

J Neurooncol. 2025 Jan 2. doi: 10.1007/s11060-024-04898-7. Online ahead of print.

# Congress of Neurological Surgeons systematic review and evidence based guideline on neuropathology for WHO grade II diffuse glioma: update

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PMID: 39747718 DOI: [10.1007/s11060-024-04898-7](https://doi.org/10.1007/s11060-024-04898-7)

## Abstract

QUESTIONS AND RECOMMENDATIONS FROM THE PRIOR VERSION OF THESE GUIDELINES WITHOUT CHANGE: TARGET POPULATION: Adult patients (age  $\geq$  18 years) who have suspected low-grade diffuse glioma.

**Question:** What are the optimal neuropathological techniques to diagnose low-grade diffuse glioma in the adult?

**Recommendation:** Level I Histopathological analysis of a representative surgical sample of the lesion should be used to provide the diagnosis of low-grade diffuse glioma. Level III Both frozen section and cytopathologic/smear evaluation should be used to aid the intra-operative assessment of low-grade diffuse glioma diagnosis. A resection specimen is preferred over a biopsy specimen, to minimize the potential for sampling error issues.

**Target population:** Patients with histologically-proven WHO grade II diffuse glioma.

**Question:** In adult patients (age  $\geq$  18 years) with histologically-proven WHO grade II diffuse glioma, is testing for IDH1 mutation (R132H and/or others) warranted? If so, is there a preferred method?

**Recommendation:** Level II IDH gene mutation assessment, via IDH1 R132H antibody and/or IDH1/2 mutation hotspot sequencing, is highly-specific for low-grade diffuse glioma, and is recommended as an additional test for classification and prognosis.

**Target population:** Patients with histologically-proven WHO grade II diffuse glioma.

**Question:** In adult patients (age  $\geq$  18 years) with histologically-proven WHO grade II diffuse glioma, is testing for 1p/19q loss warranted? If so, is there a preferred method?

**Recommendation:** Level III 1p/19q loss-of-heterozygosity testing, by FISH, array-CGH or PCR, is recommended as an additional test in oligodendroglial cases for prognosis and potential treatment planning.

**Target population:** Patients with histologically proven WHO grade II diffuse glioma.

**Question:** In adult patients (age  $>$  18 years) with histologically-proven WHO grade II diffuse glioma, is methyl-guanine methyl-transferase (MGMT) promoter methylation testing warranted? If so, is there a

preferred method?

**Recommendation:** There is insufficient evidence to recommend MGMT promoter methylation testing as a routine for low-grade diffuse gliomas. It is recommended that patients be enrolled in properly designed clinical trials to assess the value of this and related markers for this target population.

**Target population:** Patients with histologically-proven WHO grade II diffuse glioma.

**Question:** In adult patients (age  $\geq$  18 years) with histologically proven WHO grade II diffuse glioma, is Ki-67/MIB1 immunohistochemistry warranted? If so, is there a preferred method to quantitate results?

**Recommendation:** Level III Ki67/MIB1 immunohistochemistry is recommended as an option for prognostic assessment.

**New recommendation:** TARGET POPULATION: Adult patients (age  $\geq$  18 years) who have suspected WHO grade II diffuse glioma.

**Question:** Is testing for ATRX mutations helpful for predicting survival and making treatment recommendations?

**Recommendation:** There is insufficient evidence to recommend ATRX mutation testing as a means of predicting survival or making treatment recommendations.

**Target population:** Adult patients (age  $\geq$  18 years) who have suspected WHO grade II diffuse glioma.

**Question:** Does the addition of intraoperative optical histologic methods provide accuracy beyond the use of conventional histologic methods in diagnosis and management?

**Recommendation:** There is insufficient evidence at this time to suggest that intraoperative optical histologic methods offer increased diagnostic accuracy when compared to conventional techniques.

**Keywords:** Histopathology; Low-grade glioma; Molecular Markers.

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