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Differentiation of glioblastoma and cerebral metastasis using MR-derived tissue oxygenation and perfusion: a machine learning approach

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Purpose: This prospective clinical study was aimed at differentiating glioblastoma and cerebral metastasis, two tumor entities that often show similar radiological features, by means of combined MR oxygenation and perfusion imaging. Their distinction is highly important due to vastly differing therapy algorithms as well as patient outcomes. It was hypothesized that the infiltrative growth pattern of glioblastomas and the lack thereof in brain metastases would make it possible to distinguish the two groups based on their metabolic parameters in and around the contrast-enhancing part of the tumor.
Materials and Methods: Fifteen previously untreated patients were recruited, seven of which suffered from glioblastoma (median age: 68 years, range: 54 – 84 years) with the remaining eight showing one or multiple brain metastases (median age 66 years, range: 50 – 78 years). All patients underwent preoperative MRI scans including multi-gradient echo and pseudo-continuous arterial spin labeling sequences. Three regions of interest were segmented in post-processing: contrast-enhancing tumor (CET), contralateral normal-appearing brain tissue (cNAB) and peritumoral non-enhancing T2-weighted fluid-attenuated inversion recovery hyperintense area (NET2). For these regions, oxygen extraction fraction (OEF) and cerebral blood flow (CBF) were estimated, yielding a third parameter: cerebral metabolic rate of oxygen ($CMRO_2$). Two different machine learning-based approaches were employed to calculate OEF: an artificial neural network (ANN) and X-means clustering, both estimating the solution of the quantitative susceptibility mapping and quantitative blood-oxygen-level-dependent model (QSM + qBOLD). ANN results were used for statistical analysis and as features for training a support-vector machine algorithm for binary classification of tumor type. Classification performance was determined with receiver operating characteristic (ROC) analysis.
Results: We demonstrated that OEF in CET was significantly lower (p = 0.03) in glioblastomas than metastases, all features (OEF, CBF and $CMRO_2$) were significantly higher (p = 0.01) in CET than NET2 for metastasis patients only, and the ratios of CET/NET2 for CBF (p = 0.04) and $CMRO_2$ (p = 0.01) were significantly higher for metastasis patients than for glioblastoma patients. For glioblastoma patients, OEF was shown to be significantly lower (p = 0.02) in CET than in cNAB. In ROC analysis, the ratios of $CMRO_2$ and CBF in CET divided by NET2 were found to be the best single characteristics for classification with areas under the curve of 0.85 and 0.80, respectively. The best multiparametric classification model was found when training the classifier on two features: OEF in CET and the $CMRO_2$ ratio of CET/NET2. The resulting model had an area under the ROC curve of 0.94 with 93% classification accuracy.
Conclusion: The differences in oxygenation and perfusion between glioblastomas and brain metastases support the research hypothesis and allow for robust, non-invasive differential diagnosis of the tumor entity. While classification performance was found to be in line with previous MR-based publications that mainly investigated perfusion metrics such as cerebral blood flow and volume, the voxelwise estimation of $CMRO_2$ presents a major advantage in that it may also yield an insight into the likely response to radiation, antiangiogenic and chemotherapy, especially in glioblastoma. This makes the methods employed in this study promising candidates for implementation into the clinical routine, not least to complement anatomical MRI sequences without the need for additional application of contrast agent. In the long run, they have the potential to add to or even replace brain biopsies due to the good classification accuracy and the absence of typical complications of an invasive procedure. However, further research with larger patient populations is required before the QSM + qBOLD model can find its way into clinical decision making.