MAXIMUM ENTROPY RECONSTRUCTED ECHO PLANAR BASED SPECTROSCOPIC IMAGING AND DIFFUSION WEIGHTED IMAGING IN PROSTATE CANCER

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Introduction: In the United States, 90% of men with prostate cancer (PCa) are older than 60 years, diagnosed by early detection with the serum prostate-specific antigen (PSA) blood test, and have disease believed to be confined to the prostate gland (1). In vivo proton MRS provides biochemical information on the prostate tissues by providing relative concentrations of citrate (Cit), creatine (Cr), choline (Ch) and polyamines that are used to detect and diagnose PCa (2). The challenging task in 1D MRS spectra of PCa is the quantification of individual metabolites, due to spectral overlap of metabolites because of limited spectral dispersion at clinically used magnetic field strengths of less than 3T. Conventional phase encoded MRSI is relatively inefficient and time-consuming because it involves a large number of phase encodings. The applicability of compressed sensing (CS) (3) to four dimensional (4D) echo planar based J-Resolved spectroscopic imaging (EP-JRESI) in order to accelerate data acquisition using nonuniform under sampling (NUS) (4). This could be significantly reduced without sacrificing the spectral quality while maintaining high spatial resolution as well as the 4D EP-JRESI detect more metabolites (mI, glutamate, glutamine, spermine and lactate) compared to long TE conventional method. In this study maximum entropy (MaxEnt) method was used to reconstruct the 4D EP-JRESI data. Diffusion weighted imaging (DWI) has the ability to qualitatively and quantitatively represent the diffusion of water molecules by the apparent diffusion coefficient (ADC), which indirectly reflects tissue cellularity (5). The major goal of the study is to demonstrate the feasibility of correlating MaxEnt reconstructed 4D EP-JRESI data with DWI-MRI in PCa patients in 3T.

Materials and Methods: 4D EP-JRESI and DWI) were recorded in eighteen PCa patients ranging in age from 46–73 years (mean, 65 years using Siemens 3T MRI Scanner (Siemens Medical Systems, Germany). This study was approved by the Institutional Review Board, and informed consent was obtained from each patient. The mean delay between biopsy and MRI was 8 weeks. A 4D NUS EP-JRESI sequence was implemented on a Siemens 3T Trio-Tim scanner and the volume of interest (VOI) was localized using three slice-selective radio-frequency (RF) pulses (90^0-180^0-180^0). The CS-based reconstruction will enable a stable and accurate reconstruction from the NUS based EP-JRESI data (25% of t_1 and k_y increments) with a reduced total time. The parameters for the EPJRESI were: TR/TE/Avg = 1.5s/30ms/1-2, 16 phase encoding steps, 512 complex points with an F2 bandwidth of 1190Hz. For the second dimension (F1), 64 increments with bandwidths of 1000Hz were used. A 25% NUS was imposed along the incremented spectral and spatial dimensions. The individual voxel volume in human prostate was 1ml. MaxEnt is a constrained convex optimization algorithm that uses a variant of the conjugate gradient method to iteratively solve the inverse problem (6):

$$\text{maximize } S_{1/2}(f) \text{ s.t. } \|F^{-1}\ Kf\text{-}D\|_2 \le \sigma \qquad (1)$$

where f is the estimated fully-sampled spectrum at each iteration, F-1 is the inverse Fourier transform, K is the NUS matrix, D is the time-domain measured data, σ is the noise standard deviation, and S1/2(f) is the spin-½ entropy of the estimated spectrum (7). In addition, DWI-MRI was acquired with the following parameters: (TR/TE 3200/60 ms, bandwidth 1250 Hz in the EPI frequency direction) with b values of 0, 100, 400 and 800 s/mm^2.

Receiver operating characteristic (ROC) curve analyses based on logistic regression models were performed to predict the MRSI and ADC values. P values < 0.05 were considered statistically significant.

Results: Figure 1 show the ratios of myo-inositol (mI), spermine (Spm) and Cit with respect to Cr as well as (Ch+Cr). Fig.2 shows the ADC values between cancer and non-cancer locations of PCa patients. An investigation of the measurement of EP-JRESI with DWI data showed interesting results in this study. Since Ch and Cr are not always well resolved, adding to the uncertainty, we have calculated two different ratios (Cr, (Ch+Cr)). Table 1 shows the receiver operating characteristic (ROC) curve analyses based on logistic regression models were performed to predict the EP-JRESI and ADC values. Combining both EP-JRESI and ADC gives 100% accuracy in this selected group of patients. We have detected myo-inositol, glutamine, glutamate, spermine in addition to Cit, Cr and Ch. The NUS based 4D EP-JRESI data were processed using MATLAB based post processing. We have found significant ($p< 0.05$) decrease of Cit, spm, with respect to (Ch+Cr) in cancer locations compared to non-cancer locations. Also decreased trend of mI was observed with respect to (Ch+Cr) ratio. Similar trends followed in Cr ratio except mI. However, because of the small number of samples in each group the differences in mI/Cr , mI/(Ch+Cr) did not reach statistical significance. The ROI based mean ADC values of cancer and non-cancer locations in the peripheral zones were: (0.985+0.164) and (1.453+0.168). The statistical significance ($p <0.05$) was observed between cancer and non-cancer locations.

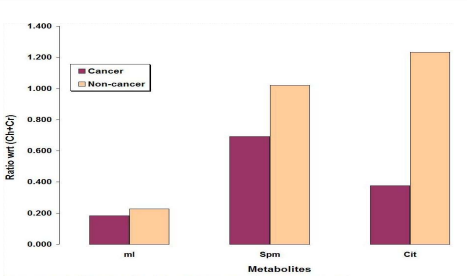

Fig 1. Metabolites ratios with respect to (Ch+Cr)

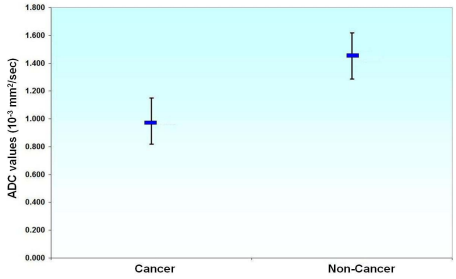

Fig 2. ADC values from Cancer and non-cancer

Parameter (%)	MRSI	ADC
Sensitivity	86.7	95.2
Specificity	95.5	95.0
PPV	91.3	94.3
NPV	92.8	93.0
Accuracy	91.5	93.1
AUC	97.0	97.4

Table.1. Findings from EP-JRESI and DWI

Discussion: Normal prostate epithelial cells produce and accumulate a large amount of Cit which is secreted as a major component of the prostatic fluid. Compared to normal tissue, decreased levels of Cit are previously observed in PCa tissue by ex vivo MRS (8).why ex vivo only Decrease in polyamines is associated with prostate cancer (9). Additionally, the very low putrescine concentration in our study confirms that the polyamine peak predominantly consists of Spm. Spm cannot be fully separated from the Ch peak using 1D spectral based MRSI, but with EP-JRESI we were able to detect and quantify nicely. The increase of mI/Cr was discussed in PCa earlier which agreed with our result (10) and decrease of mI/(Ch+Cr) may be the overlap of Ch and Cr which needs to be investigated in the future. The lower mean ADC values in the more aggressive tumors in our study may be due to higher cellular density in poorly differentiated tumors, resulting in more restricted movement of water protons (11).

Conclusion: It is evident from our preliminary investigation using a 3T MRI scanner that NUS based 4D EP-JRESI with MaxEnt reconstruction facilitates unambiguous detection of less T2-weighted metabolites compared to conventional 1D MRSI. DWI is potentially useful in PCa detection and localization. Our pilot findings demonstrate a possible clinical application of the 4D NUS EP-JRESI sequence in combination with DWI which may be useful in localizing PCa for diagnosis, monitoring, biopsy, treatment planning and staging as well as potentially for response assessment.

References:

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