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Influence of gray level and space discretization on brain tumor heterogeneity measures obtained from magnetic resonance images

David Molina [a,*], Julián Pérez-Beteta [a], Alicia Martínez-González [a], Juan Martino [b], Carlos Velásquez [b], Estanislao Arana [c], Víctor M. Pérez-García [a]

[a] Instituto de Matemática Aplicada a la Ciencia y la Ingeniería, Universidad de Castilla-La Mancha, Spain
[b] Hospital Universitario Marqués de Valdecilla and Fundación Instituto de Investigación Marqués de Valdecilla, Spain
[c] Instituto Valenciano de Oncología, Spain

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ABSTRACT

Purpose: Tumor heterogeneity in medical imaging is a current research trend due to its potential relationship with tumor malignancy. The aim of this study is to analyze the effect of dynamic range and matrix size changes on the results of different heterogeneity measures.
Materials and methods: Four patients harboring three glioblastomas and one metastasis were considered. Sixteen textural heterogeneity measures were computed for each patient, with a configuration including co-occurrence matrices (CM) features (local heterogeneity) and run-length matrices (RLM) features (regional heterogeneity). The coefficient of variation measured agreement between the textural measures in two types of experiments: (i) fixing the matrix size and changing the dynamic range and (ii) fixing the dynamic range and changing the matrix size.
Results: None of the measures considered were robust under dynamic range changes. The CM Entropy and the RLM high gray-level run emphasis (HGRE) were the outstanding textural features due to their robustness under matrix size changes. Also, the RLM low gray-level run emphasis (LGRE) provided robust results when the dynamic range considered was sufficiently high (more than 8 levels). All of the remaining textural features were not robust.
Conclusion: Tumor texture studies based on images with different characteristics (e.g. multi-center studies) should first fix the dynamic range to be considered. For studies involving images of different resolutions either (i) only robust measures should be used (in our study CM entropy, RLM HGRE and/or RLM LGRE) or (ii) images should be resampled to match those of the lowest resolution before computing the textural features.

1. Introduction

Tumors are heterogeneous entities, encompassing a mixture of different types of cells, which may differ in their morphology, genetics and biological behavior [1]. High intratumoral heterogeneity has been related to poorer prognosis, which could be secondary to intrinsic aggressive biology or treatment resistance [1,2]. However, intratumoral heterogeneity is not ascertained by biopsy samples as they do not represent the full extent of phenotypic or genetic variations [3]. Radiomics is a high throughput process of image feature extraction which uses these features to predict response and patient survival and to gather biological information about the disease [4]. One of the objectives of radiomics is the characterization of neoplasm heterogeneity from tumor images [5].

Texture analysis refers to a variety of mathematical methods used to quantify the spatial variations in gray levels within an image to derive so-called 'texture features', which provide a measurement of intralesional heterogeneity. These techniques have attracted much attention recently [6–8], being used to define prognostic biomarkers [9–12], characterize tumors [13], and guide radiotherapy treatment [14,15], to cite a few applications.

Many methods have been proposed to quantify tumor heterogeneity from imaging data. First-order features such as those derived from histograms relate the gray-level distribution within the whole tumor [12,13,16]. These features do not take into account the relative spatial position of pixels, but only the frequency of appearance of each gray level within the tumor.

Second-order heterogeneity features describe graylevel relations between nearby pairs of pixels. These features take the spatial distribution into account but in a local way. In this study,

* Correspondence to: University of Castilla-La Mancha, Applied Mathematics Researcher, Instituto de Matemática Aplicada a la Ciencia y la Ingeniería (IMACI), C/ Camilo José Cela, s/n cp. 13071 Ciudad Real, Spain
E-mail address: david.molina@uclm.es (D. Molina).

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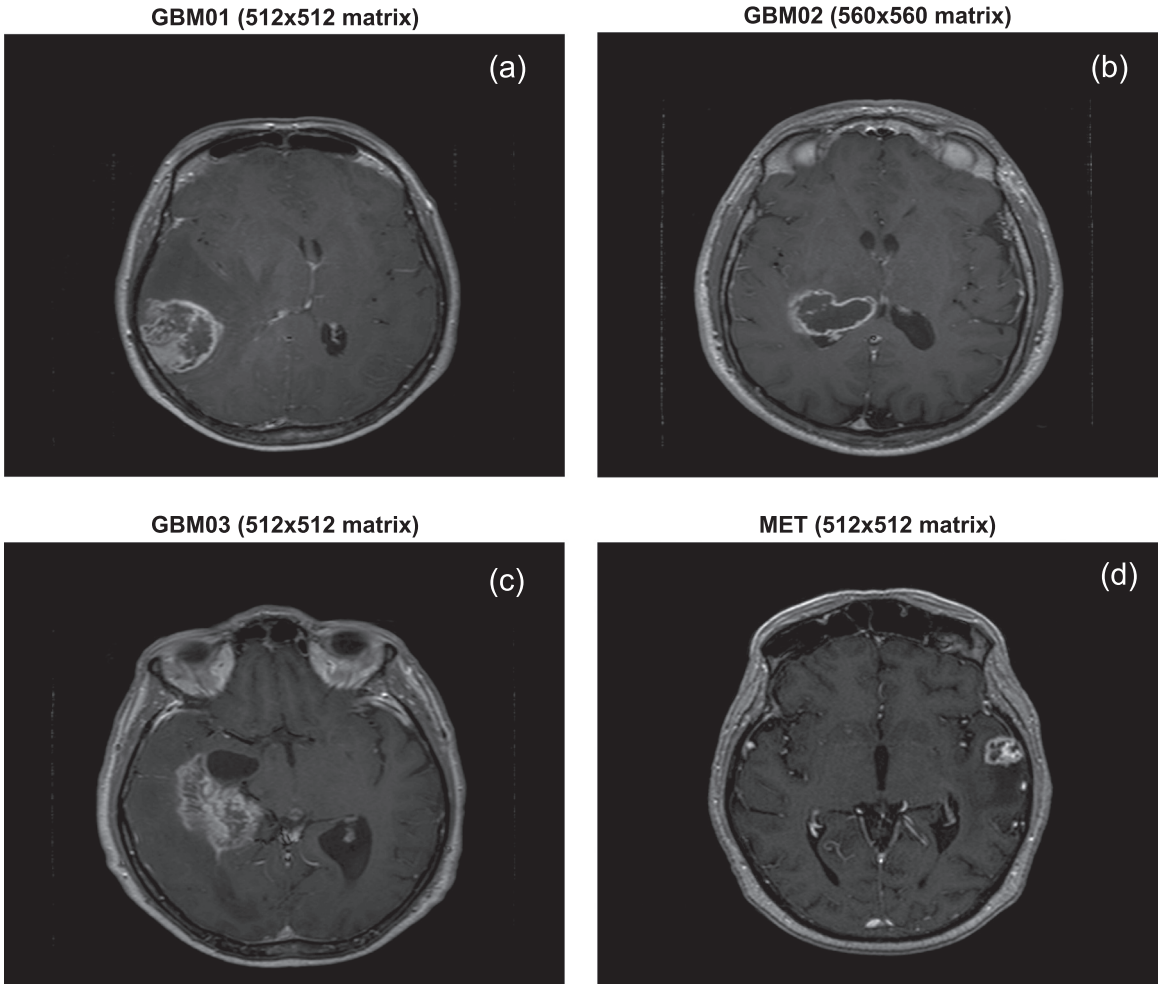

Fig. 1. The four segmented tumors considered: a diffuse GBM with necrotic areas (GBM1), a GBM with a well-defined rim (GBM2) and a diffuse GBM (GBM3). The MET tumor showed irregular contrast-enhancing areas. The title of each subplot indicates the raw matrix size.

we considered the use of the well-known co-occurrence matrices (CM) as a second-order texture description method. The CM was proposed by Haralick et al. [17] and describes the arrangements of pairs of elements (pixels) within the image [18]. It measures relations between two voxels at a time, and is usually considered to provide information on the local texture of images.

Third-order features quantify the heterogeneity by measuring the distributions and sizes of areas (groups of pixels) within the tumor having the same gray-level values. The RLM was proposed by Galloway [19] and characterizes large areas within the tumor (groups of voxels) to provide information of regional heterogeneity [20].

The CM and RLM texture methods have been extensively used [10–12,21–23]. However, if textural features are used in clinical practice, they have to be robust under the typical variations found between different commercial machines that involve acquisition protocols and/or matrix sizes [24]. The same considerations apply when trying to compare results measured from images obtained using different machines in multi-center clinical trials.

The influence of the acquisition protocol on textural measures has been controversial in the literature and may depend on the specific measure, type of tumor, etc. [25–28]. Mayerhoefer et al. [25] and Waugh et al. [26] studied the influence of different clinical breast MRI protocols and parameters on the results of several textural features. Their results showed that spatial resolution is the most important factor influencing the results of textural measures, while changes to other protocol parameters did not change the outcome of texture analyses so significantly.

Collewet et al. [27] studied the effects of two MRI acquisition protocols and four image intensity normalization methods for texture classification. Their results suggested that dynamic range discretization is also important for classification, as one of the four methods considered performed significantly better than the others.

However, the individual and combined effect of spatial and dynamic range discretization has not received attention. To our knowledge, no study has considered the problem of texture measurement robustness for brain tumor magnetic resonance (MR) images in spite of the known need for improved reliability of textural measure calculation [4].

Thus, the aim of this study was to analyze the robustness of the most common second and third-order heterogeneity measures in brain tumor medical images under changes of matrix size and dynamic range and to provide recommendations of practical utility for the choice of measures, dynamic ranges and/or matrix sizes to be used.

2. Materials and methods

2.1. Patients

Three men and a woman were studied, aged 59 ± 2.06 years. Three patients with glioblastoma (GBM) were selected from a