Imaging Biomarker Analysis of Structural MR Images for Glioma Grading

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Purpose:

Preoperative differentiation between low and high grade gliomas is critical for adapting appropriate treatment strategies. However biopsy based diagnosis presents limitations in assessing tumor diffusive and solid growth patterns, respectively, due to the potential subsampling of tumor areas, as well as the associated patient risk. The purpose of this study is to investigate the value of non-invasive Imaging Biomarker analysis, in terms of Texture Analysis of 3-D Magnetic Resonance (MRI) T1-wheighted post-contrast, T2-wheighted, Diffusion Tensor Imaging (DTI) data and Machine Learning classification, in the evaluation of tumor heterogeneity towards glioma grading.

Methods and Materials:

Twenty patients initially diagnosed with Low or High Grade Gliomas (10 LGG & 10 HGG) underwent MRI performed on a 3-Tesla MR whole-body scanner (SignaHDx; GE Healthcare, Waukesha, WI, USA).

Conventional MRI protocol included pre-contrast sagittal and transverse T1-weighted fast spin-echo (FSE) (repetition time (TR) / echo time (TE) 700ms/9.3ms), transverse T2-weighted FSE (TR/TE 2640ms/102ms), coronal T2-weighted FSE (TR/TE 2920ms/102ms), and T2-weighted fluid attenuation inversion recovery (FLAIR) (TR/TE 8500ms/130ms). Post-contrast T1-weighted FSE (TR/TE 700ms/9.3ms) axial images were also obtained. DTI was performed prior to contrast media injection, in the axial plane with single-shot spin-echo echo planar: TR/TE 8000ms/89.8ms, gradients applied in 25 nonlinear directions, b=0 and 1000 s/mm2, FOV=24mm, slice thickness=4mm with gap=1mm and NEX=1. FSL software (FMRIB Software Library v5.0 - fsl.fmrib.ox.ac.uk/) was utilized for Diffusion Tensor estimation and Mean Diffusivity (MD), Fractional Anisotropy (FA), Pure Isotropy (p) and Pure Anisotropy (q) parametric maps generation.

A semi-automated k-medians clustering segmentation method, based on T1-C, T2 and DTI parametric maps, for tumor delineation and building of 3-D whole lesion tumor models, excluding edema and hemorrhage regions (Fig. 1), was implemented in Matlab R2015b (https://www.mathworks.com).

10 Histogram features and 16 Textural features based on Co-occurrence and Run Length matrices, averaged over the 13 3-D possible directions and considering i=1-5 different pixel displacements (d_i), were calculated on every parametric map (T1-C, T2-FSE, T2-FLAIR, MD, FA, p, q), resulting in a total amount of 490 distinct features for each patient. Histogram and Texture Analysis were implemented in Matlab R2015b and MaZda ver. 5 software (http://www.eletel.p.lodz.pl/programy/mazda), respectively.

Weka 3.8 software (https://www.cs.waikato.ac.nz/ml/weka/) was utilized for performing the Machine Learning classification. In the beginning, a feature selection process, based on a Support Vector Machine – Recursive Feature Elimination (SVM-RFE) algorithm, was utilized. Subsequently, a minimum amount of important features, according to feature ranking scores provided by SVM-RFE were obtained for training a linear SVM classifier. Both SVM-RFE and linear SVM classifier were implemented based on Weka 3.8 default parameters.

A schematic representation of the analysis workflow is depicted in Fig. 2.

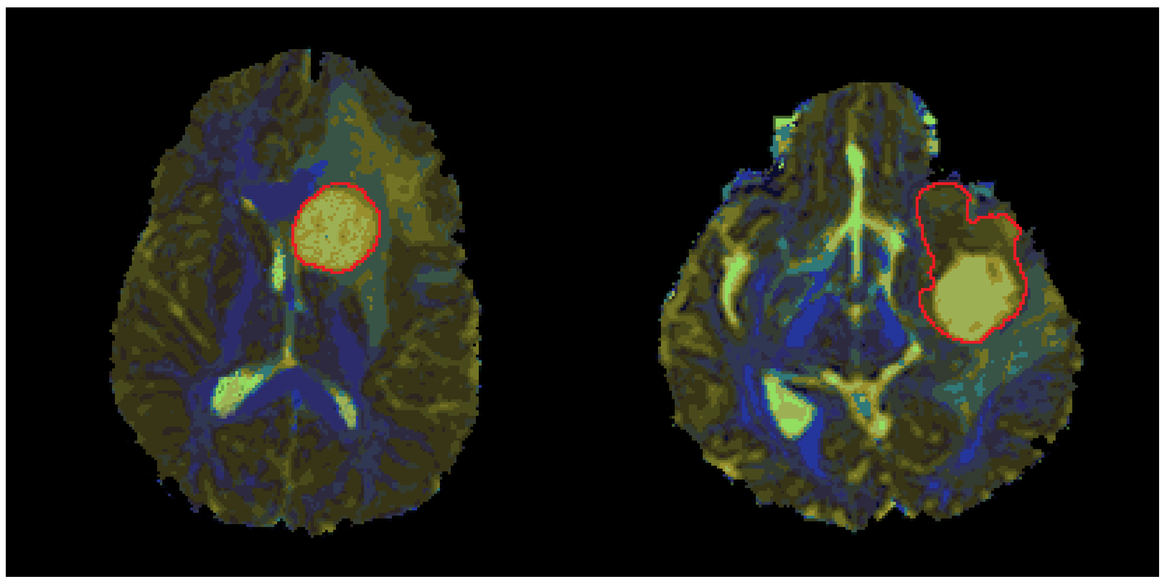

Fig. 1. Whole brain segmented maps of a LGG (left) and a HGG (right) case, resulting from the k-medians clustering of the DTI isotropic, anisotropic and T2-wheighted components feature space. The different colors presented (k=16) correspond to distinct brain tissue diffusion properties, which facilitate the precise definition of healthy tissue, tumor core and peritumoral edema. The final delineation of tumor core (red outline) is the outcome of the further combination with T1-wheighted post-contrast imaging.

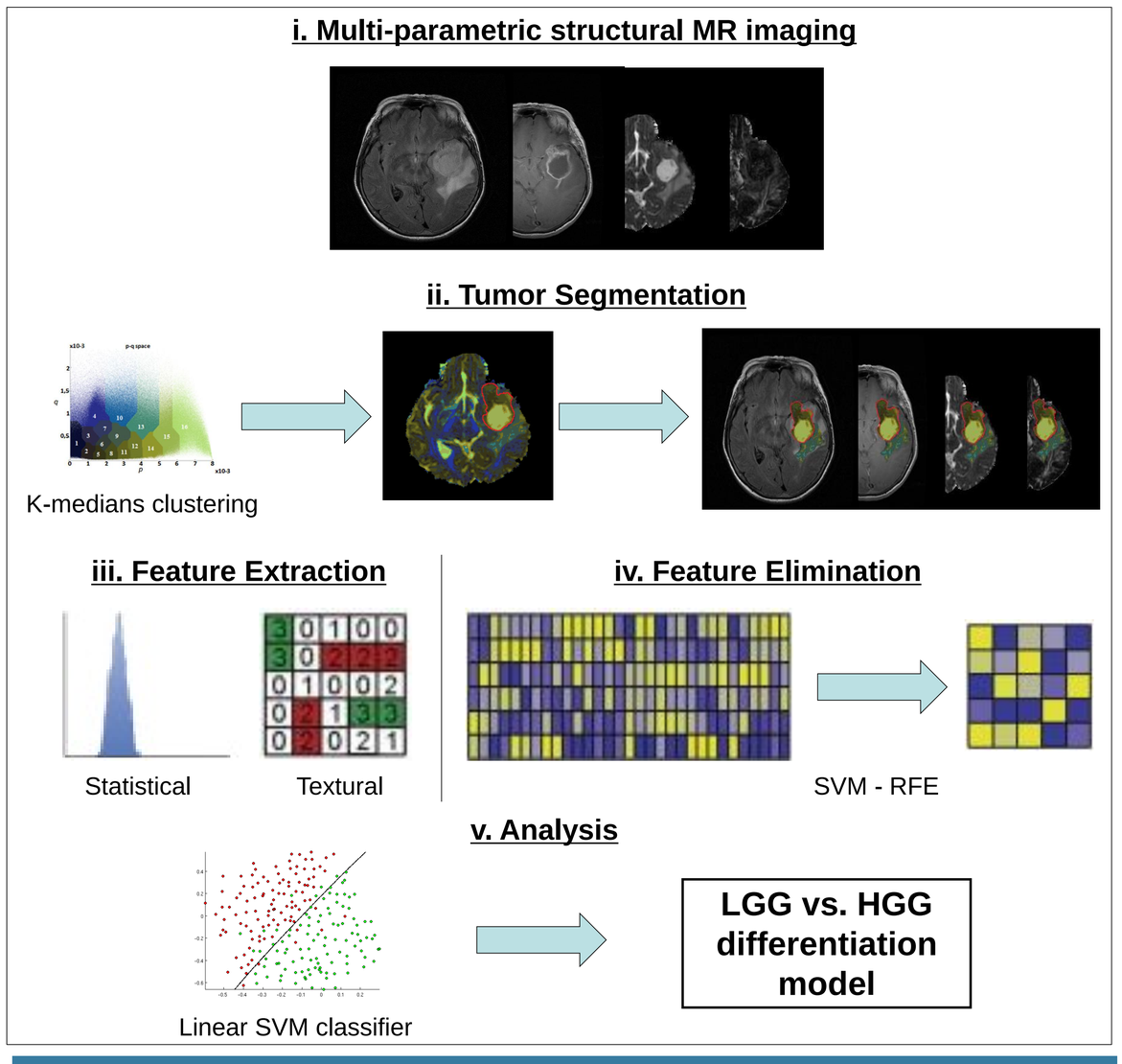

Fig. 2. The qualitative Imaging Biomarker Analysis workflow of the current study.

Results:

The evaluation of different feature subsets resulted in the adoption of 5 Histogram-based (q median, FA skewness, T2-FLAIR minimum, T1-C range, T1-C kurtosis) and 4 Textural-based (T1-C d_4 entropy, MD d_5 difference entropy, MD d_5 inverse difference moment, MD d_3 angular second moment) SVM-RFE top-ranked features, for training and testing the linear SVM classifier with leave-one-out cross validation (LOOCV), achieving: 95% Accuracy, 95% Sensitivity, 93.9% Specificity and 94.4% Area Under Curve.

Conclusion:

The pilot evaluation of the proposed method highlights the value of the advanced qualitative analysis of MRI data in identifying Imaging Biomarkers for the global non-invasive assessment of brain tumor heterogeneity. In conclusion, results demonstrate the potential role of Texture Analysis and Machine Learning in 3-D structural MRI, for pre-treatment Gliomas grade differentiation.