Automated Prostate Cancer Detection from Magnetic Resonance Spectroscopy (MRS) using a Hierarchical Non-linear Dimensionality Reduction Scheme

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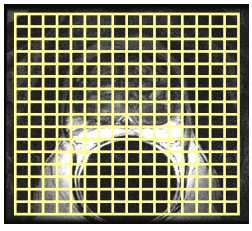
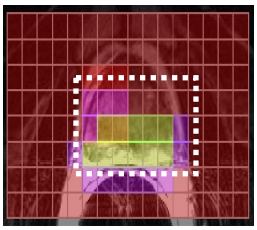
Background: The current standard for prostate cancer detection is transrectal ultrasound (TRUS) guided symmetrical needle biopsy which has a high false negative rate associated with it. Most previous automated analysis work for MRS for cancer detection has focused on developing fitting techniques that yield peak areas or relative metabolic concentrations of different metabolites like choline, creatine and citrate. The automated peak finding algorithms suffer from problems like peak overlap and peak distortion associated with the noisy data. Other methods like Principal Component Analysis (PCA) (1) and z-score method (2) are also limited with PCA being a linear reduction method while biomedical data is inherently non-linear (3) and z-score suffering from low sensitivity and specificity. Here we present a novel approach that integrates nonlinear dimensionality reduction (DR) method with an unsupervised hierarchical clustering algorithm to identify spectra corresponding to cancer on prostate MRS thereby obviating the need for peak detection on a per spectra basis.

Methods: Ground truth location for cancer on prostate was determined from the sextant location and maximum size of cancer available from the ACRIN database, from where a total of 18 MRS studies were obtained. We apply nonlinear reduction method (Isomaps/ LLE) to embed the high dimensional spectral data in a low dimensional space so that objects that are adjacent in the high dimensional ambient space are mapped to nearby points in the output embedding. Hierarchical unsupervised k-means clustering is applied to distinguish non-informative (spectra lying outside the prostate) from informative spectra (within prostate). The objects in the dominant background cluster, which correspond to the spectra lying outside the prostate, are pruned and eliminated from subsequent analysis. The recursive scheme alternates between computing the low dimensional embedding of all the spectra in the 3D MRS scene and the unsupervised clustering algorithm to identify and eliminate non-informative spectra. This scheme is recursed until the sub-clusters corresponding to cancer spectra are identified. We performed 3 fold and 5 fold cross validation on our studies to obtain the sensitivity, specificity and PPV value of our method. We also compare our method with previously used methods like PCA and z-score.

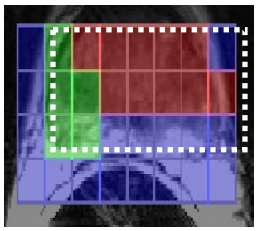
Results:



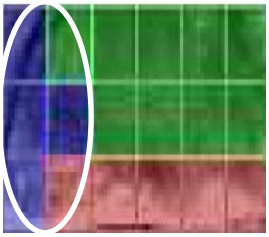
N×N Spectra



N×N/2 spectra

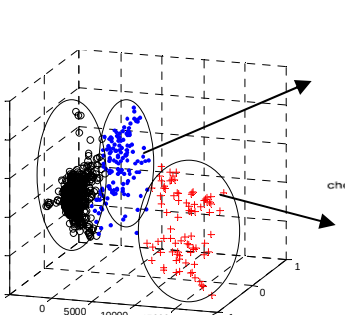


N/8 spectra

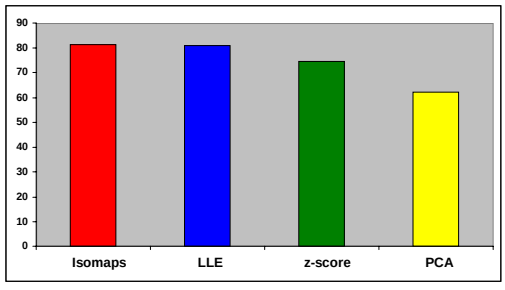


Prostate spectra

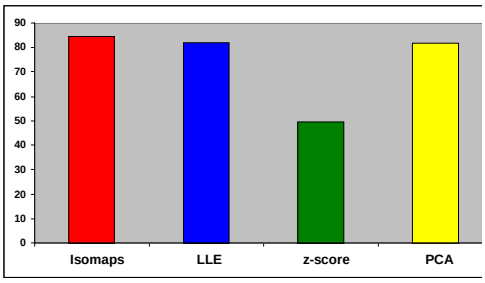
Fig 1: Hierarchical clustering scheme startin from N×N to classification of prostate spectr All the spectra are classified into 3 classes each level considering prostate spectra cou either belong to cancer, benign other tissu classes like BPH, HGPIN. Also note th cancer was present on the right side of t prostate in this slice which could be clear identified as the circled class.



(a)



(b)



(c)

Fig 2: (a) Lower dimensional embedding representation of all the spectra. Note that if two spectra are similar they will fall into same class after classification and if different they will fall into different classes (as shown in the figure- cancer and benign spectra in different classes in lower dimensional embedding) (b)-(c) Comparison of non-linear DR methods with PCA and z-score for 3-fold cross validation of (b) sensitivity for Isomaps-Red (81.43), LLE-Blue (81.23), z-score-Green (74.75) and PCA-Yellow (62.26) c) specificity for Isomaps (84.36), LLE (82.18), z-score (49.75), and PCA (81.80)

Conclusion: We were able to automatically identify suspicious regions on prostate using MRS with a high sensitivity (~82%) and specificity (~83%) using non-linear dimensionality reduction method and hierarchical clustering scheme. Our method also outperformed linear reduction method (PCA) and the popular z-score method which were found to have low sensitivity and specificity.

References: (1) Kurhanewicz, J., et al.: Analysis of a Complex of Statistical Variables into Principal Components. Magnetic Resonance in Medicine
(2) McKnight, T., et al.: An Automated Technique for the Quantitative Assessment of 3D-MRSI Data from Patients with Glioma. Journal of Magnetic Resonance Imaging
(3) Lee, G., et al: An Empirical Comparison of Dimensionality Reduction Methods for Classifying Gene and Protein Expression Datasets. ISBRA (2007)