Magnetic resonance spectroscopy of localized prostate cancer: assessment of antitumor effects of intra-prostatic hormone deprivation therapy

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INTRODUCTION

A typical treatment of low or medium grade prostate cancer (PCa) includes various types of testosterone deprivation therapies, often associated with hormonal side effects. A less invasive treatment with fewer side effects would be a desirable option.

Currently, T_2- and DWI is commonly used during the follow-up of patients undergoing therapy. However, these techniques are of limited diagnostic value. ^{1}H-MRS improves the ability of MRI to monitor the treatment response.[1] Spectral intensities of detectable metabolites (Cho, PA, Cr, Cit) decrease with increasing exposure during therapy. The final step is metabolic atrophy, where signals from metabolites are undetectable. Metabolic atrophy is indicative of successful treatment because the growth of normal and cancer cells cannot occur without metabolism.

The aim of this study was to assess usefulness of ^{1}H-MRS for monitoring the treatment efficiency of a novel transrectally injected intraprostatic drug Liproca® Depot formulation.

METHODS

Eleven PCa patients scheduled for prostatectomy participated in this study. Liproca® Depot is composed of 2-hydroxyflutamide (2-HOF) encapsulated in a calcium sulphate drug carrier matrix (NanoZolid® technology, LIDDS, Sweden).[2,3] Following intraprostatic injection of Liproca® Depot (containing 30 mg 2-HOF per mL prostate), the depot solidifies in vivo forming a solid depot which dissolves and releases 2-HOF gradually over a prolonged period of time (~6 months). Single-voxel ^{1}H-MRS and 2D MRSI of the prostates were performed before injection and 6 weeks after the injection. All measurements were performed with a 3T scanner (Achieva, Philips) using a surface phase-array coil for receiving. Spectroscopic experiments and data processing were described elsewhere.[4]

RESULTS

Figure 1 shows single-voxel and 2D MRSI spectra of a representative patient before the drug injection into the prostate and 6 weeks after the treatment. Cho, PA, Cr, and Cit intensities decreased (Fig. 1 c and f). Consequently SNR decreased. These features reveal the presence of partial metabolic atrophy. Cit concentration decreased faster than Cho and Cr, resulting in an increase of (Cho+PA+Cr)/Cit ratio. Median (Cho+PA+Cr)/Cit ratio increase was 71% (range: 12-110%), and median SNR decrease was 44% (range: 22-80%). These finding suggest that therapy has not reached its full effect after 6 weeks. Anti-androgen related side effects, typical for oral use of the same drug, were not detected.

DISCUSSION

The study formulation was designed to deliver a higher initial release rate (burst) followed by a slower and prolonged drug release (maintenance). Our results have shown that intra-prostatic injection of Liproca® Depot caused an overall reduction in prostate tissue metabolism interpreted as cellular (metabolic) atrophy. The increase in (Cho+PA+Cr)/Cit spectral intensity ratio and SNR decrease after the treatment reveal an antitumor treatment effect.

CONCLUSION

This study support the use of both single-voxel MRS and MRSI to detect metabolic atrophy in PCa patients treated with long-term hormone-deprivation therapy.
The detected metabolic atrophy confirmed an antitumor effect of the study formulation.

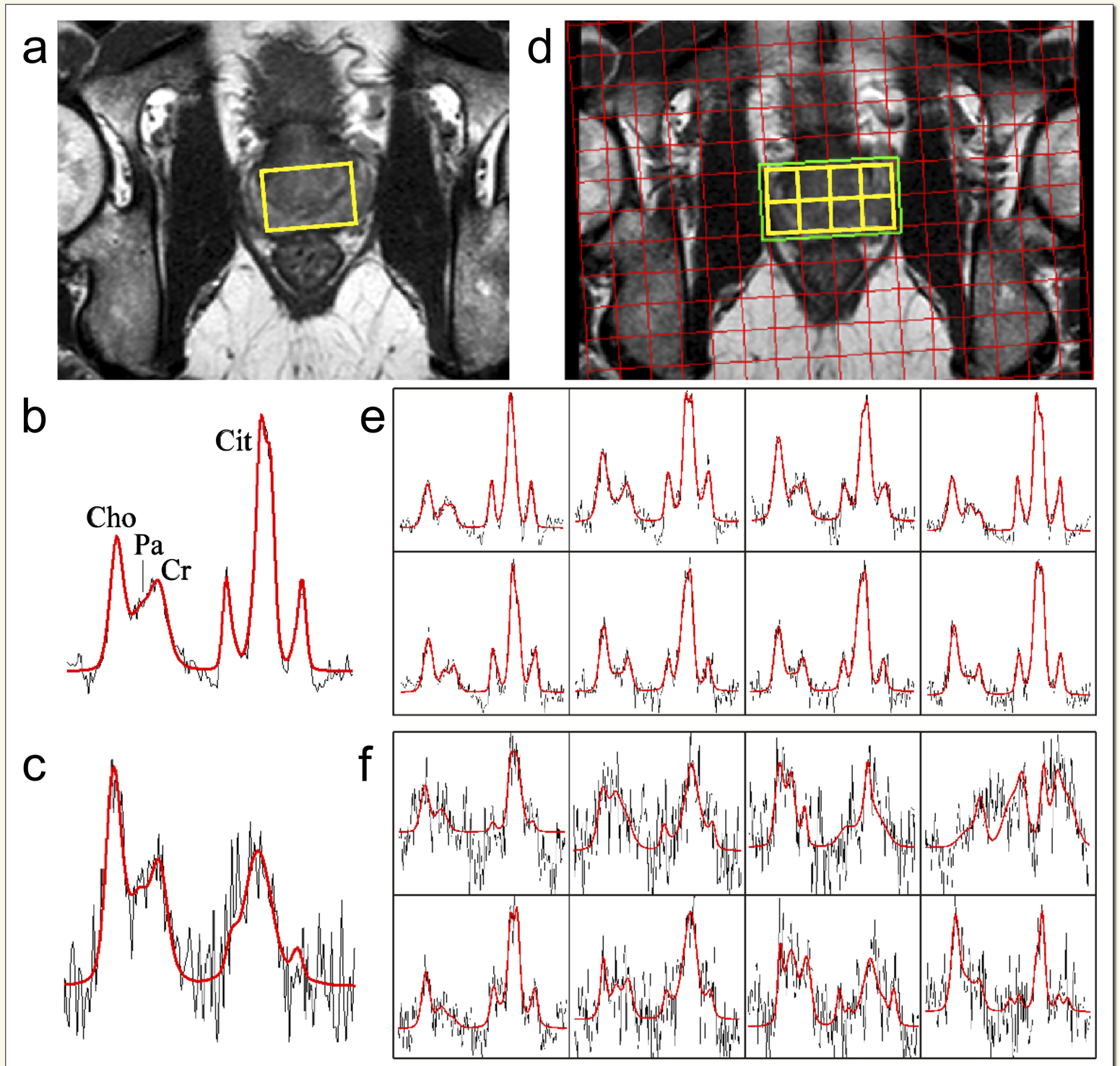

Figure 1: MR spectra of representative patient. (a-c) Single-voxel MRS and (d-f) 2D MRSI of the prostate.
(a) Typical voxel position in axial plane (yellow rectangle), (b) Spectrum before treatment (Cit concentration 16.2 mM),
(c) Spectrum after treatment (Cit content 6.7 mM). (d) 2D MRSI voxels (yellow squares) in axial plane,
(e) Spectra before treatment, (f) Spectra after treatment.

REFERENCES

1. Mueller-Lisse UG, Swanson MG, Vigneron DB, et al.: Magnetic resonance spectroscopy in patients with locally confined prostate cancer: association of prostatic citrate and metabolic atrophy with time on hormone deprivation therapy. Eur Radiol. 2007;17:371-378.
2. Ahlström H, Tammela T, Häggman M, et al.: An intraprostatic modified release formulation with 2-hydroxyflutamide for patients with localized prostate cancer. The Journal of Urology 2017;198:1333-1339.
3. Thomas MV, Puleo DA.: Calcium sulfate: Properties and clinical applications. J Biomed Mat Res. 2009;88(2):597-610.
4. Weis J, Jorulf H, Bergman A, et al.: MR spectroscopy of the human prostate using surface coil at 3T: metabolite ratios, age-dependent effects, and diagnostic possibilities. J Magn Reson Imag. 2011;34:1277-1284.