COMBINING HR-MAS AND *IN VIVO* MRI AND MRSI INFORMATION FOR ROBUST BRAIN TUMOR RECOGNITION

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Abstract— **In this study we propose to classify short echo-time brain MRSI data by using multimodal information coming from magnetic resonance imaging (MRI), magnetic resonance spectroscopic imaging (MRSI) and high resolution magic angle spinning (HR-MAS), and to develop an advanced pattern recognition method that could help clinicians in diagnosing brain tumors. We study the impact of using HR-MAS information in combination with *in vivo* information for classifying brain tumors and we investigate which parameters influence our classification results.**

To integrate HR-MAS, MRSI and MRI information a harmonization of all the input spaces is required due to the fact that we have to manage the use of very different information/data, obtained with different measurement techniques, as well as the use of data coming from different clinical centers. The problem is overcome by extracting common characteristic features from all the different data types.

The pattern recognition technique used in this study is Canonical Correlation Analysis (CCA), a statistical method developed to assess the relation between two sets of variables. The method has recently been successfully applied to prostate and brain data and is able to simultaneously exploit the spectral as well as the spatial information characterizing the MRSI data.

Here, the performance of CCA when making use of different feature vector approaches is analyzed and compared.

Keywords— **multimodal information, canonical correlation analysis, brain tumor classification, pattern recognition.**

I. Introduction

Previous studies have already proved that the use of HR-MAS data can bring added value to *in vivo* MRSI, as we can more easily distinguish the metabolites characterizing the different tissue types. In fact, as shown in Fig. 1, compared to *in vivo* MRS/MRSI, HR-MAS spectra are characterized by narrow line widths and large signal to noise ratios. In particular, with HR-MAS an important number of metabolites can be identified [1].

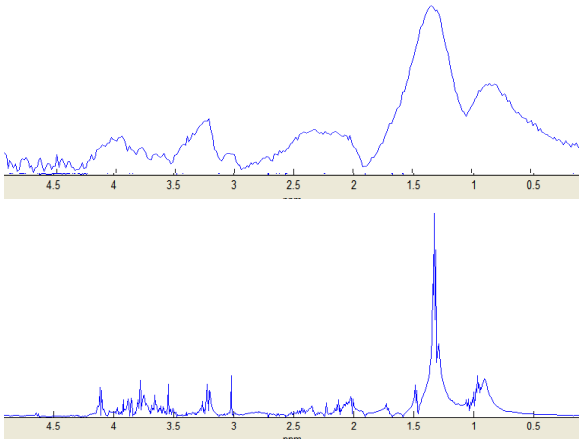

Fig.1 Comparison of in-vivo (top) and ex-vivo (bottom) spectra measured in a patient with GBM (scales are fitted; displayed region [0, 4.7] ppm).

We propose a classification method that makes use of multimodal information coming from 3 different measurement techniques: HR-MAS, MRI and MRSI. This method is based on CCA, an accurate and efficient tissue segmentation and classification technique that has recently been successfully applied to prostate and brain tumor recognition [2,3]. The performance of CCA is here further investigated by introducing the HR-MAS information as a prior knowledge. The results obtained by the new approach are compared with the results obtained by the approach described in [3], further called classical approach.

II. Materials and Methods

A. Materials

The tissue subspace models used in this study were obtained by exploiting information coming from HR-MAS measurements on 100 patients with 4 different tumor types

and stored at -80^{0}C until use. The biopsies were gathered in 4 brain tumor classes: 27 glioblastomas (GBM), 18 grade II, 6 grade III, 49 meningiomas (MNG). 1D PRESAT (pulse-and-acquire) data were acquired at 11.7 T (500 MHz for 1H) at 0-4 ^{0}C and 4,000 Hz spinnning rate using BRUKER Analytik GmbH spectrometers. The acquired signals were preprocessed. The water components were removed by HLSVD-PRO [4]. The filtered 1D "presat" signals were normalized (divided by the L2 norm of the frequency domain signal between 0.25 and 4.2 ppm), aligned with respect to the Alanine doublet at 1.47 ppm, and corrected for the baseline (by subtracting the product of the signal and an apodization function) to obtain the preprocessed signals [5].

The method was evaluated on a number of 14 images coming from patients with brain tumor diagnosed by consensus on a histopathological study. The MR data was acquired with a 1.5 T Siemens Vision whole body scanner. For every patient first 4 MR images were acquired: T1 weighted (TE/TR=15/644ms), T2 weighted (TE/TR=16/3100ms), proton density weighted (TE/TR=98/3100ms) and a Gadolinium enhanced T1 image (15 ml 0.5 M Gd-DTPA). MRSI data were acquired, using a 2D STEAM pulse sequence, with the following parameters: 16x16x1024 samples, TR/TE/TM=2000 or 2500/20/30 ms, slice thickness = 12.5 or 15 mm, FOV = 200 mm, spectral width = 1000 Hz and NS=2. Eddy current correction was performed, followed by water removal, baseline correction [6] followed by the subtraction of the residual from the original time domain signal. Finally, all spectra were normalized with respect to the water signal.

B. Canonical Correlation Analysis

CCA represents the multi-channel generalization of ordinary correlation analysis, which quantifies the relation between two random variables *x* and *y* by means of the so-called correlation coefficient:

$$\rho = \frac{Cov[x, y]}{\sqrt{V[x]V[y]}} \tag{1}$$

CCA can be applied to multichannel signal processing as follows: consider two zero-mean multivariate random vectors $x = [x_1(t), \ldots, x_m(t)]^T$ and $y = [y_1(t), \ldots, y_n(t)]^T$, with $t = 1, \ldots, N$, where the superscript T denotes the transpose. The following linear combinations of the components in x and y are defined, which respectively represent two new scalar random variables X and Y:

$$\begin{aligned} X &= \omega_{x_1} x_1 + \cdots + \omega_{x_m} x_m = \omega_x^T x \\ Y &= \omega_{y_1} y_1 + \cdots + \omega_{y_n} y_n = \omega_y^T y \end{aligned} \tag{2}$$

CCA computes the coefficients ω_x and ω_y that maximize the correlation between X and Y.

In the tissue segmentation approach proposed in [2], the aim is to detect those voxels whose spectra correlate best with model tissue spectra, defined as prior knowledge, by simultaneously exploiting the spectral-spatial information characterizing the MRSI data. CCA is applied for each voxel and the class of the model tissue giving rise to the largest canonical correlation coefficient is assigned to the voxel under investigation. The results are then exploited in order to construct nosologic images in which all the detected tissues are visualized.

III. Results and discussion

The purpose of our study is to analyze the behavior of a method that combines multimodal information. To this aim, a harmonization of the input space is required and this step is performed by a dimension reduction of the available data. The input pattern for developing the tissue subspace model was considered either as a set of quantified values from HR-MAS spectra or as the combination of the quantified values from HR-MAS and imaging intensities from MRI measurements. Tests were performed for both cases and compared with the results obtained by the classical approach.

For extracting common characteristic features and reducing the input space, peak integration, a frequency domain quantification method based on the integration of the area under the peaks of interest, was used. The following metabolites were considered [7] *L2* (lipids at 0.9ppm), *L1* (lipids at 1.3 ppm), *Lac* (3CH3-group), *Ala* (1CH3-group), *NAA* (2CH3-group), *Glx* (3CH2-group), *Cr* (N(CH3)-group), *Cho* (N(CH3)3-group), *Tau* (1CH2-group), *mI* (1CH-, 3CH-, 4CH- and 6CH-group) + *Gly* (2CH2-group).

The *y* variable in CCA, called subspace model, consists of a multivariate vector. Specifically, the first component (*y1*) was defined as the mean of the feature vectors extracted from the HR-MAS signals by peak integration. The second component (*y2*) was defined as the first principal component of the matrix containing all the mean-centered HR-MAS feature vectors.

$$\begin{cases} y1(n) = \dfrac{1}{M}\displaystyle\sum_{i=1}^{M} S_i(\omega_n) \\ y2(n) = 1^{st}\, PC \end{cases} \tag{3}$$

The performance of CCA was analyzed by considering two different approaches: in the first one the feature vectors contain 10 HR-MAS metabolite estimates, while in the second approach, the feature vectors contain 14 entries (10

HR-MAS metabolite estimates and 4 MRI variables). The results of the method were analyzed for both cases. Then, we compared the results with the nosologic images obtained by the classical approach (10 MRSI metabolites estimates and 4 MRI variables [3]).

For each case under investigation, each voxel was assigned to a certain tissue type by applying CCA between the tissue subspace models (y variable) defined a priori, and the voxel under investigation (x variable). The considered voxel was assigned to the tissue type described by the subspace model with the highest canonical correlation coefficient. The final result is a nosologic image where the detected tissue types are visualized by different colors.

In order to exploit the spatial information the x variable was defined as a multivariate vector that contains information not only from the voxel under investigation but also from the surrounding voxels. Different spatial models can be used to define the x variable. In this study, CCA was applied by adopting the symmetric 3x3 spatial model.

The patient from Fig. 2 was diagnosed with ***glioblastoma*** tumor located in the upper-right corner of our grid image.

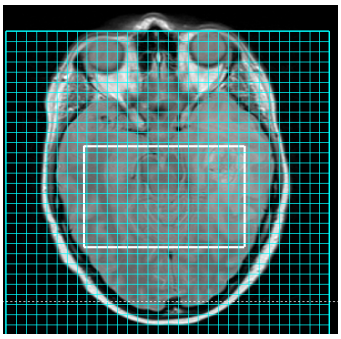

Fig.2 MRSI image of a patient affected by a glioblastoma tumor (upper-right corner of the image)

In Fig. 3-5, we report the results obtained by applying the different approaches of CCA (10 HR-MAS feature vector approach, 14 HR-MAS feature vector approach, classical approach) for the same case.

In all the different approaches the area of the tumor is correctly detected, but while the classical method detects a big area of glioblastoma surrounded by tissue belonging to meningioma (see Fig 3), in the new 10 feature vector approach the main part of the tumor area is classified as glioblastoma surrounded by voxels of grade II tumor (see Fig. 4). As a patient can not present in the same area of the brain both meningioma and glioblastoma tumor types, we believe that the new approach is closer to clinical reality.

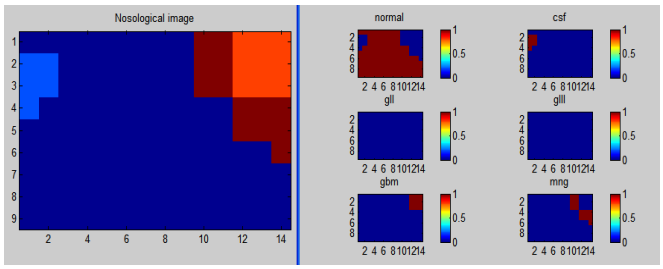

Fig. 3 Nosologic image and corresponding tissue correlation maps obtained by CCA using the classical approach

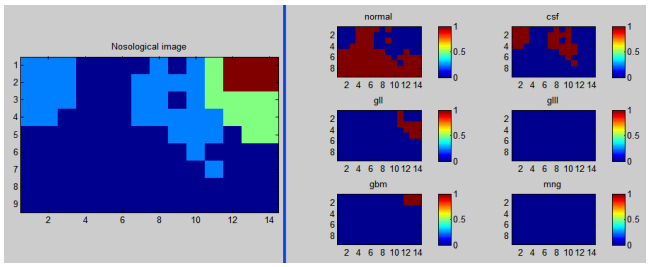

Fig. 4 Nosologic image and corresponding tissue correlation maps obtained by CCA using the 10 HR-MAS feature vector approach

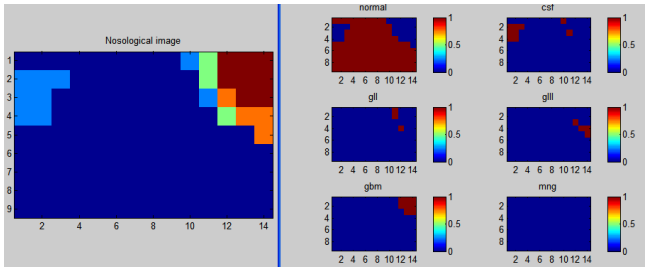

Fig. 5 Nosologic image and corresponding tissue correlation maps obtained by CCA using the 14 HR-MAS feature vector approach

We notice for this specific case that the added value of MRI to our model vector did not bring any new information in detecting the area of the tumor tissue, but influenced the classification of the voxels in the tumor area, detecting a big area of glioblastoma tumor surrounded by grade II and grade III voxels (see Fig. 5).

IV. Conclusions

In this study CCA was applied to segment short echo-time brain MRSI data by using as prior knowledge information coming from HR-MAS or HR-MAS and MRI data. We studied the possibility of combining multimodal information; we investigated which parameters influence our classification results and the impact of HR-MAS information in

combination with *in vivo* information for brain tumor recognition.

For the cases we were investigating, exploiting multimodal information improved the accuracy and the performance of the classifiers. The model that performed best is the model that uses multimodal information coming from HR-MAS and MRI data.

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