Prostate Spectroscopy Analysis with LCModel: Development of 3T Scoring Criteria

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INTRODUCTION: Prostate spectroscopy has been extensively studied at 1.5 Tesla while the promise of increased SNR and spectral resolution of higher field strengths has not been fully realized to date. There are many challenges to performing prostate spectroscopy at 3 Tesla including the availability of endorectal coils, the development of acquisition methods and improvement of post processing for spectral quantitation. To date, many investigators have demonstrated the ability to perform prostate imaging studies at 3T with an emphasis on increased SNR and spatial resolution whether it be for imaging or spectroscopy. However, no studies have demonstrated a way to classify spectra acquired at 3T. The challenge of defining a classifier results from the difficulty in quantifying the data. In order to maintain SNR the shortest echo time is desired; at 3T this is approximately 100 ms, resulting in an out-of-phase citrate peak and significant polyamine signal. The challenge of quantifying this data will be addressed in this work by using LCModel [1] and a simulated basis set, the results from which a "normal" ratio (total choline to citrate) mean and standard deviation will be defined and used to score the non-normal spectra.

METHODS: A diagnostic MRI exam including 3D spectroscopic imaging (3DSI) was performed on 50 patients with biopsy proven prostate cancer. All but 6 of the studies, which had poor quality spectroscopy data, were used in this analysis. Imaging was performed on a Philips Intera 3T (Philips Medical Systems, Best, The Netherlands) with a 1.5T endorectal coil re-tuned to 128MHz (MRinnervu; Medrad, Pittsburgh, PA). The 3DSI acquisition used PRESS and outer volume suppression for localization along with the following parameters: TR=960ms, TE=100ms, matrix=12x12, slices=12, nominal voxel size = 0.22 cm^3, 60% scan percentage and BASING for residual water and lipid. Spectroscopy voxels from the 3DSI data were chosen on a per sextant basis. Selected voxels were required to be at least 70% in the peripheral zone without contribution from the periurethral area. In the event there was a homogeneous low signal intensity lesion observed on T2W imaging and early wash-in-washout on dynamic contrast enhanced MRI, a voxel was chosen at that location of the sextant. Hemorrhagic areas, as indicated by hyperintensity on T1W images, were excluded.

Spectral quantification was performed with LCModel using a simulated basis set created by solving the Liouville equation and making use of each metabolites chemical shift and *J*-coupling information along with the RF pulses and timing details of the acquisition sequence [2]. The metabolites of interest consisted of the choline containing compounds (glycerophosphocholine (GPC), phosphocholine (PCho) and choline (Cho)), spermine (Spm) which represents the polyamine signal, creatine (Cre) and citrate (Cit). The choline containing compounds were grouped together as total choline (tCho) in the analysis. While it is important to have the individual components for fitting, only their combined result is considered reliable based on the Cramer-Rao Lower Bound (CRLB).

As all patients studied were diagnosed with prostate cancer, we attempted to obtain "normal" voxels from sextants that were at least one sextant removed from any benign or malignant process as determined on biopsy. For example, if inflammation was observed in the left apex and Gleason grade 6 was observed in the right apex and mid gland then only the voxel from the left base would be used as a "normal" voxel. From these voxels, 3 were removed as outliers as they were outside 1.5 times the interquartile range. After this process, 18 voxels were chosen with which to calculate the mean and standard deviation of tCho/Cit in normal voxels. These values were then used to generate a 5 point scoring system as proposed by Jung *et. al.* based on the number of normal standard deviations a particular voxel's tCho/Cit ratio was above the normal mean [3]. Remaining voxels were then categorized based on biopsy pathology: Gleason score 6 cancer (46 voxels), Gleason score 7 (43 voxels), Gleason score 8 and higher (15 voxels), prostatic intraepithelial neoplasia (PIN) (6 voxels), and inflammation (26 voxels). Voxels not in one of these categories consisted primarily of sextants normal on biopsy but adjacent to abnormal sextants and were not considered further in this analysis.

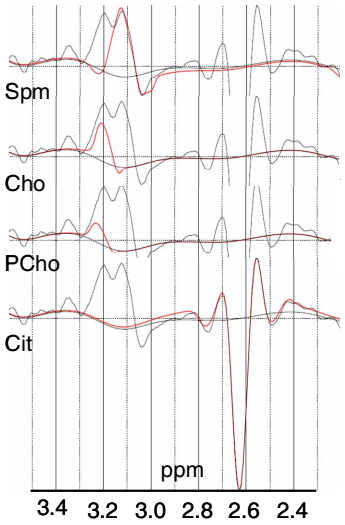

Fig. 1: Individual metabolite contributions from the basis set to the in vivo spectrum acquired in this study.

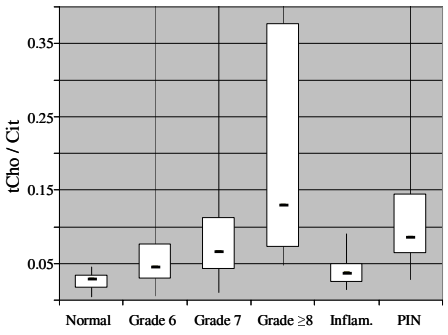

Fig. 2: Box plots showing the distribution of tCho/Cit ratios with respect to sextant matched biopsy results.

RESULTS AND DISCUSSION: A typical in vivo spectrum from a relatively normal voxel is shown in **Fig. 1** along with the individual metabolite contributions used to fit the data (shown in red and identified by the name on the left). There was no significant contribution form GPC or Cre in the fitting in this case therefore these metabolites are not shown. All the biopsy categorized voxels are displayed in the box plot of **Fig 2**. The horizontal dash within each category represents the median tCho/Cit ratio which separates the second and the third quartiles while the lower and upper whiskers represent the first and fourth quartiles respectively. As there are some extremely large values due to near zero Cit values the plot was truncated to highlight the increasing trend with grade as observed by the median value in each group.

The mean and standard deviation of tCho/Cit in the 18 normal voxels was 0.0253±0.0123. This information was used to score each voxel from **Fig. 2** on a scale from 1 to 5 depending on how many normal standard deviations it was from the normal average. The higher the score the more likely it is cancer. The scored data is shown in **Fig. 3** while still separated into columns by tissue type. While these results seem very reasonable there is much overlap between the normal and Gleason grade 6 and 7 cancer. This data gives us initial insight into the potential of such a classification for 3T data processed with LCModel. However, verification must be performed with more complete pathologic correlation beyond that of biopsy. There is a tremendous potential for sampling error even if the spectroscopy voxels were located directly at the sites of biopsy as it is typical that only a fraction of cores are positive for cancer and each core is much smaller than a single spectroscopy voxel.

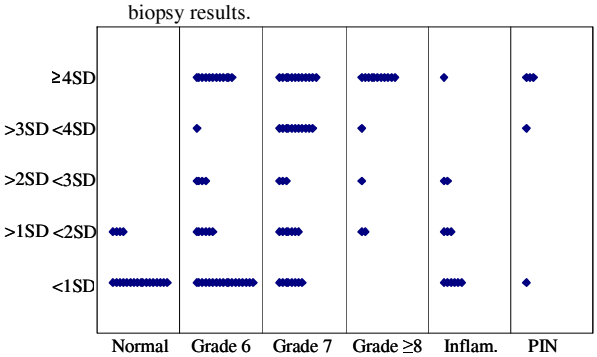

Fig. 3: Voxels in each category are scored based on the number of normal standard deviations its tCho/Cit ratio was from the normal mean. The more voxels in a given category with the same score, the longer the horizontal blue stripe.

Despite the absence of a definitive gold standard, this study demonstrates the feasibility of quantifying 3T 3DSI data with LCModel based on a simulated basis set. Until now, the challenge of quantifying 3T prostate spectroscopy data has prevented the development of scoring strategies similar to those at 1.5T. This is an important step toward realizing the potential of high field prostate spectroscopy studies.

REFERENCES: [1] Provencher. MRM 1993;30(6):672. [2] Henry et. al. MRM 2006;55(2):250. [3] Jung et. al. Radiology 2004;233(3)701.
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