

International Stereotactic Radiosurgery Society (ISRS) practice guidelines for radiosurgery in recurrent high-grade glioma.

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Neuro Oncol Neuro Oncol 310 neuroncol 100887420 neuonc Neuro-Oncology 1522-8517 1523-5866 Oxford University Press PMC12979047 PMC12979047.1 12979047 12979047 41143546 10.1093/neuonc/noaf247 noaf247 1 Guidelines AcademicSubjects/MED00300 AcademicSubjects/MED00310 International Stereotactic Radiosurgery Society (ISRS) practice guidelines for radiosurgery in recurrent high-grade glioma <https://orcid.org/0000-0002-0889-3371> Pinzi Valentina MD, PhD Department of Neurosurgery, Unit of Radiotherapy, Fondazione IRCCS Istituto Neurologico C Besta, Milan, Italy (V.P., L.F.) <https://orcid.org/0000-0001-6927-0402> Kotecha Rupesh Department of Radiation Oncology, Miami Cancer Institute, Baptist Health South Florida, Miami, Florida (R.K.) Sahgal Arjun Department of Radiation Oncology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada (A.S.) Gorgulho Alessandra Department of Neurosurgery, State University of São Paulo, NeuroSapiens Group, São Paulo, Brazil (A.G.) D'Or Institute for Research and Education, São Paulo, Brazil (A.G.) Lim-Fat Mary Jane Division of Neurology, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada (M.J.L.-F.) Levivier Marc Department of Clinical Neurosciences, Neurosurgery Service and Gamma Knife Center, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland (M.L.) Ma Lijun Department of Radiation Oncology, University of Southern California, Los Angeles, California (L.M.) <https://orcid.org/0000-0002-3820-8654> Paddick Ian Queen Square Radiosurgery Centre, National Hospital for Neurology and Neurosurgery, London, UK (I.P.) Regis Jean Aix-Marseille Université, Institut National de la Santé et de la Recherche Médicale, Institut de Neurosciences des Systèmes (INS) UMR1106, Marseille, France (J.R.) Sheehan Jason P Department of Neurological Surgery, University of Virginia, Charlottesville, Virginia (J.P.S.) Suh John H Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, Ohio (J.H.S.) Yomo Shoji Division of Radiation Oncology, Aizawa Comprehensive Cancer Center, Aizawa Hospital, Matsumoto, Japan (S.Y.) Fariselli Laura Department of Neurosurgery, Unit of Radiotherapy, Fondazione IRCCS Istituto Neurologico C Besta, Milan, Italy (V.P., L.F.) Corresponding Author: Valentina Pinzi, Department of Neurosurgery, Unit of Radiotherapy, Fondazione IRCCS Istituto Neurologico C. Besta, via G. Celoria 11, 20133 Milan, Italy (valentinapinzi@yahoo.it ; valentina.pinzi@istituto-besta.it). 2 2026 27 10 2025 28 2 509385 353 370 18 3 2025 17 10 2025 26 1 2026 27 10 2026 13 03 2026 13 03 2026 © The Author(s) 2025. Published by Oxford University Press on behalf of the Society for Neuro-Oncology. All rights reserved. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com. 2025 <https://academic.oup.com/pages/standard-publication-reuse-rights> This article is published and distributed under the terms of the Oxford University Press, Standard Journals Publication Model (<https://academic.oup.com/pages/standard-publication-reuse-rights>) Abstract Background

Recurrence invariably occurs in patients with high-grade glioma (HGG) despite maximal definitive therapy. Currently, there is no standard-of-care salvage treatment approach and re-irradiation is considered an option for select patients. Various radiotherapy fractionation schedules have been investigated, including the use of stereotactic radiosurgery (SRS). The aim of this study was to provide clinical practice recommendations on behalf of the International Stereotactic Radiosurgery Society (ISRS) specific to salvage SRS for recurrent-HGG. We define SRS as focal radiation in a single fraction and hypofractionated radiosurgery (HFSRS) as focal radiation delivered over 2-5 fractions.

A literature review and meta-analysis were performed according to PRISMA guidelines. Recommendations were formulated according to DELPHI methodology.

Sixty-two studies met the eligibility criteria for analyses, resulting in 2640 recurrent HGG patients. Stereotactic radiosurgery to a median total dose of 16 Gy was performed in 75% of patients, and HFSRS to the remaining 25% with a median total dose and number of fractions of 25 Gy and 5 fractions, respectively. The median overall survival from re-irradiation was 10.2 months. The pooled neurological toxicity rates were lower with HFSRS compared to SRS (4% vs. 7%, $P = 0.001$). A cumulative EQD2 greater than 120-130 Gy was significantly associated with a greater risk of radiation necrosis ($P = 0.003$).

Focal re-irradiation with 16 Gy in single fraction or 24-25 Gy in 3-5 fractions, is safe and appears to be effective for recurrent-HGG. We also present clinical practice recommendations on behalf of the ISRS. Given the limited prospective data, no definitive conclusions can be drawn.