

Abstract

PURPOSE: Because lactate accumulation is considered a surrogate for hypoxia and tumor radiation resistance, we studied the spatial distribution of the lactate-to-N-acetyl-aspartate ratio (LNR) before radiation therapy (RT) with 3D proton magnetic resonance spectroscopic imaging (3D-\(^1\)H-MRSI) and assessed its impact on local tumor control in glioblastoma (GBM).

METHODS AND MATERIALS: Fourteen patients with newly diagnosed GBM included in a phase 2 chemoradiation therapy trial constituted our database. Magnetic resonance imaging (MRI) and MRSI data before RT were evaluated and correlated to MRI data at relapse. The optimal threshold for tumor-associated LNR was determined with receiver-operating-characteristic (ROC) curve analysis of the pre-RT LNR values and MRI characteristics of the tumor. This threshold was used to segment pre-RT normalized LNR maps. Two spatial analyses were performed: (1) a pre-RT volumetric comparison of abnormal LNR areas with regions of MRI-defined lesions and a choline (Cho)-to-N-acetyl-aspartate (NAA) ratio $\geq2$ (CNR2); and (2) a voxel-by-voxel spatial analysis of 4,186,185 voxels with the intention of evaluating whether pre-RT abnormal LNR areas were predictive of the site of local recurrence.

RESULTS: A LNR of $\geq0.4$ (LNR-0.4) discriminated between tumor-associated and normal LNR values with 88.8% sensitivity and 97.6% specificity. LNR-0.4 voxels were spatially different from those of MRI-defined lesions, representing 44% of contrast enhancement, 64% of central necrosis, and 26% of fluid-attenuated inversion recovery (FLAIR) abnormality volumes before RT. They extended beyond the overlap with CNR2 for most patients (median: 20 cm\(^3\); range: 6-49 cm\(^3\)). LNR-0.4 voxels were significantly predictive of local recurrence, regarded as contrast enhancement at relapse: 71% of voxels with a LNR-0.4 before RT were contrast enhanced at relapse versus 10% of voxels with a normal LNR (P<.01).

CONCLUSIONS: Pre-RT LNR-0.4 in GBM indicates tumor areas that are likely to relapse. Further investigations are needed to confirm lactate imaging as a tool to define additional biological target volumes for dose painting.

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