Quantitative J-resolved prostate spectroscopy using two-dimensional prior-knowledge fitting

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Introduction

Magnetic resonance spectroscopy can be used for the detection of metabolic changes associated with prostate cancer. Proton MR spectra of cancerous prostate tissue exhibit largely reduced citrate levels and an increase in choline-containing compounds compared to healthy tissue [1]. Additional potential metabolic markers for prostate cancer (e.g. spermine and myo-inositol) have been identified, although their patho-physiological role is not well understood [2, 3]. In numerous clinical studies, quantitative results have been obtained using peak integration, sometimes in combination with simple line fitting. However, in one-dimensional (1D) spectra, there is a strong overlap of detectable metabolites in the chemical shift range between 3.0 and 3.3 ppm (creatine, choline, myo-inositol, taurine and polyamines). Two-dimensional (2D) spectroscopy methods can reduce this overlap and hence facilitate peak assignment and metabolite quantification [4]. Recently Schulte *et al.* proposed a 2D fitting procedure dubbed ProFit (Prior-Knowledge Fitting) for fitting *J*PRESS brain spectra as linear combinations of 2D basis spectra [5]. In the present work, the ProFit method was adapted to fit and quantify *J*PRESS prostate spectra from healthy subjects. It is shown that at least six metabolites can be objectively and reliably quantified *in vivo* with this method.

Materials and Methods

Single voxel *J*PRESS prostate spectra were measured from seven healthy subjects on a Philips Achieva 3T system with a two-element surface coil. For encoding the indirect spectral dimension, the echo time was varied in the range from 49 to 247 ms. The ProFit method combines a non-linear least-squares algorithm, which optimises the model parameters (chemical shifts, line widths, phases and line shape), with a linear least-squares algorithm for the determination of metabolite concentrations [5]. To exclude signal from lipids and residual water, and to reduce the numerical burden, the optimisation was limited to the spectral region $\{(f_1, f_2) \mid -28\ \text{Hz} < f_1 < 28\ \text{Hz} \wedge 2.2\ \text{ppm} < f_2 < 4.1\ \text{ppm}\}$. The 2D basis spectra were simulated numerically, using chemical shifts and coupling constants from literature. Ten basis metabolites with significant resonances in the fit region were used for the fit: creatine (Cr), choline (Cho), phosphorylcholine (PCh), citrate (Cit), spermine (Spm), myo-inositol (MI), scyllo-inositol (Scy), taurine (Tau), glutamate (Glu) and glutamine (Gln). To reduce the degrees of freedom for the fit, the polyamine resonance was merely modelled with a spermine basis spectrum although it also contains minor contributions from spermidine and putrescine. Glycerophosphorylcholine was not accounted for in the basis set since its main resonances are almost identical with those of PCh. The determined concentration ratios were corrected for relaxation effects, using T_1 and T_2 values from literature [6].

Results

Figure 1 shows a typical *J*PRESS prostate spectrum, the fitted spectrum and the fit residual. Besides the prominent citrate multiplet at 2.6 ppm, there is a large number of hardly distinguishable coupled and uncoupled resonances in the spectral region between 3.0 and 3.3 ppm. At 2.05 ppm, a broad resonance with a strong inter-subject amplitude fluctuation was observed. It was attributed to lipid signal from outside the prostate due to imperfect volume selection and therefore not included in the fit region. Table 1 shows the determined metabolite concentrations averaged over seven subjects as ratios to Cr. Quality measures for the concentrations were determined in the form of Cramér-Rao lower bounds (CRLBs), from which confidence values for the ratios could be calculated. Additionally, the inter-subject standard deviations (SDs) of the metabolite ratios are shown. Due to their mutual overlap, Cho and PCh as well as Glu and Gln have large CRLBs and can therefore be more reliably quantified as sums Glx = Glu + Gln and t-Cho = Cho + PCh.

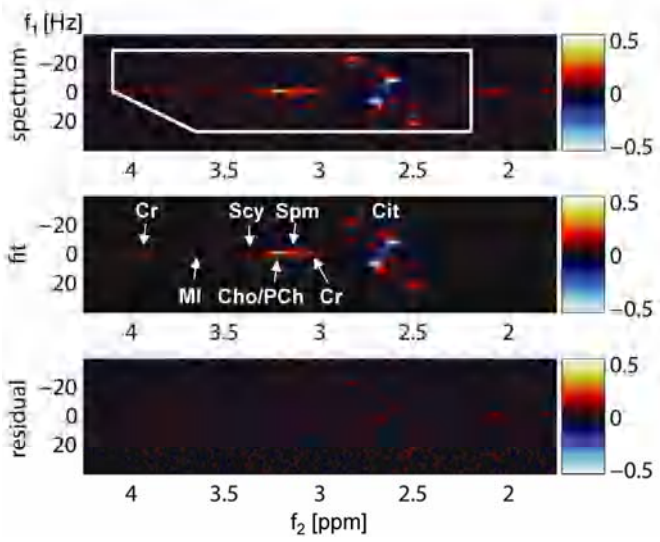

Fig. 1: *J*PRESS prostate spectrum (top), its fit (middle) and the fit residual (bottom) as logarithmically scaled colour plots. The white box defines the spectral region of interest where the cost function of the fit was minimised.

metabolite	ratio to Cr	CRLB [%]	Error [%]	SD [%]
Cr	1.00	5.4	-	-
Cho	0.12	27.4	28.0	39.0
PCh	0.53	7.5	9.3	17.1
Cit	9.10	1.4	5.6	43.4
Spm	2.47	4.3	7.0	37.0
MI	1.93	6.9	8.8	24.4
Scy	0.19	14.3	15.4	42.5
Tau	0.44	35.9	36.4	48.7
Cho+PCh	0.65	4.0	6.7	12.3
Glu+Gln	0.71	29.3	29.9	33.9

Table 1: Metabolite concentrations in healthy prostate tissue (as ratios to Cr) determined with ProFit and averaged over seven healthy subjects. The CRLBs are objective metabolite-specific quality measures for the accuracy of the quantitation results, from which error margins for the ratios to Cr were calculated. The inter-subject standard deviations of the metabolite ratios are shown in the last column.

Discussion

The quality of the *J*PRESS spectra showed a large inter-subject variation, especially in terms of signal-to-noise ratio. This is due to the acquisition with surface coils and a varying B_1 inhomogeneity in human prostates. In the average, six metabolites could be quantified with reasonable precision (CRLBs < 20 %), namely Cr, t-Cho, Cit, Spm, MI and Scy. For some metabolites, particularly Cit and Spm, the relative inter-subject SD is many times larger than the error estimate calculated from the CRLBs. This can be explained with varying amounts of glandular and stromal tissue in the volume of interest since Cit and Spm are mainly found in glandular tissue. Compared to results obtained by Swanson *et al.* [6] through quantification of 1D *in vitro* spectra, the proposed method yields similar concentrations for t-Cho and Spm, but significantly higher values for Cit and MI. This discrepancy might be partly due to *J* modulation, which can give rise to a considerably decreased signal intensity for coupled resonances at certain echo times. *J* modulation is taken into account when the spectrum is fitted using metabolite basis spectra like in this work, but it is not considered when the quantification is done via simple constrained peak fitting. Since ProFit is based on a linear combination of two-dimensional basis spectra, it incorporates the maximum amount of prior knowledge and yields metabolite concentration ratios which are independent of sequence and echo time.

References:

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6. Swanson *et al.*, MRM 2006; 55: 1257-1264.