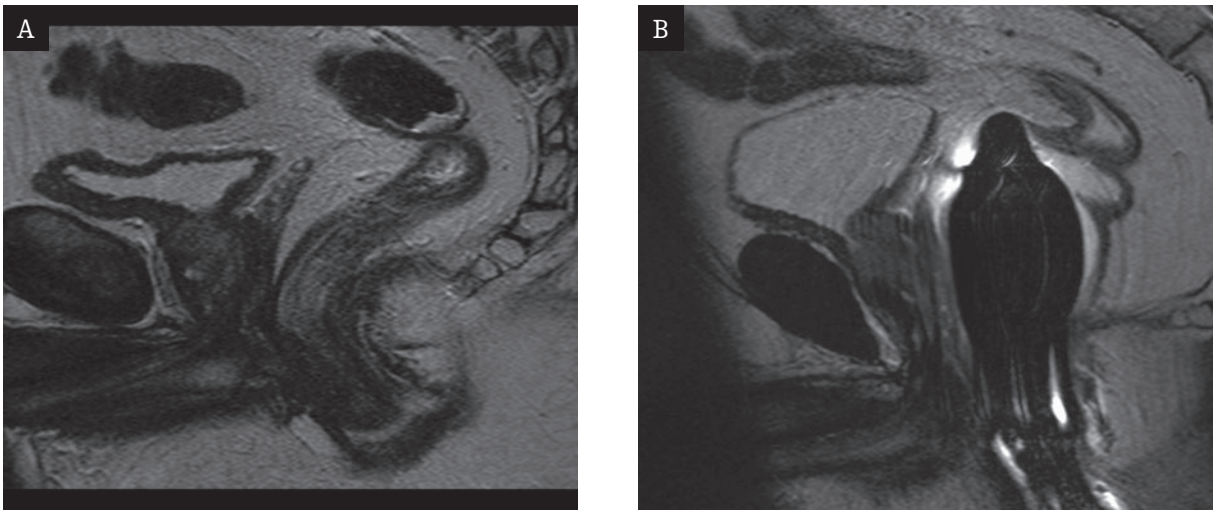
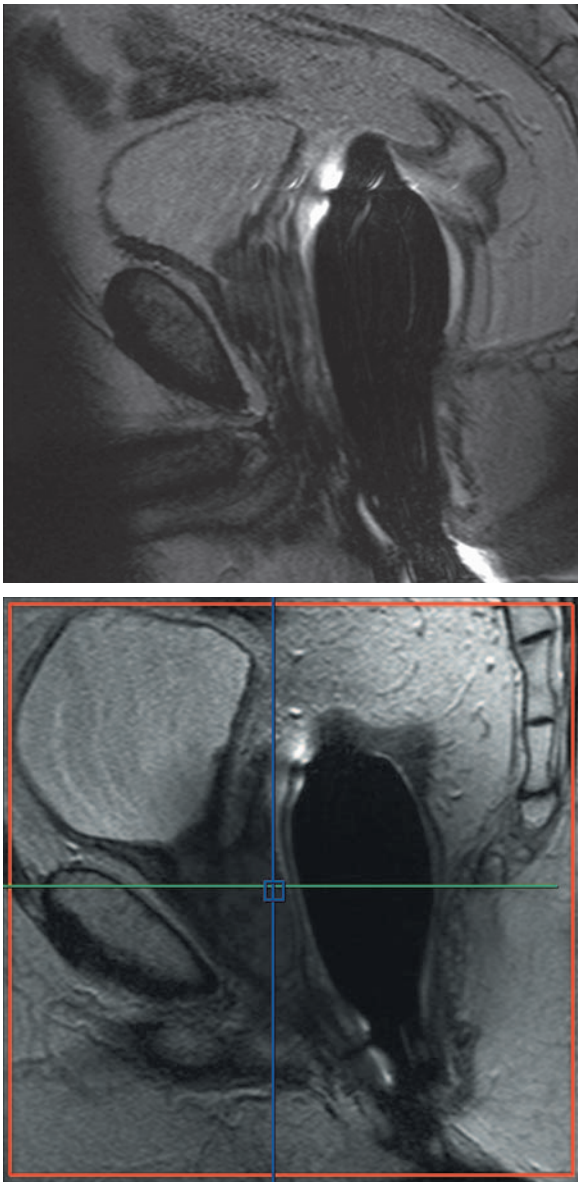


Figure 16. Influence of endorectal coil use. T2-weighted images in sagittal plane. **A**) image obtained from a surface coil, natural shape of the prostate gland; **B**) clearly visible endorectal coil; the gland is pressed, there are artifacts originating from the coil.



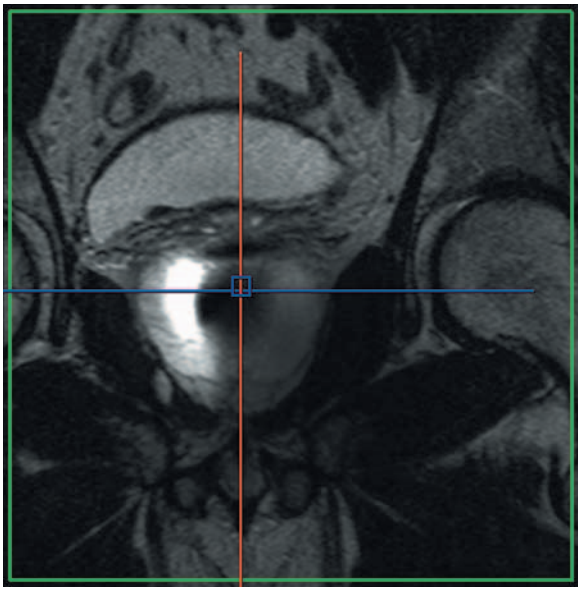


Figure 17. Artifacts caused by endorectal coil – areas of extremely intensive signal and ghost artifact. 1,5T.

To summarize: SNR theoretically should increase proportionally to magnetic field strength ($SNR=S/N\sim B_0^2/B_0=B_0$). It means that the doubling in SNR should be achieved with use of a 3.0T versus 1.5T [23, 24]. In realistic experiment conditions, the expected gain in SNR was not fully realized due to intrinsic factors like shorter T2 time and longer T1 relaxation time at 3T [Fig. 15].

Gonen et al. [25] confirmed that with $TE>0$ and $TR<\infty$, the gain is not 100% according to the equation:

$$\left.\frac{S^{3T}}{S^{1.5T}}\right|_{TE=140} = \left.\frac{S^{3T}}{S^{1.5T}}\right|_{TE=0} \bullet \exp\left[\frac{TE}{T_2^{1.5T}\bullet T_2^{3T}}\left(T_2^{3T}-T_2^{1.5T}\right)\right] \le 1.5$$

Alternatively, SNR can be traded in several ways:

1. shorter acquisition time: for example, the number of averages can be reduced without any side effect of SNR,

that means: to achieve the spectrum at 3T with the same SNR as at 1.5T, the number of averages can be reduced, fewer averages = substantial time savings;
2. smaller voxel dimensions: (SNR~ voxel size, volume, that means the bigger voxel the higher SNR because it consists of more spins contributing to the signal); to obtain the spectrum at 3T with the same SNR as at 1.5T, it is possible to resize (diminish) voxel volume in SVS and CSI_3D sequences (multivoxel, chemical shift imaging) which improves spatial resolution;
3. usage of a surface coil in stead of an endorectal one.

Diagnostic sensitivity of surface coils drops drastically with increasing distance from the examined object and because of that investigators have designed surface coils to fit particular anatomic structures. A surface coil provides good SNR in imaging tissues in close range from the coil [26]. The rapid fall-off in sensitivity below 20% can be noticed if distance between the coil and the anatomic structure being imaged exceeds the coil diameter. Despite that fact, SNR obtained at 3T using a surface coil can be compared to SNR from an endorectal coil at 1.5T. The surface coil increases patient comfort and limits to necessary minimum preparation of rhe patient prior to the examination. On the other hand, the endorectal coil causes prostate gland pressure and change of its shape and can be a source of an artifact [Fig. 16, 17].

Conclusions

1. Prostate examination using a surface coil at 3T allows to obtain spectrum of the same or better quality compared to spectrum obtained at 1,5T using an endorectal coil.
2. Cho and Cr peaks separation is more possible at 3T then at 1.5T; the difference is significant statistically;
3. Cit peak was always visible as a multiplet at 3T and never at 1.5T;
4. Spermine peak was detected in 10/150 spectrums (6.6%).

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