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## Cortical nonenhancing tumor infiltration: a predictive imaging biomarker for IDH-mutant glioma

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## Abstract

**Objective:** The aim of this study was to evaluate the cortical nonenhancing tumor infiltration (CONTIN) sign as a predictive imaging biomarker for IDH-mutant gliomas, including diffuse gliomas with and without contrast enhancement.

**Methods:** Imaging data were collected from patients with diffuse gliomas (grades 2-4) at Beijing Tiantan Hospital (BTH) from January 2019 to December 2021 (training set, n = 526) and from the University of California, San Francisco, preoperative diffuse glioma MRI dataset (UCSF PDGM; validation set, n = 501). Two independent reviewers assessed the CONTIN sign and other radiological features to develop a diagnostic strategy.

**Results:** Interrater agreement for the CONTIN sign was almost perfect ( $\kappa = 0.812$ ). In the BTH cohort, the prevalence of the CONTIN sign in IDH-mutant gliomas was 90.1% overall, with a rate of 92.2% (106/115) in contrast-enhancing gliomas and 88.9% (168/189) in nonenhancing gliomas. In the UCSF PDGM cohort, the overall prevalence was 85.4%, with 81.4% in contrast-enhancing gliomas and 88.3% in nonenhancing gliomas. In contrast-enhancing gliomas, the CONTIN sign significantly improved sensitivity compared with the T2-FLAIR mismatch (T2FMM) sign, with an increase from 14.8% to 92.2% in the BTH cohort and from 23.3% to 81.4% in the UCSF PDGM cohort. Additionally, the CONTIN sign had a high specificity (82.8% in the BTH cohort, 87.4% in the UCSF PDGM cohort) and negative predictive value (94.6% in the BTH cohort, 97.6% in the UCSF PDGM cohort). By integrating the CONTIN sign with T2FMM, contrast enhancement, age at diagnosis, and other features, a reliable diagnostic protocol for IDH-mutant gliomas was established.

**Conclusions:** The CONTIN sign was a robust imaging biomarker for identifying IDH mutation status in diffuse glioma, particularly for those with contrast enhancement. Preoperative knowledge of IDH mutation status can enhance patient counseling and inform treatment decision-making.

**Keywords:** biomarker; cortical nonenhancing tumor infiltration sign; glioma; isocitrate dehydrogenase; neuroimaging; oncology.

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