Automatic identification of radiation necrosis in resected GBM patients using cost-sensitive OC-SVM classifier

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Introduction: Differentiating tumor recurrence from radiation necrosis in GBM patients under-going radiotherapy remains a challenge in MRI. It is due to a variety of problems in ROI analysis, such as a priori bias of ROI averaging without the knowledge of the intrinsic heterogeneity of GBM, as well as inter-observer variation in ROI placement. The differentiation between those two classes at the site of resection necessitates a high resolution voxel-by-voxel analysis. Combined features from multi-parametric MRIs demonstrated increased capability in differentiating those two entities. Meanwhile, machine learning methods like Support Vector Machine (SVM) showed remarkable advantage in dealing with classification problems in high dimensional feature space. Training of traditional SVM is based on learning using both positive and negative samples. However, only training samples for radiation necrosis are available due to the practical limitation of labeling recurrent tumor voxels. One-class SVM (OC-SVM) adapts the SVM methodology to one-class classification problem was introduced before[1]. In this paper, a cost-sensitive OC-SVM model utilizing multi-dimensional features from MRIs was proposed to automatically identify irradiation introduced necrosis at high spatial resolution. Parameters used in OC-SVM classifier training were optimized with the criteria of area under receiver operating characteristics (AUROC).

Materials and Methods: 26 patients (15 with recurrent tumor and 11 with radiation necrosis, confirmed by sequential MRIs routinely acquired every 2-3 month) were included. MRIs including contrast enhanced T1 (TR/TE=415/20ms), FLAIR (TR/TE/TI=8000/130/2000ms), T2 (TR/TE=3300/100ms), PD (TR/TE=2560/30ms), ADC, and spin-echo DSC-PWIs (TR/TE=1900/80ms) were acquired. rCBV, rCBF and MTT were estimated from PWIs using Least-Absolute-Deviation regularization software developed in-house[2]. All images were spatially aligned to post-contrast T1 scan using a rigid transform to construct an 8-dimensional feature vector for each voxel after normalization using a ROI in contralateral normal white matter. Each voxel located in the hyperintensity lesions on Gd-T1 images from 8 radiation necrosis cases was treated as one training sample. Radius Bases Function (RBF) is selected as kernel function for SVM model. Two parameters *Gamma* and *v* were under optimization. Each pair of parameters will determine a cluster of scoring classifiers corresponding to a ROC curve in ROC plane. The *Gamma* and *v* maximize the AUROC when testing on a test set are considered to be optimal, with Gamma searched from 1 to 30 at step of 1 while v from 0.02 to 0.6 at step of 0.02. The test set was organized as follows. 1) radiation necrosis voxels that never present in training samples; 2) Non-enhanced voxels in grey matter, white matter and CSF were randomly selected in both groups; 3) Enhanced voxels from recurrent tumor area in progressing cases were firstly filtered since radiation necrosis might be present. A liberal OC-SVM classifier (*Gamma*=10, *v*=0.001) preferring high sensitivity was used to remove radiation necrosis voxels as completely as possible; 4) Radiation necrosis (class label +1), non-enhanced and enhanced but non-necrosis voxels (class label -1) described in previous 3 steps were mixed equally. After parameters optimization, tangent of $y=kx+b$ and the ROC curve was selected as the optimal classifier, where k reveals the cost ratio between false positive and false negative. In our experiments k=1was used in illustration with the assumption of equal misclassification cost. A threshold T can be determined simultaneously to be applied on the score set to generate the discrete classifier.

Results: Classifier was optimized with *Gamma*=5, *v*=0.06 and *T*=-0.12. Sensitivity of 89.91% and specificity of 93.72% were achieved when testing on the test dataset. AUROC is 0.94. ROC curve for each feature element showed in Fig.1 indicated that conventional MRIs are not discriminative while rCBV, rCBF and ADC dominate classifier training. Identified radiation necrosis regions using proposed method were shown in Fig.2a for a non-progressing case, showing it exactly overlapped with the post-Gd enhanced region. An example progressing case is shown in Fig.2b indicating a majority of voxels were not identified to be in radiation necrosis state. Percentage of identified voxels in radiation necrosis cases (93.2±4.7) was significantly higher ($p<0.01$) than it in recurrent tumor cases (32.8±25.3). Distributions of identified radiation necrosis voxels were consistent with clinical outcomes.

Discussion and Conclusion: Machine learning using multiple MRI features is a promising approach to identify radiation necrosis at high spatial resolution in GBM patient under radiotherapy. This method is validated in a cohort of patients with non-progressing disease. It's fully automatic and more detailed depictions of lesions will provide necessary information for elaborated treatments. Future studies can use image guided biopsy to validate the location of radiation necrosis detected by this algorithm in progressing GBM cases.

Reference: 1. Scholkopf B et al., Estimating the support of a high-dimensional distribution; 2001 Jul. Report nr 0899-7667 (Print). p1443-1471. 2. Wong KK et al., Improved Residue Function and Reduced Flow Dependence in MR Perfusion Using Least-Absolute-Deviation Regularization, MRM, in press.

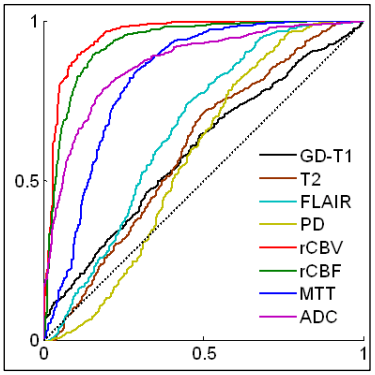

Fig.1: ROCs of different MRI features.

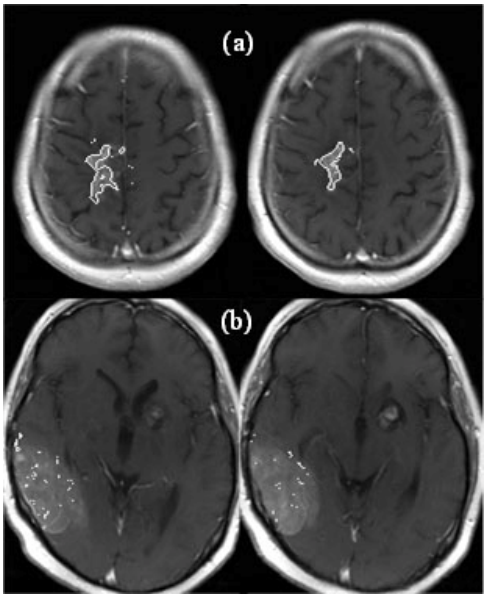

Fig.2: Identified radiation necrosis regions (bright contoured) in (a) non-progressing and progressing GBM patients.