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# Probability map prediction of relapse areas in glioblastoma patients using multi-parametric MR

Andrea Laruelo\*

*Institut Claudius Regaud, Toulouse, F-31059 France and  
Univ. of Toulouse, IRIT - INP-ENSEEIH, France*

Jose Dolz\*

*AQUILAB, Loos-les-Lille, France and  
Univ. Lille, Inserm, CHU Lille, U1189 - ONCO-THAI - Image Assisted Laser Therapy for Oncology, F-59000 Lille, France*

Soleakhena Ken

*Institut Claudius Regaud, Toulouse, F-31059 France*

Lofti Chaari

*Univ. of Toulouse, IRIT - INP-ENSEEIH, France*

Maximilien Vermandel

*Univ. Lille, Inserm, CHU Lille, U1189 - ONCO-THAI - Image Assisted Laser Therapy for Oncology, F-59000 Lille, France*

Laurent Massoptier

*AQUILAB, Loos-les-Lille, France*

Anne Laprie

*Institut Claudius Regaud, Toulouse, F-31059 France  
Université Toulouse III Paul Sabatier, Toulouse, F-31000 France and  
INSERM UMR825, Toulouse, F-31024, France*

**Purpose:** Despite post-operative radiotherapy (RT) of glioblastoma (GBM), local tumor regrowth occur in irradiated areas and are responsible for poor outcome. Identification of sites with high probability of recurrence is a promising way to define new target volumes for dose escalation in RT treatments. This study aims at assessing the value of multi-parametric magnetic resonance (mp-MR) data acquired before RT treatment in the identification of regions at risk of relapse.

**Methods:** Ten newly diagnosed GBM patients included in a clinical trial, treated in the reference arm of 60 Gy and Temozolomide, underwent magnetic resonance imaging (MRI) and MR spectroscopy (MRSI) before RT treatment and every 2 months until relapse. Quantification of MRSI was improved following the spatio-spectral regularization approach proposed in [1]. The site of relapse was considered as the new appearing contrast-enhancing (CE) areas on T1-weighted images after gadolinium injection (T1-Gd). Using a set of mp-MR data acquired before RT treatment as input, a supervised learning system was trained to generate a probability map of CE appearance of GBM. Since it has recently shown a great performance in some other brain-related classification problems, such as segmentation of brain tumor [2] or some brain structures [3], support vector machines (SVM) [4] was chosen as the learning technique. To feed the classifier, T1-Gd and FLAIR image intensities, Choline-over-NAA, Choline-over-Creatine and Lac-over-NAA metabolite ratios, and metabolite heights were used. The resolution of the MRI images was lowered to the one of the MRSI grid by averaging MRI pixel intensities within each MRSI voxel (400 MRSI voxels were considered for each subject). The region of CE was manually contoured on both the pre-RT and post-RT T1-Gd images by experienced medical staff. All voxels that enhanced at the pre-RT exam were excluded from further consideration. The learning system was trained and tested using leave-one-out-cross-validation (LOOCV) with all the patients. A grid-search strategy was employed for parameter optimization.

**Results:** For comparison purposes, generated probability maps were thresholded with a value of 0.5. Thus, only voxels with values higher than 0.5 on the probability map were considered as relapse. The sensitivity and specificity of the proposed system were 0.80 (0.19) and 0.87 (0.09), respectively. For our data, standard Choline-to-NAA index (CNI) achieved a sensitivity of 0.62 (0.25) and a specificity of 0.63 (0.13). In addition, the receiver operating characteristic (ROC) curve also shows that the presented approach outperforms CNI (Fig 1.). The SVM-based results had lower variation across patients than CNI. An example of a probability map of relapse areas generated by the proposed approach is shown in Fig.2. Relapse regions predicted by the learning scheme are in high accordance with the manually contoured region.

**Conclusions:** A learning system based on SVM trained with mp-MR data has been presented. Reported results imply that this learning scheme can provide a probability map of the area of relapse of GBM in a stable and accurate manner, as shown in Fig.1. This study suggests the potential of multi-parametric MR data in addressing specific questions in GBM imaging.

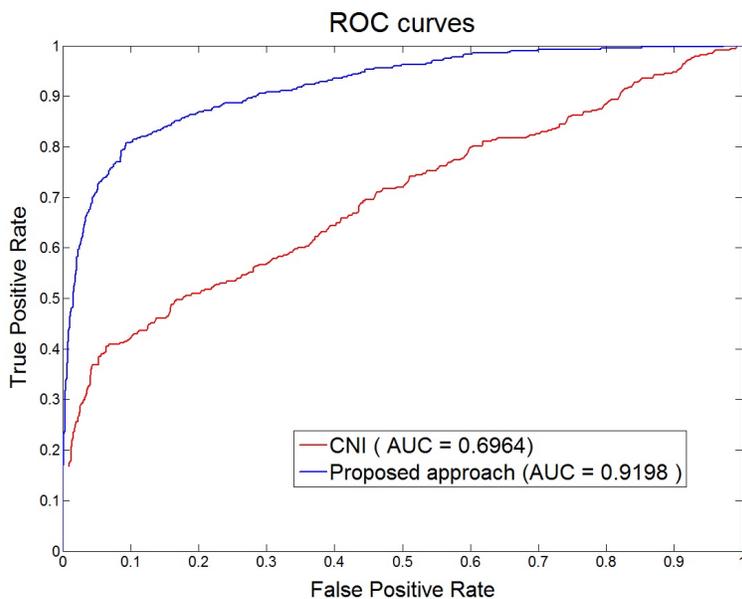


Figure. 1. Receiver operating characteristic (ROC) curve for the proposed method (blue) and for the standard CNI approach (red).

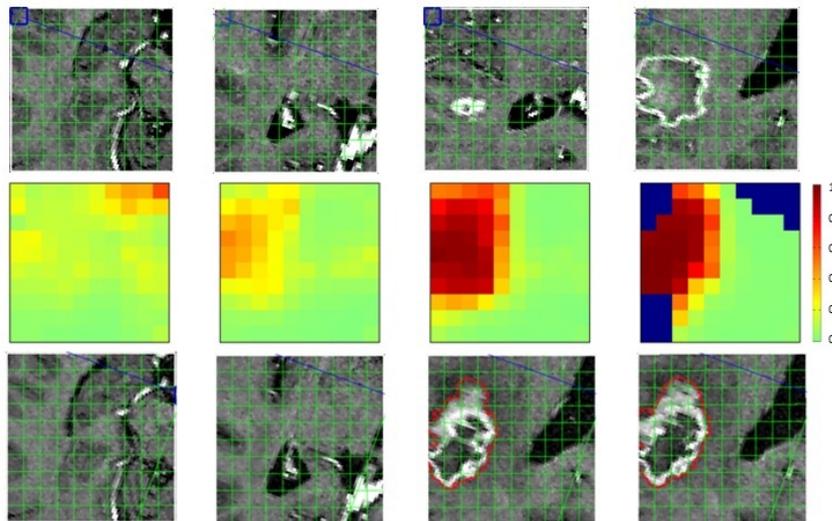


Figure. 2. Pre-RT T1-Gd (top), probability maps of GBM relapse generated by the proposed approach (middle) and reference manual contours of the relapse for a given patient (bottom). Each slice represents a slice in the axial view. Dark blue on the probability maps indicate voxels where metabolic information was not available. The areas at risk of relapse predicted by the proposed approach (using MR data acquired before RT) are in clear accordance with the manually contoured relapse regions.

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