Comparison of 2D JPRESS and 2D L-COSY on Detecting Polyamines and Citrate Metabolites for Prostate Study

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Purpose

The polyamine spermine, which plays a role in cell proliferation and differentiation, may provide additional information for early diagnosis and prognosis predicting tumor progression. It might be used as target for chemoprevention or chemotherapeutic intervention. Recently, Shukla-dave et al [Radiology 2007; 245:499-506] incorporated the polyamine level into their scoring systems for prostate cancer detection by using 1D ^{1}H MR spectroscopy. Shukla-dave et al. reported in their preliminary (Classification and Regression Tree) CART analysis that polyamine had a better performance on the detection of cancer than did the (Cho+Cr)/Cit. However, polyamine levels were only assessed qualitatively in their study because of the proximity of the (Choline, creatine and polyamine) peaks and limited spectral resolution, not allowing the polyamine levels to be integrated from the peak and quantified. Expanding 1D ^{1}H MRS to a second dimension has been shown to be useful for resolving overcrowded spectra. The application of localized 2D *J*PRESS in prostate examinations enables the spectral separation of creatine (Cr) and Cho from polyamine spermine (Spm). However, the limited spectral resolution along the second axis (F1) resulted in an overcrowded 2D JPRESS spectrum by the unavoidable strong coupling effects of Citrate, which produces complex spectra and difficulty in interpretation. A localized 2D L-COSY sequence [MRM 2001,46:58~67] had been implemented to explore the 2D COSY spectrum of prostate phantom [ISMRM 2007], which could get a better dispersion of J-cross-peaks for both polyamine spermine and citrate. The strong coupling effect resulted in a complex overcrowded 2D J resolved cross-peak pattern for analysis of citrate metabolite. In this study, 2D JPRESS and 2D L-COSY were implemented, and their capability in resolving the prostate metabolites such as polyamine spermine, citrate, choline, creatine etc were compared. The strategy about how to improve the detection and monitoring prostate cancer progression is also discussed.

Methods

All experiments were performed using a 4T scanner equipped with a SMIS console (Surrey Medical Imaging System). An in-house built birdcage coil was used for both RF transmission and signal detection. Measurements were performed on a phantom containing 90 mM citrate, 20 mM spermine, 10 mM choline and 12 mM creatine to mimic prostate tissue (pH =7.0). The 2D L-COSY sequence and 2D L-JPRESS both with the CHESS suppression was performed. A 8-step phase cycle for COSY and a 16-step phase cycling scheme was used for 2D JPRESS on all three pulses respectively. 2D L-COSY spectra were acquired using the following parameters: TR = 800ms sec, minimal TE of 18ms, 128 t_1 increments were used to sample the second frequency dimension (F_1). The raw data were acquired using 1024 complex points and the spectral window along the first dimension was 2.5 kHz, and 1.25kHz along the second dimension. For 2D JPRESS, the parameters were TR = 2000ms sec, minimal TE of 26ms, 48 t_1 increments with 330Hz spectral window. The voxel size is 15mm^3 for both sequences. The matNMR software package was employed to analyze the spectra. The raw data were apodized with exponential functions along t_1 and t_2 and zero-filled to 512 x 2048 prior to Fast Fourier Transformation. All 2D spectra were presented as contour plots. The resulting spectrum was displayed in magnitude mode.

Results

Figure 1 shows the 2D JPRESS MR spectrum obtained from the prostate phantom. In the spectrum, spermine multiplets at 3.10 ppm are still overlapped with neighboring choline and creatine peaks at 4T. It is complicated and difficult to analyze the quantitative level. The Citrate peaks are strongly coupled. The Polyamine spermine peaks only show J-resolved peaks at around 3.15ppm, but not at 2.1ppm and 1.8ppm. However, in the 2D L-COSY MR spectra (Fig. 2), spermine shows two well-separated cross-peaks at (3.1 ppm / 1.8 ppm), (1.8 ppm / 3.1 ppm) and (3.1 ppm / 2.1 ppm), and (2.1 ppm / 3.1 ppm). The diagonal peaks along $F_1 = F_2$ resembles the conventional 1D spectral resonances.

Fig1. 2D JPRESS prostate spectra

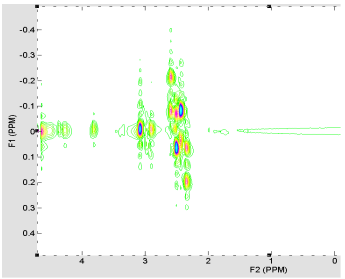
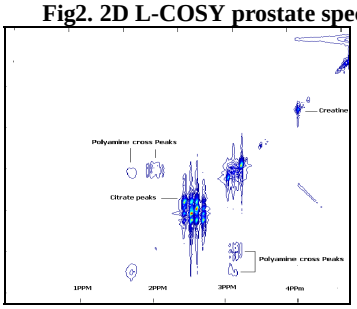


Fig2. 2D L-COSY prostate spectra



DISCUSSION

The extended second frequency dimension of two-dimensional (2D) spectroscopy can give additional information about the spins (coupling or correlation of spins etc.) or better separate them from other nuclei with a similar chemical shift. 2D JPRESS enables the separation of chemical shift and coupling information for *J*-coupled metabolites, therefore gained popularity for prostate exams. However, the strong coupling effects of citrate make the JPRESS spectra too complex to interpret. Compared with 2D JPRESS, increased spectral width (smaller t_1 incremental delays) along the new spectral dimension in 2D L-COSY, which explores the correlation of the coupled spins, resulted in an improved spectral dispersion and better separation of various 2D cross-peaks.

However 2D L-COSY (with CABINET selection) MR spectrum can only retain 50% of the sensitivity, while the JPRESS sequence retains 100% of the magnetization from a localized volume of interest (VOI). Owing to the limited spectral dispersion, the 2D *J*-resolved cross peaks were complex and identification of metabolites at low concentrations was further complicated by additional *J*-cross peaks due to inherent strong coupling for 2D JPRESS spectra. Although the new technique 2D S-PRESS enables an improved resolution, there are two characteristic 'strong coupling' doublets. However only one metabolite can be detected per measurement, which makes the MR spectra measurement not efficient if multiple metabolites need to be monitored. For 2D JPRESS, due to increased sampling rate, severe loss of metabolite signals due to T_2 decay during t_1 delays was a problem. 2D JPRESS prostate spectra, polyamine spermine J-resolved peaks are not shown at 2.1ppm and 1.8ppm(see Fig1), while the cross peaks of polyamine of 3.1ppm/2.1ppm and 3.1ppm/1.8ppm were clearly shown in 2D L-COSY spectrum (Fig2). 2D L-COSY may be better for characterizing polyamine spermine signals, but since the spectra are reconstructed in the magnitude mode, which may cause the twisted contour peaks. Presentation of 2D diagonal and cross peaks in the pure absorptive phase will facilitate better spectral resolution leading to improved spectral assignments.

In summary, spatially localized 2D spectroscopic sequences have been successfully implemented on a 4T MRI/MRS scanner. *J*-coupled connectivities have been demonstrated in several prostatic metabolites in 2D JPRESS and 2D L-COSY. Compared with the previously reported 2D JPRESS spectra using a 1.5 T MRI scanner, improved spectral dispersion and better dispersion of J-cross-peaks, facilitated recording of polyamine and citrate using 2D L-COSY. 2D L-COSY combined with 3D MRSI may improve detection of prostate cancer, or for evaluation of chemoprevention efficacy using polyamine as the biomarker.