Non-negative blind source separation techniques for describing intratumoral histopathological tissue properties within MRSI measurements

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Introduction

Magnetic resonance spectroscopic imaging (MRSI) is currently used in clinical setting in conjunction with anatomical MRI to assess the presence, extent and type of brain tumors. The accuracy of MRSI in differentiating and grading brain tumors is limited by significant variability of in vivo spectra as an effect of intra-tumoral heterogeneity [1]. In gliomas one can observe distinct histopathological tissue properties, such as viable tumor cells, necrotic tissue or regions where the tumor infiltrates normal brain. A first screening between these intratumoral histopathological tissue properties would greatly assist in an improved diagnosis and prognosis and treatment planning in gliomas. We address these problems by quantifying the abundance within each MRSI voxel for each intratumoral histopathological tissue property using a non-negative matrix factorization algorithm (NNMF). Additionally, nosologic images are drawn based on the extracted abundance maps, reflecting the presence of necrosis, viable tumor cells or infiltrations in the MRSI grid.

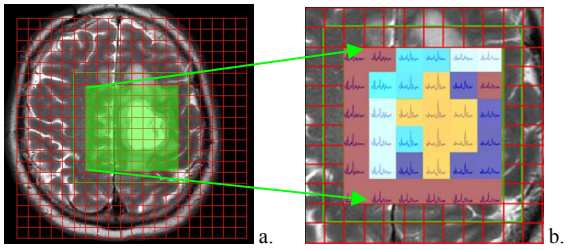
Methods and data

MRSI data, obtained in 7 patients with gliomas, histopathologically confirmed according to WHO classification, were acquired on a 3T Philips scanner, using a PRESS pulse sequence. The MRSI parameters are: 16x16x1024 samples, TR/TE=2000/35 ms, slice thickness = 10, FOV = 200 mm, spectral width = 20000 Hz and NS=1. The spectra were preprocessed using MATLAB environment by water removal with HLSVD-PRO [2], baseline correction [3] and normalization with respect to the water signal. The AQSES-MRSI quantification method [4] is used for extracting the concentration of 11 most representative metabolites (NAA, Glu, Cre, PCh, Glc, Lac, Ala, Myo, Tau and Lips at 0.9 and 1.3ppm). For each MRSI grid, non-negative matrix factorization (NNMF) [5] is applied separately on the magnitude MRSI spectra in the region of interest between 0.25 ppm and 4.2 ppm and on sets of features obtained from the spectra. Given a non-negative matrix, X, of size m x n (in our case m = number of voxels and n represents the dimension of the observations), NNMF simultaneously decomposes X into constituent spectral sources (S) and their abundance distributions (A) by minimizing the function $f(A,S)=1/2\|X-AS\|^2$ subject to non-negativity constraints on the values of A and S. For the spectra case, we used $n=512$.

For the metabolite features case, we considered either $n=11$ observations, representing the concentration of the most representative metabolites in separating tumor from normal tissue, or $n=6$ observations representing the concentration of the most representative metabolites in identifying intratumoral histopathological variability (Lips, Ala, Cr, NAA and PCh). In a first step we separate normal brain tissue voxels from voxels with predominant tumor tissue for $n=512$ and $n=11$. Then, NNMF is applied within the region with mostly predominant tumor tissue for classifying each voxel based on its predominant intratumoral histopathological property corresponding to necrotic, high cellular or infiltrations. We consider as dimension either $n=512$ or $n=6$. The results are then exploited in order to construct nosologic images, by assigning each voxel to the tissues type with the highest abundance coefficient.

Results

With NNMF we obtain reliable results when working with full magnitude spectra, as well as when considering metabolite concentrations as features. The contour of the tumor area corresponds to the contour reflected in the MRI image. Also the metabolite features/spectral sources extracted for necrotic and highly cellular regions present metabolic characteristics that are in conformity with the existing literature [1, 6]. Namely the necrotic regions present elevated levels of Lips and Lac, while in the highly cellular tumor area the PCh is present in high levels together with some contributions from Lac and Lips. In Figure 1 we illustrate the method on a patient diagnosed with glioblastoma.



a. b.

Figure 1. a. MRI T2-weighted image shows glioblastoma. The contour of the MRSI grid is marked with green on the image. b. Nosologic image showing the voxels identified as predominantly necrotic tissue (orange color), voxels with viable tumor cells (blue color; dark blue stands for high cellularity; lighter blue reflects higher levels of infiltrations from normal tissue) and voxels with predominantly normal brain tissue (dark red). This image was created using NNMF, with metabolite concentrations as features.

Conclusions

Using advanced source separation techniques we can decompose the observed MRSI grid into constituent tumor tissue sources with different predominant intratumoral histopathological properties and further quantify the abundance of each considered tissue source for being further visually explored as nosologic images. This can provide relevant additional information for a better interpretation and classification of in vivo MRSI data and therefore increase its contribution to brain tumor classification. In particular, this method can be of added value in addressing difficult questions such as the grading of glial tumors or differentiating metastasis from glioblastoma. Also it requires no previous training set which often can be a problem when dealing with new measurements or with rare tumors.

References

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