A peak phasing and alignment algorithm for automated post-processing of 3D MRSI data from the prostate of cancer patients.

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Introduction: Diagnosis and localization of suspected prostate cancer (PCa) requires TRUS-guided sextant (or more) biopsy with limited accuracy. MR Spectroscopic Imaging (MRSI) of PCa patients can provide complimentary information on the detection, localization and grading of PCa with minimal risk to the patient [1]. Currently, prostate 3D MRSI acquisition methods have matured considerably, but automatic spectral processing remains a bottleneck in the realisation of routine clinical application. For instance, processing is often hampered by variations in phase and chemical shift of metabolite peaks across the MRSI data set. Furthermore, the citrate resonance at 2.6ppm is sensitive to the salt concentration and pH of the local environment [2] affecting the relative chemical shifts of choline and citrate across an MRSI data set. To overcome these problems we present an automated method to correct for chemical shift variations and phase in MRSI data sets of prostate tumour patients.

Methods: 3D MRSI data of PCa patients was acquired at 3T (145ms TE, endorectal coil, MEGA PRESS [3]). A simulated set was generated with known chemical shift variations (s.d 3.11Hz) and phase distortions. The alignment algorithm has an initial phase correction (maximizing the correlation to the magnitude spectra) then a frequency correction based on principal component analysis [4,5]. The spectral region of interest is corrected in two separate sections: a Cho/Cr region (3.36-2.87ppm: containing the overlapping choline, creatine and polyamine signals) and a Citrate region (2.87-2.38ppm containing the citrate CH_2 resonances). The algorithm applies corrections that iteratively tend towards 0Hz. The remaining voxels are corrected by an average of neighbouring voxels. The algorithm was applied to the simulated set and five novel 3D MRSI data sets from patients. Each set is also referenced to the citrate peak maximum per spectrum using the auto phased data. Two simple (Choline +creatine)/citrate ratios (CC/C) are then calculated. The first is by integrating positive data points over the choline and creatine peaks (3.36-3.06ppm) divided by the central citrate signals (2.65-2.59ppm) and is used to compare thedistribution of CC/C for aligned, citrate-referenced and unaligned data. The second ratio is calculated from a single-data-point height at three chemical shifts (3.20 + 3.07 / 2.62ppm) and is used to display the localization of the data in an MRSI slice.

Results: The algorithm, applied to the simulated data set, showed iterative improvement in 98% of citrate peaks and 89% of the Cho/Cr region with reduced standard deviations of the known peak position to 0.68Hz and 1.65Hz respectively. Figure (a) shows the simulated data (red) overlayed with the algorithm output of correctly phased spectra (green) showing well defined – aligned - Cho/Cr and citrate regions. The median at each spectral point is shown in Figure (b) for aligned (green) and unaligned (red) data with much higher signals in the aligned "median spectra" which has greater signal to noise (x3). Figure (c) shows the quartiles and medians for the integral CC/C ratio of all voxels in the simulated set. Both citrate referencing and alignment greatly reduce the variance of the data but the median CC/C value is significantly higher (p=2x10-4) for the processed spectra due to increased choline and creatine signal aligned to the integrated region. The mean correlation coefficient of all spectra in the peak region (3.36-2.38ppm) improves from 0.04 raw data to 0.88 phased and aligned. In the five novel-patient data sets, this mean correlation coefficient over the peak region improved in each case. Principal component analysis was performed of the spectral region of interest in all spectra. The percentage of variance of the data explained by the first principal component increases, in all five data sets - after the algorithm is applied, reflecting the decrease in the variations of peak position and phase. The algorithm also improves SNR of the "Median Spectrum", and gives a dramatic reduction in CC/C ratio variance in all five data sets. Comparing the citrate referenced to the algorithm aligned data showed significantly (Mann-Whitney U test) higher CC/C ratios for algorithm-aligned data in four of the five test sets. A CC/C ratio of data height at exact frequencies (at assigned chemical shifts of the three metabolites) shows better localization and less erroneous negative voxels for aligned data over unaligned data, an example slice from one patient is given in Figure (d).

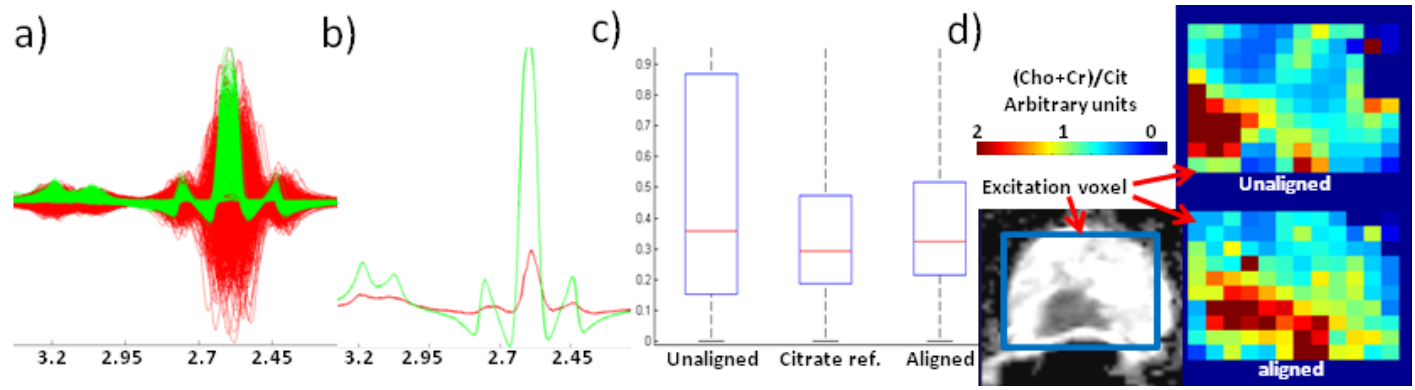

Figure: a) *Overlay of simulated 1000 spectra before (red) and after (green) alignment,* ***(b)*** *shows the median at each frequency point for this data set: a "Median Spectrum";* ***(c)*** *shows the integral CC/C ratios for the unaligned simulated data set, the same data after simple referencing to the top of citrate and for the fully aligned data;* ***(d)*** *a patient data example showing tumour position and CSI excitation voxel on an ADC map and the data-height CC/C ratios for the excitation volume voxels before and after application of the alignment algorithm.*

Discussion: Applying the new algorithm to simulated sets showed significant improvements in the alignment of prostate MRSI spectra particularly in the citrate region. Significant improvements in the alignment has also been shown for novel patient data with higher mean cross-correlation, better defined peaks in "median spectra" and lower variance in the distribution of CC/C ratios. Additionally, the algorithm measures chemical shift variations in signals that carries information on the environment of the corresponding metabolites in prostate and cancer tissues.

References:[1] Nayyar *et al.* 2009 *BJU Int.* 103,1614.[2] Van der Graaf *et al.*1996 *JMR(B)* 112,58. [3] Scheenen *et al.* 2007 *Rad.* 245, 507. [4] Witjes *et al.* 2000 *JMR* 144, 35. [5] Brown *et al.* 1996 *JMR(B)* 112, 32. **Acknowledgments:** Support by the EU RTN project FAST