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Authors

Nagarajan, Rajakumar
Iqbal, Zohaib
Burns, Brian
et al.

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Accelerated echo planar *J*-resolved spectroscopic imaging in prostate cancer: a pilot validation of non-linear reconstruction using total variation and maximum entropy

Rajakumar Nagarajan^a, Zohaib Iqbal^a, Brian Burns^a, Neil E. Wilson^a, Manoj K. Sarma^a, Daniel A. Margolis^a, Robert E. Reiter^b, Steven S. Raman^a and M. Albert Thomas^{a*}

The overlap of metabolites is a major limitation in one-dimensional (1D) spectral-based single-voxel MRS and multivoxel-based MRSI. By combining echo planar spectroscopic imaging (EPSI) with a two-dimensional (2D) *J*-resolved spectroscopic (JPRESS) sequence, 2D spectra can be recorded in multiple locations in a single slice of prostate using four-dimensional (4D) echo planar *J*-resolved spectroscopic imaging (EP-JRESI). The goal of the present work was to validate two different non-linear reconstruction methods independently using compressed sensing-based 4D EP-JRESI in prostate cancer (PCa): maximum entropy (MaxEnt) and total variation (TV). Twenty-two patients with PCa with a mean age of 63.8 years (range, 46–79 years) were investigated in this study. A 4D non-uniformly undersampled (NUS) EP-JRESI sequence was implemented on a Siemens 3-T MRI scanner. The NUS data were reconstructed using two non-linear reconstruction methods, namely MaxEnt and TV. Using both TV and MaxEnt reconstruction methods, the following observations were made in cancerous compared with non-cancerous locations: (i) higher mean (choline + creatine)/citrate metabolite ratios; (ii) increased levels of (choline + creatine)/spermine and (choline + creatine)/myo-inositol; and (iii) decreased levels of (choline + creatine)/(glutamine + glutamate). We have shown that it is possible to accelerate the 4D EP-JRESI sequence by four times and that the data can be reliably reconstructed using the TV and MaxEnt methods. The total acquisition duration was less than 13 min and we were able to detect and quantify several metabolites. Copyright © 2015 John Wiley & Sons, Ltd.

Keywords: MRS; prostate cancer; 4D EP-JRESI; citrate; myo-inositol; Glx; echo planar spectroscopic imaging

INTRODUCTION

Prostate cancer (PCa) is the most commonly diagnosed non-cutaneous malignancy in the USA and is the second leading cause of cancer-related death in men (1). One in six men will be diagnosed with PCa during their lifetime, but only one in 36 will die of this disease. Currently, the annual prostate-specific antigen (PSA) test and digital rectal examination (DRE) are routinely performed (2) for screening. The PSA screening test measures the serum level of PSA in blood samples. However, it is a controversial test because 65–75% of PSA screening gives false-positive results leading to overdiagnosis (3). The use of systematic transrectal biopsy can miss significant cancer lesions because of random sampling error (4) and the observation that one-third of significant tumors lie in the anterior part of the gland, based on studies of radical prostatectomy specimens (5). Hence, there is an immediate need for early, yet accurate, detection of PCa to improve disease outcomes.

¹H MRS enables the detection of a range of biochemicals in the prostate by making use of the proton signals in these molecules. The detection of biochemicals *in vivo* is limited to concentrations of more than 0.5–1 mM. Signals of citrate (Cit), creatine (Cr), choline (Ch) and spermine (Spm) can be detected

throughout the prostate, with increased levels of Ch and decreased levels of Cit being indicative of cancer (6–8).

* Correspondence to: M. A. Thomas, Radiological Sciences, David Geffen School of Medicine at UCLA, Los Angeles, 90095 CA, USA.
E-mail: athomas@mednet.ucla.edu

a R. Nagarajan, Z. Iqbal, B. Burns, N. E. Wilson, M. K. Sarma, D. A. Margolis, S. S. Raman, M. A. Thomas
Radiological Sciences, University of California Los Angeles, Los Angeles, CA, USA

b R. E. Reiter
Urology, University of California Los Angeles, Los Angeles, CA, USA

Abbreviations used: 1D, one-dimensional; 2D, two-dimensional; 3D, three-dimensional; 4D, four-dimensional; AUC, area under the curve; Ch, choline; Cit, citrate; Cr, creatine; DRE, digital rectal examination; EP-JRESI, echo planar *J*-resolved spectroscopic imaging; EPSI, echo planar spectroscopic imaging; Gln, glutamine; Glu, glutamate; Glx, glutamine + glutamate; JPRESS, *J*-resolved spectroscopy/spectroscopic; MaxEnt, maximum entropy; ml, myo-inositol; NPV, negative predictive value; NUS, non-uniform undersampling/non-uniformly undersampled; NWS, non-water-suppressed; PCa, prostate cancer; PPV, positive predictive value; PSA, prostate-specific antigen; PZ, peripheral zone; RF, radiofrequency; ROC, receiver operating characteristic; SNR, signal-to-noise ratio; Spm, spermine; TV, total variation; T2W, T₂-weighted; VOI, volume of interest; WS, water-suppressed.

Current limitations of single-voxel-based MRS and MRSI in the prostate are caused by the overlap of metabolite resonances, allowing the quantification of only a few metabolites (Cit, Ch, Cr and Spm) and the use of long TEs. The conventional MRSI technique can be accelerated by echo planar spectroscopic imaging (EPSI) (9–13). EPSI speeds up MRSI using an echo planar readout of one spectral and one spatial dimension, thereby achieving an acceleration factor equal to the number of points along one of the spatial dimensions. For example, a two-dimensional (2D) spatial matrix array (16×16) would be acquired 16 times faster with EPSI than with conventional MRSI. However, the acceleration may be at the cost of the signal-to-noise ratio (SNR) (11) and the spectra could be affected by Nyquist ghost artifacts (14).

A single-voxel-based 2D J-resolved spectroscopic (JPRESS) sequence has been evaluated in PCa, and has shown improved spectral dispersion because of the added spectral dimension (15,16). New computational methods have made compressed sensing feasible to accelerate MRI by exploiting the sparsity of the images in a known transform domain to reconstruct non-uniformly undersampled (NUS) k -space data (17). For further acceleration, the application of compressed sensing for MRSI is apt, exploiting sparsity in multiple dimensions of frequency and space in transform domains of wavelets and total variation (TV) (18–20). By combining EPSI with JPRESS, 2D spectra can be recorded in multiple locations in the prostate using four-dimensional (4D) echo planar J-resolved spectroscopic imaging (EP-JRESI), which combines two spectral with two spatial dimensions. A pilot feasibility has been demonstrated recently to map metabolites in the healthy human prostate and brain (21,22).

Maximum entropy (MaxEnt) reconstruction finds the spectrum that maximizes entropy whilst maintaining consistency with the measured data. MaxEnt reconstruction is an alternative non-linear reconstruction technique to compressed sensing. MaxEnt has been successfully used to reconstruct undersampled images in astronomy and multidimensional spectra in NMR (23–25), but has not been applied to the spatial-spectral domain (k_y – t_1) of 4D EP-JRESI of PCa. MaxEnt and TV algorithms have been used to reconstruct the NUS indirect spectral and spatial dimensions (21,26).

The TV algorithm was first proposed by Rudin *et al.* (27) for image denoising and, since then, has been successfully used for image restoration. In the TV algorithm, an objective function using the TV norm is minimized subject to a data fidelity term posed by the acquired projection data. Minimization of the image gradient essentially suppresses those high spatial frequency parts, such as streaking artifacts and noise, in the reconstructed images.

The goal of the present work was to validate the MaxEnt and TV non-linear reconstruction algorithms separately in patients with PCa using compressed sensing-based 4D EP-JRESI data.

MATERIALS AND METHODS

Patients

Between March 2012 and May 2013, twenty-two patients with PCa with a mean age of 63.8 years (range, 46–79 years), who subsequently underwent radical prostatectomy, were selected for the study. The patients' Gleason scores varied between 6 and 9. Their PSA levels varied from 0.7 to 22.8 ng/mL (mean, 6.23 ng/mL). These patients were scanned using a 3-T Siemens (Siemens Medical Solutions, Erlangen, Germany) MRI scanner with an endorectal 'receive' coil. The protocol combining MRI

and MRS was performed at least 8 weeks after transrectal ultrasound-guided sextant biopsy. The entire protocol was approved by the Institutional Review Board, and informed consent was obtained from each patient. PCa was histopathologically confirmed after radical prostatectomy. The voxels covering the tumorous lesions from the peripheral zone (PZ) were selected and indicated as tumor voxels, which was confirmed by the pathology report. After reconstruction, the EP-JRESI data were overlaid onto MRI images.

MRI and MRSI

A body matrix phased-array coil assembly, combined with an endorectal coil, was used in the 'receive' mode, whereas a quadrature body 'transmit' coil was used. All patients were imaged in the supine (feet-first) position. Axial images were oriented to be perpendicular to the long axis of the prostate, which was guided by the sagittal images. Axial, coronal and sagittal T_2 -weighted (T_2W) turbo spin echo images were recorded using the following parameters: TR/TE = 3850–4200 ms/96–101 ms; slice thickness, 3 mm; field of view, 20×20 cm²; echo train length, 13; data matrix, 320×256 .

A compressed sensing-based 4D EP-JRESI sequence was validated on the 3-T MRI scanner and the volume of interest (VOI) was localized using three slice-selective radiofrequency (RF) pulses (90° – 180° – 180°) (Fig. 1). The total time for the acquisition of a fully sampled 4D EP-JRESI scan (TR = 1.5 s, $16k_y \times 16k_x$, 64 – $100t_1$, $512t_2$) can be more than 25 min. The parameters for EP-JRESI were as follows: TR/TE/Avg = 1500 ms/30 ms/2; 16 phase-encoding steps; 512 complex points with an F_2 bandwidth of 1190 Hz along the detected dimension. For the second dimension (F_1), 64 increments with bandwidths of 1000 Hz were used. The in-plane spatial resolution and slice thickness were 1×1 cm² and 1 cm, respectively. As the EPSI readout simultaneously acquires one spatially encoded dimension (k_x) and one temporal dimension (t_2), we propose the use of NUS in the remaining k_y – t_1 plane, followed by compressed sensing reconstruction (MaxEnt and TV). A $4 \times$ NUS was imposed along the plane containing the incremented spectral and spatial dimensions (t_1 and k_y). Despite the mixing of spatial and spectral dimensions in the reconstruction, the sparsity requirement for reconstruction is shown to be satisfied, as required by compressed sensing. As the k_y – t_1 values are incremented, NUS can be applied along the k_y – t_1 plane.

The individual voxel volume in human prostate was 1 mL. Two sets of data were collected: one water-suppressed (WS) scan with a total scan time of 12 min and a second non-water-suppressed (NWS) scan using one average and one t_1 increment (30 s). The NWS scan was used for phase corrections (eddy current corrections). The full width at half-maximum of the water peak in the cancerous and non-cancerous locations was between 20 and 25 Hz.

Data analysis

The NUS data were reconstructed by MaxEnt and TV separately. A modified Split-Bregman algorithm (28) solves the unconstrained TV optimization problem as:

$$\min_m \|\nabla m\|_1 + \lambda \|F_u m - y\|_2 \quad [1]$$

where ∇ is the gradient operator, m is the reconstructed data, $\|x\|_1$ is the l_1 -norm, λ is a regularization parameter, F_u is the

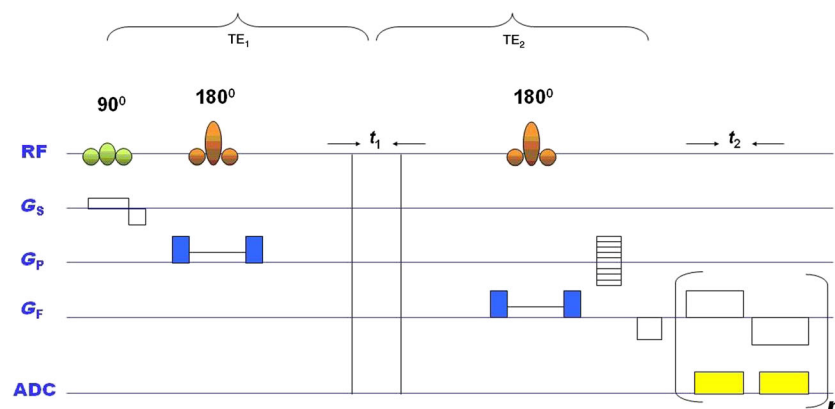


Figure 1. Schematic diagram of the four-dimensional (4D) echo planar *J*-resolved spectroscopic imaging (EP-JRESI) pulse sequence with the volume of interest (VOI) localized using point-resolved spectroscopy with three radiofrequency (RF) pulses (90°, 180°, 180°). The indirect dimension (t_1) was introduced before the last 180° pulse. ADC, analog to digital converter; G_s , G_p and G_f , gradients for slice selection, phase encoding and frequency encoding, respectively; t_2 , detected dimension; n , number of echo planar imaging bipolar readouts.

undersampled Fourier transform and y is the undersampled data. The above equation removes the incoherent artifacts caused by NUS by minimizing TV, whilst maintaining consistency with the sampled measurements. The TV regularization parameters were the same as reported by Burns *et al.* (29). We have used the Split-Bregman reconstruction method primarily for its robustness against the regularization parameters chosen. Because of the use of Bregman parameters in the reconstruction algorithm, which are calculated using the difference between the reconstruction and the sampled data at each iteration, the influence of the regularization parameters is greatly lessened compared with the use of other algorithms that solve the TV problems. Although the choice of parameters can influence the reconstruction, the algorithm allows for a wider range of possible values in order to achieve roughly the same results.

MaxEnt is a constrained convex optimization algorithm that uses a variant of the conjugate gradient method to iteratively solve the inverse problem (23,25,28):

$$\text{maximize } S_{1/2}(f) \text{ such that } \|F^{-1} Kf - D\|_2 \leq \sigma \quad [2]$$

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 measured time domain data, σ is the noise standard deviation and $S_{1/2}(f)$ is the spin - 1/2 entropy of the estimated spectrum (24). All compressed sensing 4D EP-JRESI data were processed using TV and MaxEnt reconstruction with custom MATLAB software. The reconstruction time for each method took about 25 min using an 8 GB RAM, Intel Core i7-2600 CPU @ 3.40 GHz. For the 2D data processing, the raw matrix was apodized with phase shifted and squared sine bell functions along t_1 and t_2 , and zero filled to 128×1024 prior to fast Fourier transformation along the two dimensions. All 2D spectra were presented as contour plots, and the 2D spectral matrices were not skewed by 45° about $F_1 = 0$ Hz.

Statistical analysis

Statistical analyses were performed with SPSS 21 (SPSS Inc., Chicago, IL, USA). Using logistic regression analysis, areas under the curve (AUCs) of the receiver operating characteristic (ROC) were calculated for various metabolites to discriminate between

MaxEnt and TV reconstruction methods. In addition, the paired *t*-test was used to determine the various metabolite ratios in cancerous and non-cancerous locations. $p < 0.05$ was considered to be statistically significant.

RESULTS

Using this pilot validation, 2D peaks attributed to Cit, Ch, Cr, Spm, myo-inositol (ml) and glutamate (Glu) plus glutamine (Gln) (Glu + Gln = Glx) were quantified in cancerous and non-cancerous locations using the peak integration MATLAB code. Figure 2 shows (Ch + Cr)/Cit, (Ch + Cr)/Spm, (Ch + Cr)/ml and (Ch + Cr)/Glx of cancerous and non-cancerous locations processed by TV and MaxEnt. The mean metabolite ratios ($\pm$ standard deviation, SD) of Cit, Spm, ml and Glx of the non-cancerous locations, processed using TV, were 1.158 ± 0.830 , 2.396 ± 1.95 , 5.325 ± 2.42 and 5.404 ± 2.74 , respectively. In the cancerous locations, the corresponding metabolite ratios were: 4.209 ± 2.132 , 2.808 ± 1.77 , 5.640 ± 2.18 and 5.275 ± 2.80 . Similarly, the mean metabolite ratios ($\pm$ SD) of Cit, Spm, ml and Glx of the non-cancerous locations, calculated using the MaxEnt-reconstructed data, were 1.079 ± 0.795 , 2.096 ± 1.06 , 4.967 ± 2.114 and 5.902 ± 3.40 , respectively. In the cancerous locations, the corresponding metabolite ratios were 3.620 ± 1.759 , 2.727 ± 1.46 , 6.008 ± 2.57 and 5.275 ± 3.19 .

We found that the mean Cit metabolite ratios were significantly higher in cancerous locations relative to non-cancerous locations in both the TV and MaxEnt reconstructions ($p < 0.005$). Increased levels of Spm ($p = 0.46$) and ml ($p = 0.65$) ratios, and decreased levels of Glx ($p = 0.88$) ratios, were observed in cancerous locations relative to non-cancerous locations in the TV reconstruction. Similarly, in the MaxEnt reconstruction, increased levels of Spm ($p = 0.25$) and ml ($p = 0.15$) ratios, and decreased levels of Glx ($p = 0.81$) ratios, were observed in cancerous locations relative to non-cancerous locations. None of the ratios could discriminate significantly between differing grades (Gleason scores) of PCa because of overlap of the ratio values.

Figure 3 shows spatial maps of (Ch + Cr) for the TV and MaxEnt reconstructed data acquired in a 74-year-old patient with PCa. The MaxEnt and TV reconstructions of the cancerous (Fig. 4B, D) and non-cancerous (Fig. 4C, E) locations extracted from the

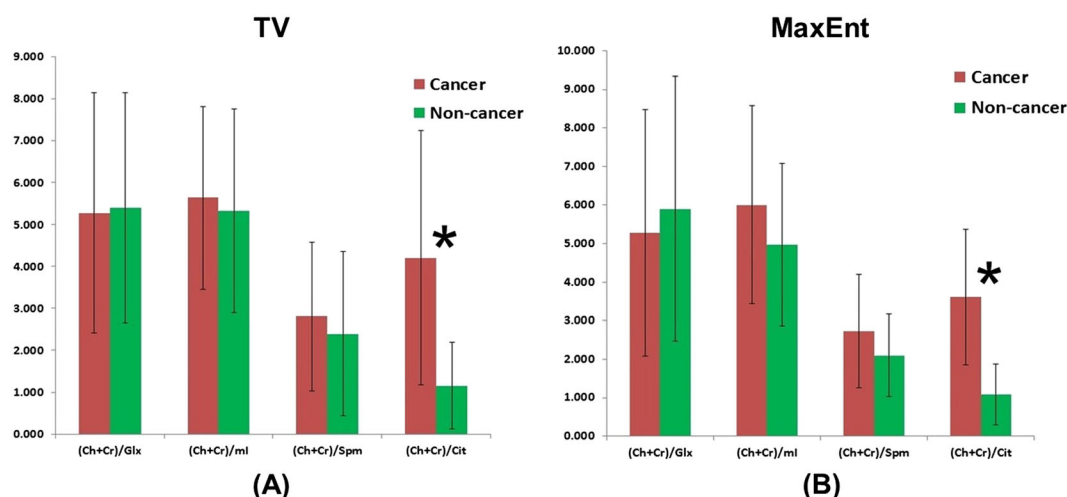


Figure 2. Metabolite ratios of citrate (Cit), spermine (Spm), myo-inositol (ml) and glutamine + glutamate (Glx) in cancerous and non-cancerous locations processed by non-linear reconstruction methods using total variation (TV) and maximum entropy (MaxEnt). Ch, choline; Cr, creatine.

JPRESS spectrum, obtained from the 4D EP-JRESI data, are shown in Fig. 4. Figure 4C illustrates the regions of interest used for peak integration. We compared and correlated the TV and MaxEnt reconstruction methods for Cit, Spm, ml and Glx in the cancerous and non-cancerous locations. The correlation of the (Ch + Cr)/Cit, (Ch + Cr)/Spm, (Ch + Cr)/ml and (Ch + Cr)/Glx ratios for the MaxEnt and TV reconstructions in the cancerous locations are shown in Fig. 5. For each patient, two to three voxels were selected in the PZ of the cancerous and non-cancerous locations, and the average values for each location were reported. A positive correlation was found for the following metabolites in the cancerous locations: (Ch + Cr)/Cit ($R^2 = 0.85$), (Ch + Cr)/Glx ($R^2 = 0.96$), (Ch + Cr)/Spm ($R^2 = 0.86$) and (Ch + Cr)/ml ($R^2 = 0.95$). The concentration of Cit is higher in healthy prostate. Hence, if the Cit peak was higher than the Ch peak, the voxel was considered to be non-cancerous for (Ch + Cr)/Cit values below 0.5 and malignant for (Ch + Cr)/Cit values above 0.5. These values were selected manually on each subject.

The results of the logistic regression analysis and consequent ROC curve analyses are given in Table 1, including the sensitivity,

specificity, positive predictive value (PPV), negative predictive value (NPV), AUC and accuracy for the classification of the MaxEnt and TV methods. ROC curve analyses for differentiating the metabolite ratios of cancerous and non-cancerous locations in MaxEnt suggest that the Cit ratio gives the best predictability, with a sensitivity of 86.4%, specificity of 90.0%, accuracy of 88.6% and AUC = 94.0%. In addition, the overall sensitivity, specificity, accuracy and AUC of ml and Spm were slightly better in MaxEnt compared with TV.

DISCUSSION

Using the NUS data with non-linear iterative reconstruction, we have validated the TV and MaxEnt reconstruction methods independently in patients with PCa using EP-JRESI in a clinically feasible time. In addition to a significantly increased Cit ratio in cancerous locations, increased metabolite ratios of Spm and ml, and decreased ratios of Glx, were found in cancerous locations compared with non-cancerous locations. Although TV and

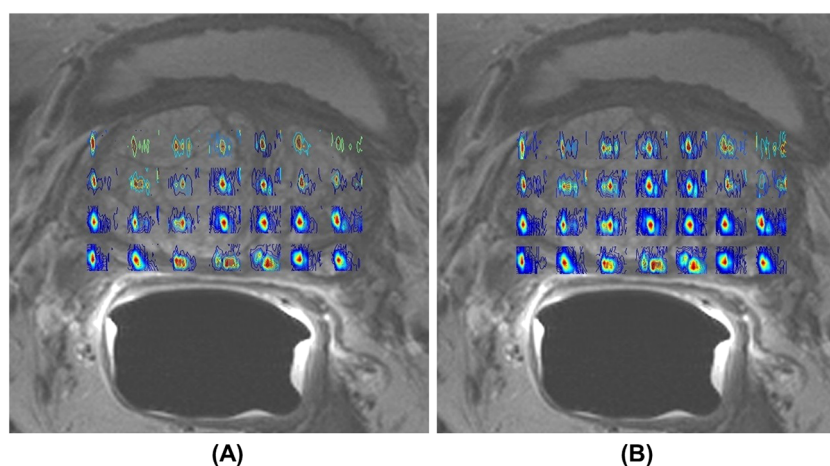


Figure 3. Spatial maps of (choline + creatine) [(Ch + Cr)] for total variation (TV) (A) and maximum entropy (MaxEnt) (B) non-linear reconstruction methods of the four-dimensional (4D) echo planar J-resolved spectroscopic imaging (EP-JRESI) data recorded in a 74-year-old patient with prostate cancer (PCa). EP-JRESI was overlaid on top of the T_2 -weighted MRI.

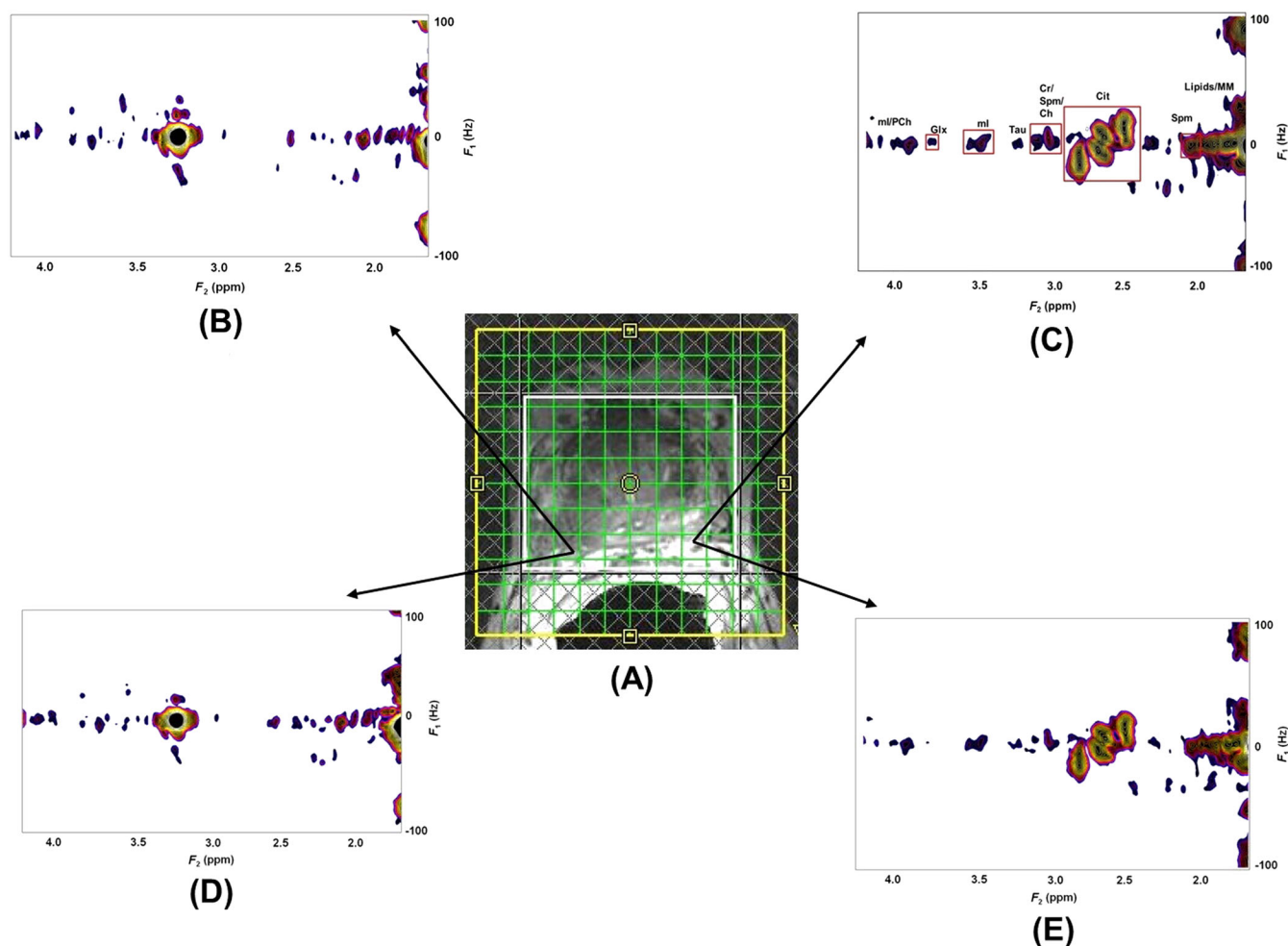


Figure 4. Echo planar J -resolved spectroscopic imaging (EP-JRESI) voxel localization on top of the T_2 -weighted MRI (A); two-dimensional (2D) J -resolved spectroscopy (JPRESS) spectra extracted from the maximum entropy (MaxEnt) and total variation (TV) reconstructions of cancerous (B, D) and non-cancerous (C, E) locations. The regions of interest used for peak integration are shown in (C); (MM, macromolecules; Cit, citrate; Glx, glutamine + glutamate; ml/PCh, myo-inositol/phosphocholine; Tau, taurine; Spm, spermine).

MaxEnt reconstruction methods showed comparable results in cancerous and non-cancerous locations, the sensitivity, accuracy and AUC were slightly increased in the MaxEnt reconstruction.

In the present study, we report the ratios of (Ch + Cr)/Cit, (Ch + Cr)/Spm, (Ch + Cr)/ml and (Ch + Cr)/Glx, because of the proximity of the total Cr peak (3.0 ppm) to the total Ch peak (3.2 ppm) in these *in vivo* MR spectra, which were therefore not always separable. In this study, significantly higher ratios of Cit were observed in the PZ of cancerous locations.

It is likely that the drop in Cit levels precedes malignant transformation (30). It has been suggested that, as a result of a metabolic switch, neoplastic cells oxidize Cit, whereas normal prostatic cells show a low Cit oxidizing capability (31). Decreased levels of zinc, which would relieve *m*-aconitase from inhibition, has been proposed as one of the reasons for the decreased level of Cit in PCa (30).

Ch is an essential component of cell membrane synthesis and phospholipid metabolism, and functions as an important methyl donor. Ch-containing molecules are an essential component of cell membranes, which are more highly concentrated in tumorous areas within the prostate than in healthy prostate tissue (32,33). Ch groups are precursors and breakdown products of the phospholipid phosphatidylcholine, a major cell membrane

compound (34). Increased Ch is observed as a result of altered phospholipid metabolism in PCa cell lines (33). This alteration is most probably a result of an increased expression and activity of choline kinase, a higher rate of Ch transport and an increased phospholipase activity (34).

The polyamines Spm, spermidine and putrescine are essential for the differentiation and proliferation of cells, the synthesis of DNA, RNA and proteins, and the stabilization of cell membranes and cytoskeletal structures (35). Previous studies have observed high levels of Spm in healthy prostate tissue and benign prostatic hyperplasia, and reduced Spm levels in malignant prostate tissue (16,36–38).

The osmoregulator ml is expressed in a variety of tissues, and its decrease was observed in PCa within human expressed prostatic secretions using high-resolution NMR (39) and in breast tumors (40). In our study, slightly increased ml ratios were observed in cancerous locations, but were not statistically significant.

Glu and Gln are difficult to resolve owing to resonance overlap. As a result, most MRS studies use the sum of Glu and Gln (expressed as Glx or Glu + Gln). Glu is extensively involved in metabolic and oncogenic pathways. Koochekpour (41) showed that serum Glu levels correlated directly with Gleason scores

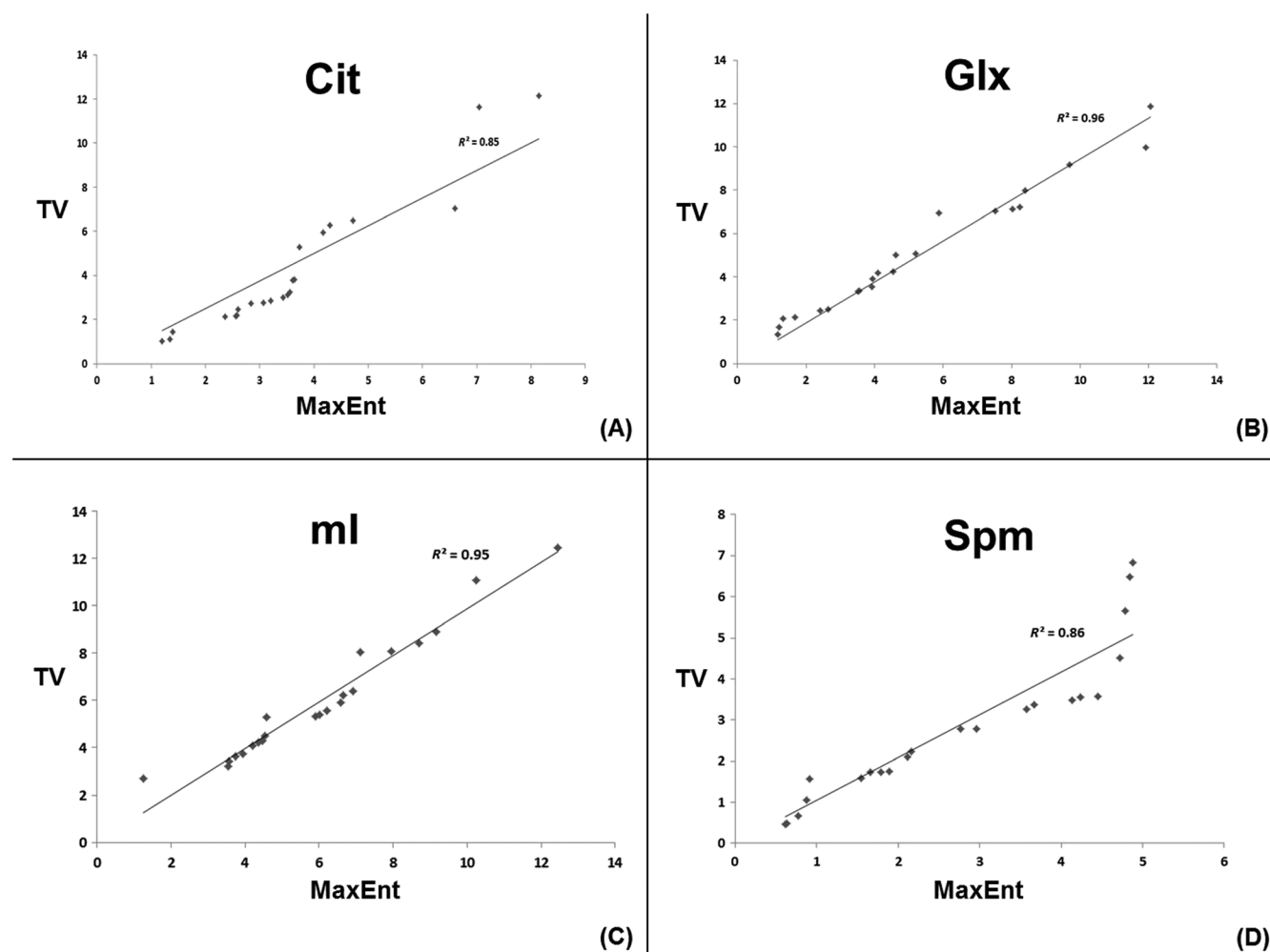


Figure 5. Correlation of maximum entropy (MaxEnt) and total variation (TV) non-linear reconstruction methods for citrate (Cit) (A), glutamine + glutamate (Glx) (B), myo-inositol (ml) (C) and spermine (Spm) (D) in cancerous locations. R^2 values are shown for each metabolite.

Table 1. Measures of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of maximum entropy (MaxEnt) and total variation (TV) methods using receiver operating characteristic (ROC) curve analysis

MaxEnt						
Metabolite	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	AUC (%)
Cit	86.4	90.0	88.6	90.5	87.0	94.0
Glx	66.6	31.8	47.7	48.3	46.7	56.9
ml	54.5	63.6	59.1	60.0	58.3	65.1
Spm	50.0	72.7	61.4	64.7	59.3	64.9
TV						
Cit	86.4	90.9	88.6	90.5	87.0	92.1
Glx	63.6	36.4	50.0	50.0	50.0	57.2
ml	40.9	59.1	50.0	50.0	50.0	58.5
Spm	50.0	63.6	56.8	57.9	56.0	58.5
Cit, citrate; Glx, glutamine + glutamate; ml, myo-inositol; Spm, spermine.						

Cit, citrate; Glx, glutamine + glutamate; ml, myo-inositol; Spm, spermine.

(<6 versus >8) and primary PCa aggressiveness. In our study, decreased Glx ratios were found in cancerous locations, but were not statistically significant.

There was an overlap between cancerous and non-cancerous locations, possibly as a result of the low SNR of the Cr peak. As

a result of patient movement and B_0 inhomogeneity, the resonances of Ch, Cr and Spm are difficult to resolve, especially in cancerous locations, adding to the uncertainty in quantification. However, the use of prior knowledge fitting (ProFit) may improve accurate metabolite (42) quantification, which warrants future

investigation. As a result of the limited patient population, we did not find any significant changes in other metabolites. In addition, this study focused on the PZ of the prostate, where only 80% of cancer occurs. The advantage of the compressed sensing-based 4D EP-JRESI sequence is that it records short TE-based spectra from multiple regions of human prostate, and additional metabolites, such as ml, Spm and Glx, to the normally detected Cit, Cr and Ch.

This pilot work demonstrated the use of slice-based 4D EP-JRESI, and future work will focus on volume-based, five-dimensional (5D) EP-JRESI in PCa (43). Compressed sensing-based 4D EP-JRESI shortens the total acquisition time, effectively enabling future potential to extend to pathological evaluations in a clinical set-up. The current validation method may require further optimization to improve the overall performance. As reported by Burns *et al.* (26), the sample mask is crucial to the SNR of each reconstructed prostate metabolite for the 4D EP-JRESI data. Further optimization of the reduction in non-linearity of the reconstructed peaks may enable accurate quantification of metabolites. In addition, future work will address the use of Poisson gap *versus* deterministic sample masks, and the optimization of the modulation functions for specific metabolites relevant to PCa.

CONCLUSION

We were able to detect metabolites in PCa using compressed sensing-based 4D EP-JRESI data acquired in clinically acceptable times (<12 min). We have shown that it is possible to undersample the 4D EP-JRESI sequence with an acceleration factor of four times, and that the data can be reliably reconstructed using the TV and MaxEnt methods. Both non-linear reconstruction methods provided comparable results.

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