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Exploiting morphology and texture of 3D tumor models in DTI for differentiating glioblastoma multiforme from solitary metastasis

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ABSTRACT

Ambiguous imaging appearance of Glioblastoma Multiforme (GBM) and solitary Metastasis (MET) is a challenge to conventional Magnetic Resonance Imaging (MRI) based diagnosis, leading to exploitation of advanced MRI techniques, such as Diffusion Tensor Imaging (DTI). In this study, 3D tumor models are generated by a DTI clustering segmentation technique, providing up to 16 brain tissue diffusivities, complemented by T1 post-contrast imaging, resulting in the identification of tumor core, whose surface is refined by a Morphological Morphing interpolation technique. The 3D models are analyzed in terms of their surface and internal signal variations characteristics towards identification of discriminant features for differentiation between GBMs and METs, utilizing a case sample composed of 10 GBMs and 10 METs. Morphology analysis of tumor core surface is assessed by 5 local curvature features. Texture analysis considers 11 first and 16 second order 3D textural features. From the 16 second order features, 11 are based on Gray Level Co-Occurrence Matrices (GLCM) and 5 on Gray Level Run Length Matrices (GLRLM), calculated from DTI isotropic and anisotropic parametric maps, corresponding to 3D tumor core segmented from the clustering technique. Also, 3 different image quantization levels (QL) were tested for both GLCM and GLRLM analysis, while 1–4 pixel displacements (D) in case of GLCM analysis. Case sample distributions of morphology and texture features were analyzed using the Mann-Whitney *U* test, with a cut-off value of 0.05 to identify discriminant features. The discriminatory performance of the derived features was analyzed with Receiver Operating Characteristic (ROC) curve analysis. Results highlight the value of all 5 local curvature descriptors to capture differences between the boundary of GBMs and METs. Histogram analysis of isotropy maps revealed statistical significant differences for median value and kurtosis, while 7 out of the 11 GLCM features were capable of discriminating heterogeneity of anisotropic diffusion properties of GBMs and METs, at QL = 6 and D = 2. Finally, all 5 GLRLM features extracted from diffusion isotropy maps seem to discriminate structural properties of GBMs and METs, at QL = 5. Results demonstrate the potential of surface morphology and texture analysis of 3D tumor imaging appearance in pre-treatment brain MRI tumor differentiation.

1. Introduction

Preoperative differentiation of brain tumors is critical for adapting treatment strategies, as well as for evaluating tumor response to therapy. However, differentiation solely relying on conventional Magnetic Resonance Imaging (MRI) remains a challenge, due to ambiguous tumor imaging characteristics. Glioblastoma Multiforme (GBM) and solitary Metastasis (MET) are common brain tumors, which represent a characteristic example of such a diagnostic problem, sharing similar characteristics, like a low signal necrotic region, the extended region of peritumoral edema, and the rim – enhancement region in T1 post contrast images, resulting from the leakage of the contrast agent, due to the Blood-Brain-Barrier (BBB) disruption.

Although histopathological analysis of biopsy samples is the gold standard for establishing diagnosis, it is not always feasible, because it is an invasive procedure, while it samples only a limited portion ◯f the lesion tissue. This has led to the exploitation of a

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variety of advanced MRI techniques, which provide structural and functional information of tumors, achieving improved performance as compared to conventional MRI. More specifically, Diffusion imaging presents tumors microstructure and micro-architecture by means of water molecules diffusion properties [1,2]. Dynamic Perfusion Imaging, resulting from the analysis of contrast agent's mobility, injected into the human body, can give detailed information regarding tumor vascularity and cellularity [3]. Finally, MR Spectroscopy is able to reveal the tumors biochemical profile in a completely noninvasive way [4].

In addition to advanced MRI techniques, image analysis schemes have been recently introduced regarding exploitation of quantitative tumor imaging parameters, in terms of tumor morphology and/or texture. The justification for morphology analysis is based on the fact that GBMs are usually invasive, mostly along white matter (WM) tracts, leading to more complex tumor boundary, while METs expand more homogeneously, in the junctions between white and gray matter, resulting in a more spherical shape (encapsulated). Recent studies reporting on morphology analysis of GBM and MET have utilized generic tumor shape features applied on 2D tumor segments derived from representative slices [5–7] and local curvature features applied on 3D tumor surfaces [8].

Texture analysis is used for the identification of tumor's signal variations, possibly connected to their underlying pathophysiological characteristics. Regarding GBMs and METs, previous studies [6,9, and 10] based on texture features, obtained from conventional or advanced MR images, have reported successful differentiation results by means of quantifying the different levels of tumors' heterogeneity.

In this study, morphology and texture features of 3D tumor models are investigated towards differentiation of GBM and MET. 3D tumor models are generated by a Diffusion Tensor Imaging (DTI) clustering segmentation technique, complemented by post-contrast T1 imaging, resulting in the identification of tumor core, whose surface is refined by a Morphological Morphing interpolation technique. Morphology analysis of tumor core surface is assessed by five local curvature features. Texture analysis considers first and second order 3D textural features, calculated from DTI isotropic and anisotropic parametric maps. Texture analysis targets the tumor core active region, exploiting the outcome of the DTI clustering segmentation technique, as tumors' necrotic and cystic components are expected to contribute less in the profile of heterogeneity. Morphology and Texture features differentiation ability is tested in terms of statistical significance of sample statistics, and Receiver Operating Characteristic (ROC) analysis.

2. Image segmentation

2.1. Image segmentation

In clinical routine, at first approximation, tumor core's rough delineation is manually performed by radiologists in MR images, with the help of T1 post contrast and T2 images, which present enhancement regarding tumor borders and edematogenous regions, respectively. However, manual segmentation of tumor core is time consuming and inaccurate, in terms of intra- or inter-operator variability errors [11]. The low degree of reproducibility of tumor manual segments is anticipated to affect subsequent measurements (imaging biomarkers), a main drawback in evaluation and comparison of reported literature results. This is important in the field of computer aided diagnosis, where a more systematic study of imaging biomarkers is required.

In the literature, a variety of semi or fully automated methods exist, which aim to distinguish and efficiently describe brain tissue's component anatomical areas (WM, GM, CSF), as well as brain tumor different parts (active, necrotic and edematogenous regions). Their clinical acceptance depends on algorithm efficiency, computation simplicity as well as degree of user's supervision [12].

In intensity based methods the generation of segmented regions relies on the classification of image voxels into groups according to their intensity. The simplest way regards the application of thresholds in image corresponding histograms. The main disadvantage of the thresholding methods is the spatial incoherence (scattering) presented in segmented regions, as this method doesn't take into account pixels neighborhood information. Region growing methods are an evolution, where segments coherence is obtained via the application of conditions by the user, such as homogeneity criteria between neighboring voxels and mostly the inclusion of manually induced seed voxels in the final segment [13].

Recently, voxel classification and clustering algorithms have become very popular in MRI segmentation [5,11,14] as an efficient description of neuroanatomical and neuropathological tissue contrast information regarding the whole brain, may be achieved with minimum user's interaction. More specifically, classification and clustering algorithms, such as k-NN, k-means and fuzzy c-means, are used for classifying image histograms data points into one or more overlapping or non-overlapping sets, presenting intensity values, accounting for similar tissue properties [11]. Also, in the recent literature, a variety of classification methods can be found, utilizing sophisticated algorithms, coming from the evolving field of machine learning [15–17].

In addition, Atlas Based methods relying in prior knowledge about brain anatomical structures stored in MR images atlases, to which the patients' images are registered. In this way, alterations in normal structure properties are correlated with various brain diseases [18].

Finally, surface-based methods, including active contours and active surfaces, implement deformable geometric models which segment anatomical structures [19].

In this study, a proposed DTI clustering segmentation technique is implemented, which classifies a given set of elements (i.e. brain voxels) into groups corresponding to similar isotropic and anisotropic diffusion properties, by means of a k-medians algorithm. Specifically, k-medians clustering is applied on the proposed p-q space [14], which is a 2D histogram of p (isotropic) and q (anisotropic) components of the diffusion tensor (Fig. 1), derived from all patient cohort. K-medians was selected, as compared to k-means or fuzzy c-means, as p and q histograms present a non-normal distribution, and moreover because the patient sample used for the classifier training in the present study is small.

Starting with K initial clusters definition, the algorithm: (i) assigns the data points into k disjoint subsets by minimizing the within cluster sum of 1-norm (cityblock) distances (Eq. (1)), between each point and the respective cluster's centroid,

$$J = \sum_{j=1}^{K} \sum_{n \in Sj} \|x_n - \mu_j\| \quad (1)$$

where x_n the nth data point and μ_j the geometric centroid of the data points in S_j, and (ii) new cluster centroids are computed (Eq. (2))

$$\mu_i = \frac{1}{|S_i^{(t)}|} \sum_{x_j \in S_i^{(t)}} x_j \quad (2)$$

Steps i and ii are repeated until convergence, i.e. the energy function J reaches its minimum value.

Selection of k = 16 according to [14], is adopted, as adequately accounting for tissue diffusivities encountered in the brain, including white matter, gray matter, cerebrospinal fluid, edema, tumor's active, cystic and necrotic regions. Initially, clusters are defined by