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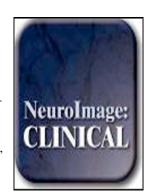
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# ACCEPTED MANUSCRIPT

# Comparison of unsupervised classification methods for brain tumor segmentation using multi-parametric MRI

N. Sauwen<sup>1,2</sup>, M. Acou<sup>3</sup>, S. Van Cauter<sup>4,5</sup>, D.M. Sima<sup>1,2</sup>, J. Veraart<sup>6</sup>, F. Maes<sup>7</sup>, U. Himmelreich<sup>8</sup>, E. Achten<sup>3</sup> and S. Van Huffel<sup>1,2</sup>

#### **Abstract**

Tumor segmentation is a particularly challenging task in high-grade gliomas (HGGs), as they are amongst the most heterogeneous tumors in oncology. An accurate delineation of the lesion and its main subcomponents contributes to optimal treatment planning, prognosis and follow-up. Conventional MRI (cMRI) is the imaging modality of choice for manual segmentation, and is also considered in the vast majority of automated segmentation studies. Advanced MRI modalities such as perfusion-weighted imaging (PWI), diffusion-weighted imaging (DWI) and magnetic resonance spectroscopic imaging (MRSI) have already shown their added value in tumor tissue characterization, hence there have been recent suggestions of combining different MRI modalities into a multiparametric MRI (MP-MRI) approach for brain tumor segmentation. In this paper, we compare the performance of several unsupervised classification methods for HGG segmentation based on MP-MRI data including cMRI, DWI, MRSI and PWI. Two independent MP-MRI datasets with a different acquisition protocol were available from different hospitals. We demonstrate that a hierarchical nonnegative matrix factorization variant which was previously introduced for MP-MRI tumor segmentation gives the best performance in terms of mean Dice-scores for the pathologic tissue classes on both datasets.

**Keywords:** Segmentation, glioma, multi-parametric MRI, unsupervised classification, non-negative matrix factorization, clustering

Abbreviations: 1H-MRSI: proton magnetic resonance spectroscopic imaging; ADC: apparent diffusion coefficient; Cho: total choline; cMRI: conventional magnetic resonance imaging; Cre: total creatine; DKI: diffusion kurtosis imaging; DSC-MRI: dynamic susceptibility-weighted contrast-enhanced magnetic resonance imaging; DTI: diffusion tensor imaging; DWI: diffusion-weighted imaging; FA: fractional anisotropy; FCM: fuzzy C-means clustering; FLAIR: fluid-attenuated inversion recovery; GBM: glioblastoma multiforme; Glx: glutamine+glutamate; Gly: glycine; GMM: Gaussian mixture modelling; HALS: hierarchical alternating least squares; HGG: high-grade glioma; hNMF: hierarchical non-negative matrix factorization; Lac: lactate; LGG: low-grade glioma; Lip: lipids; MD: mean diffusivity; mI: myo-inositol; MK: mean kurtosis; MP-MRI: multi-parametric magnetic resonance imaging; NAA: N-acetyl-aspartate; NMF: non-negative matrix factorization; NNLS: non-negative linear least-squares; PWI: perfusion-weighted imaging; rCBV: relative cerebral blood volume; ROI:

<sup>&</sup>lt;sup>1</sup> KU Leuven, Department of Electrical Engineering (ESAT), STADIUS Centre for Dynamical Systems, Signal Processing and Data Analytics, Leuven, Belgium

<sup>&</sup>lt;sup>2</sup> iMinds, Department of Medical Information Technologies, Belgium

<sup>&</sup>lt;sup>3</sup> Ghent University Hospital, Department of Radiology, Ghent, Belgium

<sup>&</sup>lt;sup>4</sup> University Hospitals of Leuven, Department of Radiology, Leuven, Belgium

<sup>&</sup>lt;sup>5</sup> Ziekenhuizen Oost-Limburg, Department of Radiology, Leuven, Belgium

<sup>&</sup>lt;sup>6</sup> University of Antwerp, iMinds Vision Lab, Department of Physics, Antwerp, Belgium

<sup>&</sup>lt;sup>7</sup> KU Leuven, Department of Electrical Engineering (ESAT), PSI Centre for Processing Speech and Images, Leuven, Belgium

<sup>&</sup>lt;sup>8</sup> KU Leuven, Biomedical MRI/MoSAIC, Department of Imaging and Pathology, Leuven, Belgium

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