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Differentiation between Brain Metastasis and Glioblastoma using MRI and two-dimensional Turbo Spectroscopic Imaging data

T. Laudadio[1,2], J. Luts[1], M. Carmen Martínez-Bisbal[3,4], Bernardo Celda[3,4] and Sabine Van Huffel[1]

[1]Department of Electrical Engineering, Division ESAT-SCD, Katholieke Universiteit Leuven, Leuven, Belgium
[2]Istituto per le Applicazioni del Calcolo "M. Picone", National Research Council, (IAC-CNR), Bari, Italy
[3]Departamento de Química-Física, Facultad de Química, Universidad de València, València, Spain
[4]CIBER of Bioengineering, Biomaterials and Nanomedicine, ISC-III, Spain

Abstract — **In this paper we propose a novel technique to differentiate brain metastases from high-grade gliomas, which represent the most aggressive and common brain lesions. In spite of the significant progresses achieved in the field of MRI in the last decades, the differentiation between these two types of tumors is still a challenge as they show a similar appearance on MRI images, but require a completely different therapeutic treatment. Here, we show that such a differentiation is actually possible and can be obtained by making use of MRI as well as of two-dimensional Turbo Spectroscopic Imaging (2D-TSI) information. Specifically, the proposed technique consists of three steps: we first detect the abnormal region on the MRI by applying a new segmentation-classification algorithm able to produce nosologic images of the brain by exploiting both MRI and 2D-TSI information; afterwards, an accurate and efficient tissue typing technique, based on a statistical method known as canonical correlation analysis, is applied to 2D-TSI data in order to detect the lesion and characterize its nature; finally, the lesion contours provided by the aforementioned methods are compared in order to differentiate glioblastoma from metastasis lesions. The latter step exploits the infiltrative nature of glioblastoma, when compared to metastasis, which can be observed on magnetic resonance spectroscopic imaging (MRSI) but not on MRI. Indeed, our studies show that the tumor region detected in the second step for glioblastoma is significantly broader than the lesion obtained in the first step and observable on the MRI image. On the contrary, such a difference does not occur in the metastasis examples.**

Keywords — **Glioblastoma, metastasis, turbo spectroscopic imaging, tissue segmentation, classification.**

I. Introduction

Nowadays, MRI is widely applied in oncology as a non-invasive diagnostic tool to localize tumors and visualize their morphology. Despite the relevant achievements determined by MRI in tumor diagnosis, its ability to differentiate some tumor types is still very limited and, in such cases, biopsy is needed in order to avoid a wrong clinical management. In this context, an important example is represented by brain metastasis and glioblastoma tumors, as they are very similar from the radiological point of view but imply completely different therapeutic decisions.

Several studies have been carried out in order to develop a robust MRI-based differentiation technique [1,2], but up to our knowledge, none of them has been included in clinical routine practice yet.

Recently, some papers have been published where the potential of magnetic resonance spectroscopy (MRS) and MRSI, in differentiating the considered brain tumors, is investigated [3,4,5]. These NMR techniques provide important metabolic information on the lesion tissues and, by studying the level alterations of the relevant metabolites, clinicians can better understand the underlying pathology.

In particular, concerning the ability of MRS/MRSI to differentiate metastases from glioblastomas, some studies suggest that the absence of creatine and a higher lipid contribution could indicate metastases, but such criteria do not seem to be completely reliable. A more interesting approach has been proposed in [6], where the metabolite ratios have been investigated in the peri-tumoral region. According to this study, glioblastoma lesions show a higher choline/creatine ratio with respect to metastases, because of their infiltrative nature.

In this paper, we further investigate the infiltration property of glioblastoma tumors and propose a new automated differentiation technique which makes use of both MRSI and MRI information, specifically of 2D-TSI data and T1, T2 and T1-enhanced MR images.

The method mainly consists of three steps: the abnormal region on the MRI is first detected by applying a new segmentation-classification algorithm able to produce nosologic images [7] of the brain by exploiting MRI as well as MRSI information; afterwards, an accurate and efficient tissue typing technique, based on a statistical method known as canonical correlation analysis (CCA), is applied to the 2D-TSI data in order to detect the lesion and characterize its nature; finally, the lesion contours provided by the aforementioned methods are compared in order to differentiate glioblastoma from metastasis lesions.

The data considered in this study were acquired by 2D-TSI sequences, which are characterized by reduced

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acquisition times compared to those required for standard MRSI. Generally, around 6 minutes are needed to collect a 2D-TSI slice with a 24x24 matrix resolution (turbo factor 3), while 30 minutes are required by standard acquisition sequences with the same spatial resolution.

In vivo studies were carried out on seven patients, four affected by glioblastoma and three by metastasis. The results of our tests show that, in the glioblastoma cases, the tumor region detected in the second step is significantly broader than the lesion obtained in the first step and observable on the MRI image, thereby revealing the infiltrative nature of high-grade gliomas. On the contrary, such a difference cannot be observed in the metastasis examples.

The paper is organized as follows: in Section II the acquisition environment and parameters of the *in vivo* studies are defined; in Section III the proposed method is briefly described; in Section IV the results are reported and, finally, in Section V the main conclusions are formulated.

II. Materials

Seven tumor patients, four affected by glioblastoma and three by metastasis, were considered for this study. The data were acquired at the Radiology Service of Clínica Quirón, and the Hospital La Ribera, Alzira, Valencia (Spain), as a part of the routine clinical preoperative MR imaging and spectroscopy protocol for the brain. All patients signed an informed consent paper, in agreement with the guidelines of the University Hospital Ethical committee. A full high-resolution MRI study including Gadolinium (Gd) injection was acquired previously to the 2D-TSI study. Other sequences completed the MRI study, including a T2 weighted image package with the same orientation in plane location of the 2D-TSI slice. The MRI information of the different regions comes from both, the T1 pre and post-Gd injection, and the images obtained with the same orientation as the spectroscopy acquisition. After imaging with turbo spin echo T2 and proton density weighted images (TR = 5154 ms, TE = 13 and 115 ms), 2D-TSI using a 90° – 180° – 180° pulse sequence were acquired in 1.5 T Philips magnets (Philips Medical Systems, The Netherlands). The multivoxel spectroscopic images consist of a grid of 24x24 voxels with a field of view of 230x230 mm and a slice thickness of 20 mm. Each volume unit dimension was 9.6x9.6x20 mm (1.8 ml). The acquired signals are long echo time signals with TE = 272 ms, and TR = 2000 ms. Each signal consists of 256 complex data points. Data processing also included zero filling to 512 points, removal of the residual water resonance by using HLSVD-PRO [8] and Fourier transformation.

III. Methods

As already described in the introduction section, the method combines the application of two segmentation-tissue typing techniques that have recently been applied to brain tumors.

The first technique, described in [9], is an accurate segmentation-classification method which provides nosologic images of the brain by exploiting both MRI and MRSI information. More precisely, a registered brain-atlas and a subject-specific abnormal tissue prior, obtained from MRSI, are used in the segmentation step. This provides a segmented image where cerebral-spinal fluid (CSF), white matter, gray matter and the abnormal region, on the T2-weighted MRI, are clearly visualized. In the classification step the tissue characterization of the abnormal region is obtained by making use of advanced supervised pattern recognition algorithms. In this specific study, the following CCA-based method is applied as pattern recognition algorithm.

The second segmentation-classification technique is described in [10] and is based on CCA, a statistical method able to simultaneously exploit the spectral and spatial information provided by the 2D-TSI data. More precisely, CCA is used to quantify the relationship between two sets of variables, spectra of the measured data and signal subspace modeling the spectra of characteristic tissue types, by means of correlation coefficients. These coefficients are afterwards exploited in order to construct nosologic images in which all the detected tissue types are visualized.

Several and important properties make the aforementioned techniques a valid alternative to other segmentation-classification ones. In particular, they both exploit the spatial information characterizing the 2D-TSI data in addition to the spectral one, and allow the use of biochemical prior knowledge that is available when working with this type of NMR data.

In this study, the two techniques are independently applied to the *in vivo* data in order to detect the tumor region and to provide its tissue characterization. Once the results are available, the extension of the two detected tumor regions is compared and the overlap is carefully checked. The aim is to verify the infiltrative nature that characterizes glioblastomas with respect to metastases, and to use such a property as a differentiation criterion to distinguish the two tumor types.

IV. Results

The screenshot in Fig. 1 shows the T2 image of the slice of interest and the corresponding spectral map of a brain

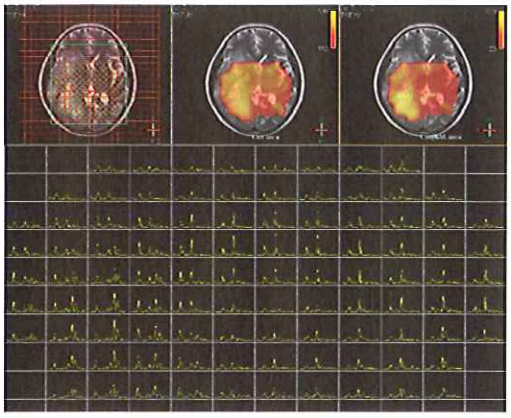


Fig. 1 *In vivo* 2D-TSI data set measured in a brain with glioblastoma.

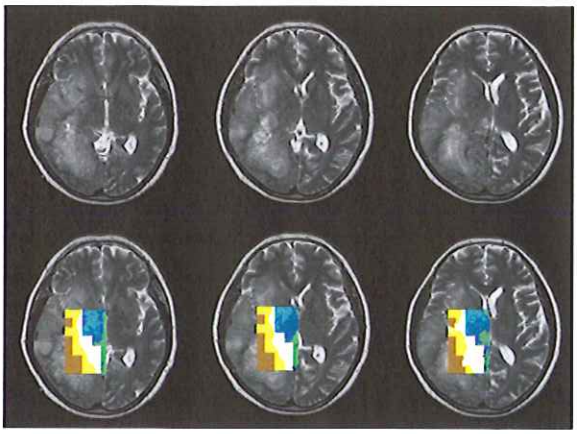


Fig. 2 Top: T2 images of three neighbor slices included in the 2D-TSI slice of Fig. 1; bottom: same images showing the segmentation results of the lesion. Colors: dark blue=gray matter; light blu=white matter; green=CSF; yellow=tumor; brown=necrosis+tumor (mixed tissue); gray-blue=normal+axonal damage; white=normal tissue on MRI, but tumor or necrosis on MRSI.

affected by glioblastoma. The suspicious region is located on the left-hand side of the MRI image.

Fig. 2 shows the segmentation-classification results provided by the proposed method for the lesion when processing the above 2D-TSI slice and three contiguous MRI slices contained in it. In fact, the thickness of the former is 20mm, while the latter slices are only 5mm thick. The considered MRI slices show similar, but not equal, anatomical information and they can help us to better understand the tissue distribution in the 2D-TSI voxels. In particular, the results obtained by the two segmentation-classification techniques are combined and shown in the bottom images. The detected tissues are denoted by different colors (see caption). In particular, the white pixels represent normal tissue on MRI, i.e. when applying the first step of the method, but pathological tissue (tumor or necrosis) tissue on 2D-TSI, obtained by CCA in the second step. As we can observe, CCA detects, as tumor or necrosis tissue, voxels that are completely outside the boundary of the tumor visible on the MRI. Such voxels reveal the infiltrative nature of this type of tumor, which can be retrieved from 2D-TSI, but not from MRI data.

Fig. 3 shows the T2 image of the slice of interest, along with the corresponding spectral map, of a metastasis example. The tumor is located in the bottom right-hand side of the image. In Fig. 4 the results obtained by the two segmentation-classification techniques are combined and visualized for three neighbor MRI slices contained in the considered 2D-TSI slice. Also in this case, the detected tissues are visualized by different colors (defined as in the previous example). In particular, the white pixels denote normal tissue on MRI, but tumor or necrosis tissue obtained by CCA by processing the 2D-TSI data. At the first glance, it seems that also metastasis is characterized by infiltration, since white pixels are present in these results as well. Nevertheless, a more careful inspection of the results reveals that, at least in one of the three slices, the detected white pixels belong to voxels that are not completely outside the boundary of the tumor visible on the MRI and, therefore, such pixels do not represent infiltration but partial volume. This fact highlights the importance of the inspection of all the MRI information contained inside the MRSI slice. Similar results were obtained when processing the other glioblastoma and metastasis examples.

V. Conclusions

In this paper a new technique is proposed to differentiate glioblastoma from metastasis lesions. The proposed approach exploits the infiltrative nature of glioblastoma tumors that has been suggested in the literature. Here, such a property is further investigated and exploited in order to develop a semi-automatic algorithm that, making use of MRI and 2D-TSI information, allows a visual differentiation between the two tumor types. Nevertheless, it is worth stressing that extensive validation studies need to be carried out in order to verify the actual degree of reliability of the method.

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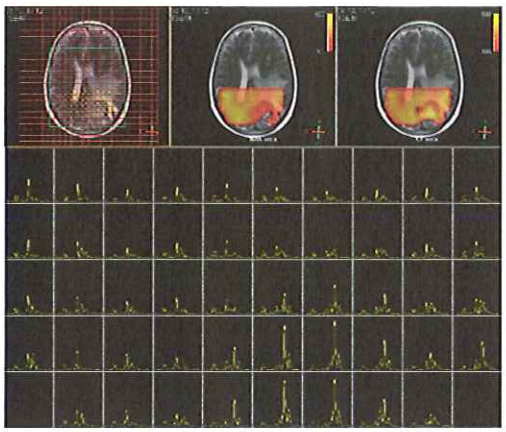


Fig. 3 *In vivo* 2D-TSI data set measured in a brain with a metastasis tumor.

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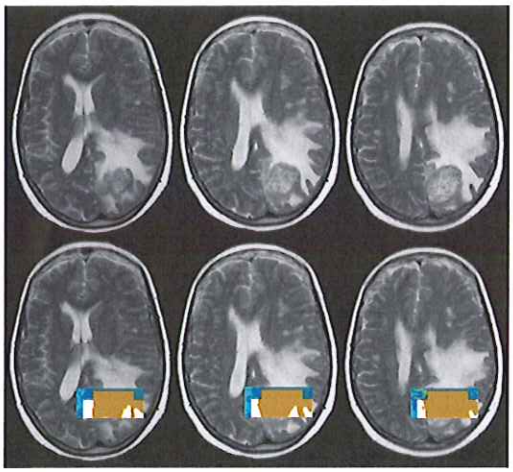


Fig. 4 Top: T2 images of three neighbor slices included in the 2D-TSI slice of Fig. 3; bottom: same images showing the segmentation results of the lesion. Colors: dark blue=gray matter; light blue=white matter; green=CSF; yellow=tumor; brown=necrosis+tumor (mixed tissue); gray-blue=normal+axonal damage; white=normal tissue on MRI, but tumor or necrosis on MRSI.

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Author: Laudadio Teresa
Institute: Istituto per le Applicazioni del Calcolo M. Picone
Street: Via Amendola 122/D
City: Bari
Country: Italy
Email: t.laudadio@ba.iac.cnr.it