Congress of Neurological Surgeons systematic review and evidence-based guidelines for the role of radiotherapy in the management of patients with diffuse low grade glioma in adults: update

Review Published: 24 July 2025

(2025) Cite this article

Journal of Neuro-Oncology

Aims and scope

Submit manuscript

Simon S. Lo, Lia M. Halasz, Serah Choi, Priya Kumthekar, Tony J. C. Wang, Hui-Kuo Shu, Andrew E. Sloan & Jeffrey J. Olson

Abstract

Target population: These recommendations apply to adults with newly diagnosed WHO Grade 2 diffuse glioma.

Questions and Recommendations from the Prior Version of These Guidelines Without Change

Question What is the optimal role of external beam radiotherapy in the management of adult patients with newly diagnosed low-grade glioma (LGG) in terms of improving outcome (i.e. survival, complications, seizure control or other reported outcomes of interest)?

Recommendations Level I Radiotherapy is recommended in the management of newly diagnosed low-grade glioma in adults to prolong progression free survival, irrespective of extent of resection.

Level II Radiotherapy is recommended in the management of newly diagnosed low grade glioma in adults as an equivalent alternative to observation in preserving cognitive function, irrespective of extent of resection.

Level III Radiotherapy is recommended in the management of newly diagnosed low grade glioma in adults to improve seizure control in patients with epilepsy and subtotal resection.

Level III Radiotherapy is recommended in the management of newly diagnosed low-grade glioma in adults to prolong overall survival in patients with subtotal resection.

Level III Consideration of the risk of radiation induced morbidity, including cognitive decline, imaging abnormalities, metabolic dysfunction and malignant transformation, is recommended when the delivery of radiotherapy is selected in the management of newly diagnosed low grade glioma in adults.

Question Which radiation strategies (dose, timing, fractionation, stereotactic radiation, brachytherapy, chemotherapy) improve outcomes compared to standard external beam radiation therapy in the initial management of low grade gliomas in adults?

Recommendations Level I Lower dose radiotherapy is recommended as an equivalent alternative to higher dose immediate postoperative radiotherapy (45–50.4 vs. 59.4–64.8 Gy) in the management of newly diagnosed low-grade glioma in adults with reduced toxicity.

Level III Delaying radiotherapy until recurrence or progression is recommended as an equivalent alternative to immediate postoperative radiotherapy in the management of newly diagnosed low-grade glioma in adults but may result in shorter time to progression.

Level III The addition of chemotherapy to radiotherapy is not recommended over whole brain radiotherapy alone in the management of low-grade glioma, as it provides no additional survival benefit.

Level III Limited-field radiotherapy is recommended over whole brain radiotherapy in the management of low-grade glioma.

Level III Either stereotactic radiosurgery or brachytherapy are recommended as acceptable alternatives to external radiotherapy in selected patients.

Question Do specific factors (e.g. age, volume, extent of resection, genetic subtype) identify subgroups with better outcomes following radiation therapy than the general population of adults

with newly diagnosed low-grade gliomas?

Recommendations Level II It is recommended that age greater than 40 years, astrocytic pathology, diameter greater than 6 cm, tumor crossing the midline and preoperative neurological deficit be considered as negative prognostic indicators when predicting overall survival in adult low grade glioma patients treated with radiotherapy.

Level II It is recommended that smaller tumor size, extent of surgical resection and higher mini-mental status exam be considered as positive prognostic indicators when predicting overall survival and progression free survival in patients in adult low grade glioma patients treated with radiotherapy.

Level II I It is recommended that seizures at presentation, presence of oligodendroglial histological component and 1p19q deletion (along with additional relevant factors—see Table 1) be considered as positive prognostic indicators when predicting response to radiotherapy in adults with low grade gliomas.

Level III It is recommended that increasing age, decreasing performance status, decreasing cognition, presence of astrocytic histological component (along with additional relevant factors (see Tables 1, 2) be considered as negative prognostic indicators when predicting response to radiotherapy.

New Questions and Recommendations

Question In adult patients with pathology confirmed WHO Grade 2 diffuse glioma is proton therapy superior to standard radiation therapy result in terms of overall survival, progression free survival, local control, complications, neurocognitive preservation, and quality of life (QOL)?

Recommendation There is insufficient evidence to provide guidance on the superiority or inferiority of proton radiation effect compared to standard radiation therapy on WHO Grade 2 diffuse glioma in terms of overall survival, progression free survival, local control, complications, neurocognitive preservation, and quality of life.

Question In adult patients with pathology confirmed WHO Grade 2 diffuse glioma receiving radiotherapy, do the molecular markers IDH-1 status, *MGMT* promoter methylation status and 1p19q presence or absence result in better prediction of overall survival, progression free survival, local control, complications, neurocognitive preservation, and quality of life?

Recommendation Level III It is suggested that 1p/19q deletion status be used as a positive

prognostic indicator regarding the effect of radiation therapy on progression free survival and overall survival for WHO grade II diffuse gliomas.

Data availability

This clinical systematic review and evidence-based guideline was developed by a physician volunteer task force as an educational tool that reflects the current state of knowledge at the time of completion. Each chapter is designed to provide an accurate review of the subject matter covered. This guideline is disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a competent physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

References

1. Ryken TC, Parney I, Buatti J, Kalkanis SN, Olson JJ (2015) The role of radiotherapy in the management of patients with diffuse low grade glioma: a systematic review and evidence-based

clinical practice guideline. J Neuro-Oncol Rev 125(3):551–583. https://doi.org/10.1007/s11060-015-1948-1

Article CAS Google Scholar

2. Morshed RA, Young JS, Hervey-Jumper SL, Berger MS (2019) The management of low-grade gliomas in adults. J Neurosurg Sci Rev 63(4):450–457. https://doi.org/10.23736/S0390-5616.19.04701-5

Article Google Scholar

3. Schiff D et al (2019) Recent developments and future directions in adult lower-grade gliomas: Society for Neuro-Oncology (SNO) and European Association of Neuro-Oncology (EANO) consensus. Neuro Oncol 21(7):837–853. https://doi.org/10.1093/neuonc/noz033

Article CAS PubMed PubMed Central Google Scholar

4. Weller M et al (2017) European Association for Neuro-Oncology (EANO) guideline on the diagnosis and treatment of adult astrocytic and oligodendroglial gliomas. Lancet Oncol Rev 18(6):e315–e329. https://doi.org/10.1016/S1470-2045(17)30194-8

Article Google Scholar

5. Wood MD, Halfpenny AM, Moore SR (2019) Applications of molecular neuro-oncology—a review of diffuse glioma integrated diagnosis and emerging molecular entities. Diagn Pathol. https://doi.org/10.1186/s13000-019-0802-8

Article PubMed PubMed Central Google Scholar

6. G. Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice, in *Clinical Practice Guidelines We Can Trust*, R. Graham, M. Mancher, D. Miller Wolman, S. Greenfield, and E. Steinberg Eds. Washington (DC): National Academies Press (US) Copyright 2011 by the National Academy of Sciences. All rights reserved. (2011).

7. Louis DN et al (2016) The 2016 world health organization classification of tumors of the central nervous system: a summary. Acta Neuropathol 131(6):803–820. https://doi.org/10.1007/s00401-016-1545-1

Article PubMed Google Scholar

8. Louis DN et al (2021) The 2021 WHO classification of tumors of the central nervous system: a summary. Neuro Oncol 23(8):1231–1251. https://doi.org/10.1093/neuonc/noab106

Article CAS PubMed PubMed Central Google Scholar

9. Ziu M, Olson JJ (2016) Update on the evidence-based clinical practice parameter guidelines for the treatment of adults with diffuse low grade glioma: the role of initial chemotherapy. J Neuro-Oncol. https://doi.org/10.1007/s11060-016-2137-6

Article Google Scholar

10. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. https://doi.org/10.1371/journal.pmed.1000097

Article PubMed PubMed Central Google Scholar

11. Shih HA et al (2015) Proton therapy for low-grade gliomas: results from a prospective trial. Cancer 121(10):1712–1719. https://doi.org/10.1002/cncr.29237

Article PubMed Google Scholar

12. Sherman JC et al (2016) Neurocognitive effects of proton radiation therapy in adults with low-grade glioma. J Neuro-Oncol 126(1):157–164. https://doi.org/10.1007/s11060-015-1952-5

Article CAS Google Scholar

13. Tabrizi S et al (2019) Long-term outcomes and late adverse effects of a prospective study on proton radiotherapy for patients with low-grade glioma. Radiother Oncol 137:95–101. https://doi.org/10.1016/j.radonc.2019.04.027

Article PubMed PubMed Central Google Scholar

14. Dworkin M et al (2019) Increase of pseudoprogression and other treatment related effects in low-grade glioma patients treated with proton radiation and temozolomide. J Neuro-Oncol 142(1):69–77. https://doi.org/10.1007/s11060-018-03063-1

Article CAS Google Scholar

15. Ducray F et al (2013) Ongoing and prolonged response in adult low-grade gliomas treated with radiotherapy. J Neurooncol 115(2):261–265. https://doi.org/10.1007/s11060-013-1224-1

Article CAS PubMed Google Scholar

16. Etxaniz O et al (2017) IDH mutation status trumps the Pignatti risk score as a prognostic marker in low-grade gliomas. J Neurooncol 135(2):273–284. https://doi.org/10.1007/s11060-017-2570-1

Article PubMed Google Scholar

17. Bell EH et al (2018) Association of MGMT promoter methylation status with survival outcomes in patients with high-risk glioma treated with radiotherapy and temozolomide: an analysis from the NRG oncology/RTOG 0424 trial. JAMA Oncol 4(10):1405–1409. https://doi.org/10.1001/jamaoncol.2018.1977

Article PubMed Google Scholar

18. Bell EH et al (2020) Comprehensive genomic analysis in NRG oncology/RTOG 9802: a phase III trial of radiation versus radiation plus procarbazine, lomustine (CCNU), and vincristine in high-risk low-grade glioma. J Clin Oncol 38(29):3407–3417. https://doi.org/10.1200/jco.19.02983

Article CAS PubMed PubMed Central Google Scholar

19. Hudson EM et al (2024) Hitting the target: developing high-quality evidence for proton beam therapy through randomised controlled trials. Clin Oncol. https://doi.org/10.1016/j.clon.2023.11.027

Article Google Scholar

Acknowledgements

The guidelines task force would like to acknowledge the CNS Guidelines Committee for their contributions throughout the development of the guideline, the AANS/CNS Joint Guidelines Review Committee, as well as the contributions Trish Rehring, MPH, Director for Evidence-Based Practice Initiatives for the CNS. Through-out the review process, the reviewers and authors were blinded from one another. At this time the guidelines task force would like to acknowledge the following individual peer reviewers for their contributions: Stav Tjoumakaris MD, Koji Ebersole, MD, Cara Sedney, MD, Andrew P. Carlson, MD, Brian J. Williams, MD, Jamie J. Van Gompel, MD, Matthew Shepard, MD and Emanuela Binello, MD.

Funding

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons, which received no funding from outside commercial sources to support the development of this document.

Author information

Authors and Affiliations

Departments of Radiation Oncology and Neurological Surgery, University of Washington School of Medicine, 1959 NE Pacific Street, Box 356043, Seattle, WA, 98195, USA
Simon S. Lo & Lia M. Halasz

Department of Radiation Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA
Serah Choi

Division of Neurology (Neuro-Oncology), Northwestern Medicine, Feinberg School of Medicine, Lurie Cancer Center, Chicago, IL, USA
Priya Kumthekar

Department of Radiation Oncology, Columbia University Medical Center, New York, NY, USA
Tony J. C. Wang

Department of Radiation Oncology, Emory University, Atlanta, GA, USA
Hui-Kuo Shu

Department of Neurosurgery, Premier Health, Dayton, OH, USA
Andrew E. Sloan

Department of Neurological Surgery, Emory University, Atlanta, GA, USA

Jeffrey J. Olson

Contributions

SL wrote the main manuscript. LH, SC, PK, TW and HKS conducted the systematic review. JJO led the guideline task force. All authors reviewed the manuscript.

Corresponding author

Correspondence to Simon S. Lo.

Ethics declarations

Conflict of interest

All Guideline Task Force members were required to disclose all potential COIs prior to beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Review Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of task force members with possible conflicts and restrict the writing, reviewing, and/or voting privileges of that person to topics that are unrelated to the possible COIs. The task force has not made any disclosures.

Additional information

Publisher's Note

Sponsored by: Congress of Neurological Surgeons (CNS) and the Section on Tumors

Endorsement: Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS)

Rights and permissions

About this article

Cite this article

Lo, S.S., Halasz, L.M., Choi, S. *et al.* Congress of Neurological Surgeons systematic review and evidence-based guidelines for the role of radiotherapy in the management of patients with diffuse low grade glioma in adults: update. *J Neurooncol* (2025). https://doi.org/10.1007/s11060-025-05074-1

Received	Accepted	Published
28 February 2025	06 May 2025	24 July 2025

DOI
https://doi.org/10.1007/s11060-025-05074-1

Keywords

Low grade glioma Radiotherapy Prognostic factor Proton therapy IDH mutation 1p/19q deletion