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Original Article

Patterns of care in primary brain tumour Reirradiation: A survey by the ESTRO CNS focus Group

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A B S T R A C T

Background: Reirradiation is increasingly considered for patients with recurrent primary brain tumours, yet clinical practices vary significantly due to limited evidence and a lack of standardized guidelines. This survey aimed to map European practice patterns in brain tumour reirradiation.
Methods: A 23-item web-based survey was developed by the ESTRO CNS Focus Group to assess institutional characteristics, clinical decision-making, and technical aspects of reirradiation. Distributed via email and social media, the survey collected responses between June–July 2025. Descriptive statistics were applied.
Results: Eighty responses from 28 European countries were analysed. High-grade gliomas were the most frequently reirradiated tumours (>80 %), followed by meningioma (56 %, low-grade glioma (49 %), and ependymoma (44 %). Conventional photon radiotherapy (RT) was the predominant technique across all tumour types, with varying use of hypofractionation, stereotactic RT, and proton therapy. Target volume definition and margin size varied by histology, with larger margins and inclusion of edema/cavities more frequent in gliomas. MRI-CT fusion was standard for planning. Concurrent systemic treatment was used mainly in high-grade gliomas. Organ at risk dose recovery and cumulative constraints were commonly considered, but threshold values and recovery models differed. Main barriers included fear of toxicities, including radiation necrosis and limited evidence.
Conclusion: This survey reveals high heterogeneity in brain tumour reirradiation practices across Europe, especially regarding dose, technique, and target definition. Despite shared principles, consensus is lacking for rarer tumour types. These findings underscore the need for harmonized guidelines and prospective data to optimize patient care.

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Introduction

Radiotherapy (RT) remains a cornerstone in the management of primary brain tumours. However, recurrences within previously irradiated volumes present a complex clinical challenge. In the absence of an established standard of care in case of recurrence for most such entities, reirradiation is increasingly considered a feasible salvage strategy for patients with recurrent primary and metastatic brain tumours [1–4]. Advances in imaging and radiation delivery techniques enable precise targeting while minimizing dose to surrounding healthy tissue, and with preclinical and clinical data suggesting notable capacity for repair in the central nervous system (CNS). Therefore, a second course of radiotherapy in appropriately selected patients is a safe and efficient approach [5–7].

While retrospective and some prospective data suggest potential clinical benefit across various tumour histologies, including high grade glioma (HGG), low grade glioma (LGG), ependymoma (EPD), medulloblastoma (MBL), meningiomas and several benign tumours, the absence of widely accepted guidelines and variability in institutional practices continue to limit clinical implementation [2,8–10]. Numerous factors influence the decision to offer reirradiation, including tumour histology and grade, prior treatments, time interval since the initial course, patient performance status, most suitable techniques and alternative treatment options, including surgical and systemic treatments [3,11–13]. International efforts to standardize reirradiation practices have begun to address clinical questions regarding dose constraints, imaging, target delineation, and patient selection. Nevertheless, significant variability remains in how reirradiation is implemented in clinical settings, particularly in the treatment of rarer tumour entities [4]. To date, there is limited information on how reirradiation is applied across European centres, specifically for primary brain tumours.

To address this knowledge gap, this study aimed to map current European practices in primary brain tumour reirradiation, and provide an overview of clinical patterns, focusing on clinical decision-making, technical aspects of treatment, and potential limitations, to inform future efforts toward harmonizing practices.

Methods

This cross-sectional, web-based survey was developed by the European Society for Radiotherapy and Oncology (ESTRO) CNS Focus Group (FG), following the ESTRO-recommended methodology for survey-based research [14]. The questionnaire included 23 items in multiple formats (single-response, multiple-response, open-ended), covering institutional characteristics, clinical aspects of brain tumour reirradiation and technical aspects regarding contouring, dose prescription and organs-at-risk (OARs) management. Content validation was performed through iterative expert review and formal pre-testing involved 10 FG members, who provided structured feedback on clarity, scope, and usability. The final version was distributed in English on the SurveyMonkey™ (SurveyMonkey Inc., San Mateo, California, USA) platform. It was disseminated using a dual-channel strategy, by direct email invitation sent by ESTRO and an open call via social media. Responses were collected between 2nd of June- 21st of July 2025, and one reminder was issued midway through the data collection period to encourage completion. Participation was voluntary and anonymous, and no incentives were offered. Completion implied informed consent, in line with the general data protetion regulations. No ethical approval was required. No duplicate submissions were detected. Since participation was open and the eligible population size unknown, response rate could not be calculated. All partially completed responses were retained and included in the analysis. No imputation was applied for missing data. Descriptive statistic was applied.

Results

Ninety-one responses from 37 countries were collected and 11 answers from extra- European countries were excluded. Eighty responders from 28 European countries completed at least one section of the survey. Most responders were from Romania (16 %), Germany (15 %), and United Kingdom (12 %). Most participants worked in university hospitals (50 %) and comprehensive cancer centres (24 %), non-university clinics and practices or outpatient centres (12 %). Their roles in the radiotherapy team were radiation oncologist (84 %), medical physicist (9 %), radiation therapist or dosimetrist (7 %). Most centres were high-volume centres, with $>$ 90 primary brain tumour patients treated per year, with a minority (12 %) of responders coming from centres treating $<$ 30 primary brain tumour patients per year. In terms of reirradiation of primary brain tumour patients, 58 % performed it for less than 20 patients per year, whereas only 7 % of responders treated more than 60 patients per year with reirradiation.

The most frequent reradiated tumour entities were high grade gliomas, both Isocitrate dehydrogenase, wild type (IDHwt) (performed by 88 % of responders) and IDH mutant (IDHmt) (81 %). Fifty-six percent of professionals prescribed reirradiation of grade 2–3 (G2-3) meningioma, 49 % for LGG, 44 % for ependymoma, 42 % for medulloblastoma and 40 % for grade one (G1) meningioma. Other benign tumours (such as craniopharyngioma, pituitary adenoma, acoustic neuromas/vestibular schwannoma) were considered for reirradiation only by 18 % of clinicians.

The decision to reirradiate based on resection extent varied by tumour type (Fig. 1). For grade 1 meningiomas, 57 % of respondents reirradiated only if re-resection was not feasible, while for benign tumours, this criterion was reported by 50 %. Among other tumour types, a notable proportion of respondents reirradiated regardless of resection extent, including 39 % for HGG IDHwt and 37 % for HGG IDHmt. Decisions based solely on gross total resection were rare across all tumour types (<5 %).

Contouring practices vary notably by tumour type. Edema is most frequently included in the CTV for HGG (30 % in IDHmt and 32 % in IDHwt) and LGG (22 %), while its inclusion is rare in meningiomas, medulloblastomas, ependymomas, and benign tumours (CTV inclusion $\leq$ 21 %). Post-resection cavities are most often included for HGG IDHwt (73 %) and IDHmt (60 %), while inclusion is lower in benign tumours (17 %) and meningioma G1 (28 %). GTV–CTV margins are largest for HGGs (median 5 mm) and smallest for benign tumours and meningioma G1 (median 0–1 mm). Fig. 2 presents a detailed overview of the contouring practices for each tumour type.

Conventional fractionation is the predominant modality for reirradiation. It is widely used for LGG, HGG, meningiomas (G1, G2-3), ependymomas, and medulloblastomas, with $>$ 50 % usage reported by 38–56 % of responders. Moderately hypofractionated RT is also commonly applied, especially in HGG, where $>$ 50 % of patients are treated as such by more than half of the clinicians. Fractionated stereotactic RT is also occasionally used, mainly for G1 meningioma and other benign tumours and LGG, with 33–46 % of responders reporting using it for $>$ 50 % of these tumour types. Single fraction SRS is reported as rarely (<10 % of the patients) or never used by over 50 % of responders for LGG and HGG, with only 10 % of responders reportedly using it for $>$ 50 % of ependymoma and meningioma cases. Proton therapy sees moderate use in meningioma, ependymoma and medulloblastoma (10–20 % of participants use or refer more than half of these patients for protons), but it is reportedly never used by the majority of centres (50–78 %) for LGG or HGG. Carbon ion therapy and brachytherapy are the least adopted techniques, with 75–88 % of centres reporting they never use them nor refer to specialised centres across all tumour types.

For conventional fractionation (1.6–2 Gy/fraction), the most common total dose was 54 Gy, used by 29 % of responders. Other frequently reported regimens included 32–34 Gy, 36 Gy, 39.6–40 Gy, and 50–50.4

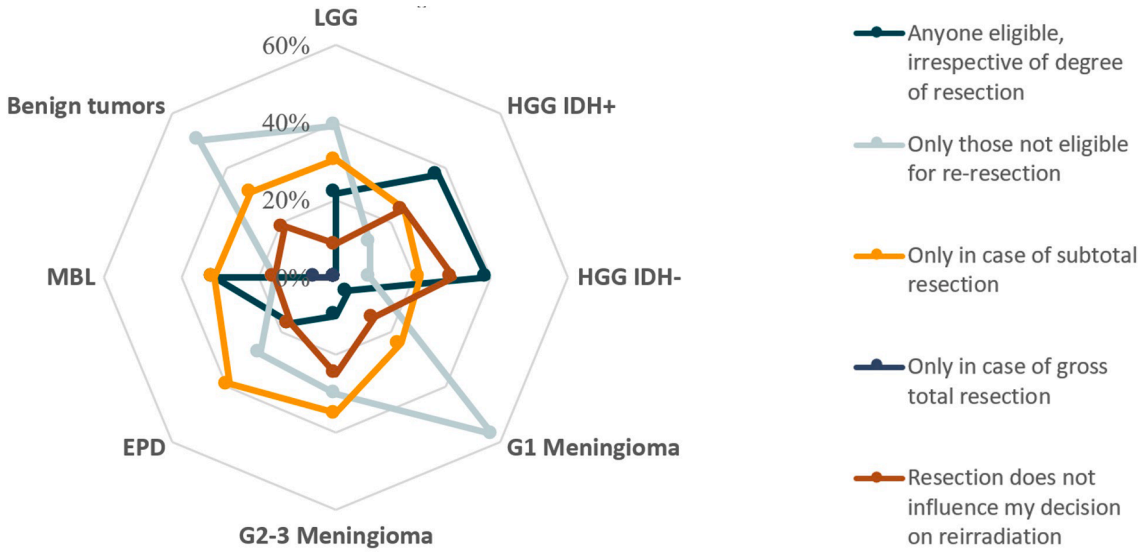

Fig. 1. Reirradiation in the post-reoperation setting. Spider graphic showing the criteria to perform reirradiation depending on the resection of the relapsed tumour. Percentages of respondents are shown for each tumour type. LGG = Low grade glioma, HGG IDH+ – High grade glioma with IDH mutation, HGG IDH- – High grade glioma with IDH wild type, MBL- Medulloblastoma, EPD- Ependymoma, G = tumour grade.

Gy (each by 14 % of responders), while 59.4–60 Gy and 45 Gy were less common (10 % and 5 %, respectively). In the moderate hypofractionation category (2.5–3.5 Gy/fraction), the most used regimen was 35 Gy, reported by 44 % of respondents. Other schemes such as 30–32 Gy, 37.5–39 Gy, and 40–40.05 Gy were each reported by 16–24 % of participants. Regarding fractionated stereotactic radiotherapy (FSRT) (5–9 Gy/fraction), a wide range of prescriptions was observed. The most frequently used doses were 35–36 Gy (36 %) and 30 Gy (24 %), with others using 24–25 Gy or 27–27.5 Gy (reported by 16 % each). For single-fraction radiosurgery, practice was notably heterogeneous. The most used prescription was 10–12 Gy (used by 42 % of respondents), followed by 18–20 Gy (26 %) and 14–15 Gy (16 %). Higher single doses of 24–25 Gy were reported by 16 % as well.

For treatment preparation, 76 % of responders used standard MRI registered to simulation CT, 57 % also used multiparametric or functional MRI and 52 % registered amino-acid PET/MRI to the simulation CT. Ten percent used CT-simulation only and no responder reported on using MRI-only workflows.

The use of concurrent systemic therapy during reirradiation varied by tumour type. Chemotherapy was most frequently prescribed for high-grade gliomas, with 42 % of respondents using it for both IDHmt and IDHwt cases. In these groups, antiangiogenic agents were also used (25 %/35 %, respectively), and targeted therapy was rarely reported (<8 %). In contrast, many respondents did not use systemic therapy for other tumour types: >75 % did not prescribe it any for low-grade gliomas, meningiomas, ependymomas, and benign tumours. However, medulloblastoma had slightly more systemic therapy use, with 21 % prescribing chemotherapy. The use of systemic therapy did not significantly alter radiotherapy planning. Most respondents (>80 % for each tumour entity) reported that they do not adjust margins, total dose, or dose per fraction when prescribing concurrent systemic treatment. Only a small proportion of respondents (<14 %) indicated that they use smaller margins, lower total dose, or smaller dose per fraction. Forty percent of responders never prescribe prophylactic steroids (before reirradiation), only in symptomatic patients during reirradiation. However, 32 % use prophylactic steroids in selected cases, based on previous symptoms (during the first RT course) and 20 % use them routinely.

Among clinical limitations and potential contraindications for reirradiation, the most impactful factors were the presence of multiple comorbidities and limited life expectancy, considered by 81 % of responders as very limiting or an absolute contraindication. Low performance score and previous/ persistent high-grade RT-related brain toxicity were also considered very limiting by 57 % of responders. Tumour location near critical structures, exceeding cumulative doses and too large tumour volumes each rated as very limiting by 80 % of respondents. Factors like steroid treatment requirement for symptom control and advanced age, as well as overlap with previous CTV were generally seen as less restrictive, with half of respondents considering them not limiting.

Fifty-three percent of participants considered 6–9 months as a minimum time interval since the first RT course, in case of overlapping fields, whereas 25 % consider 3–6 months as being enough, and 20 % suggesting > 1 year as minimum time interval between RT courses. In response to whether the prescribed dose or fractionation at reirradiation depends on the time elapsed since the initial radiotherapy course, responses were evenly split: 50 % of participants indicated no influence, while the other 50 % reported prescribing higher total doses when longer intervals had passed.

When asked which structures are considered for dose recovery between radiotherapy courses, most respondents reported accounting for recovery in the brainstem (80 %), optic structures (65 %), brain (60 %), and spinal cord (60 %). In contrast, recovery was less frequently considered for other cranial nerves, cochlea, hippocampi, and pituitary/ hypothalamus (each < 15 %). OAR constraints depend on the time interval between RT courses, as recovery is considered by 48 % of responders, 38 % use cumulative OAR constraints and 10 % use the same constraints for reirradiation as for the first course, with dose discount for the first course. Most respondents reported using Equivalent Dose in 2 Gy fractions (EQD2) recalculation (90 %), followed by biological effective dose (BED) recalculation (47 %). Physical plan summation was performed using rigid registration by 43 % and deformable registration by 33 %, while only 5 % indicated not performing dose accumulation at all. For brainstem, the accepted maximum cummulative dose (Dmax) commonly ranged between 70–80 Gy EQD2, with several specifying upper limits of 100 Gy or 94–100 Gy EQD2 (D0.1 cc). For the brain parenchyma, mean dose constraints were typically set at ≤ 40–50 Gy or ≤ 120 Gy EQD2, cumulative. Optic structures (chiasm, nerves, tracts) shared similar thresholds, with most respondents indicating limits of 70–75 Gy or < 108 Gy EQD2. A subset also used 100 Gy BED or specified 80 Gy EQD2 to D0.03 cc. For the spinal cord, common constraints included a Dmax of 60–70 Gy or 70 Gy EQD2 to D0.03 cc, with some respondents noting ≤ 45 Gy EQD2 if prior dose had been substantial.

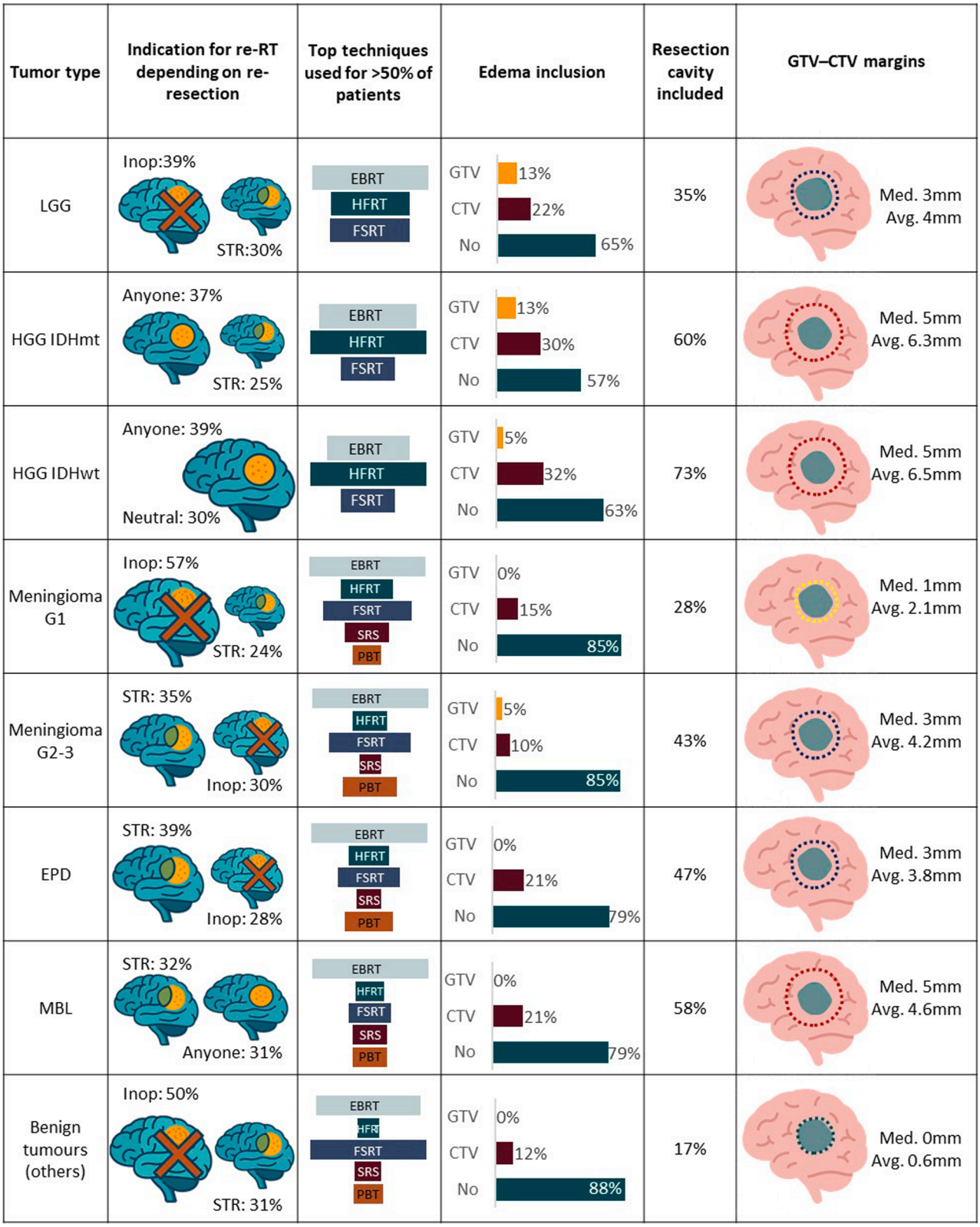

Fig. 2. Summary of radiotherapy indications, techniques used and contouring practices across tumour types. All percentages represent the proportion of responses. LGG = Low grade glioma, HGG IDH+ – High grade glioma with IDH mutation, HGG IDH- – High grade glioma with IDH wild type, MBL- Medulloblastoma, EPD- Ependymoma, G = tumour grade; Anyone = Anyone eligible, irrespective of degree of resection, Inop= Only those not eligible for re-resection, STR= Only in case of subtotal resection, GTR=Only in case of gross total resection; Neutral = Resection does not influence the decision on reirradiation; EBRT- Conventional EBRT, HFRT- Hypofractionated RT, FSRT- Fractionated Stereotactic RT, SRS- single fraction SRS, PBT- Proton therapy; Red cross = inoperable; GTV = Gross Tumour Volume, CTV= Clinical Target Volume, No = edema is not included in the target volume; Med = Median, Avg. = Average. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Regarding pituitary and hippocampi, dose constraints were more variable or absent. Some reported no specific constraints or deemed them not applicable. However, a few mentioned mean dose thresholds of 45–50 Gy EQD2 for the pituitary and $\leq$ 12 Gy BED per hippocampus to minimize neurocognitive toxicity.

The most reported reason to withhold reirradiation was fear of radiation necrosis, cited by 85 % of respondents, followed by concerns about other toxicities (57 %). A third of participants also expressed reservations due to insufficient evidence regarding survival benefit or safety. Fewer respondents pointed to lack of training (24 %) or infrastructure limitations (10 %).

Discussion

This study provides a comprehensive overview of current clinical practices regarding reirradiation of primary brain tumours across Europe. While there is growing clinical interest in this approach, our data highlight the considerable heterogeneity in indications, techniques, and decision-making processes, while also identifying some areas of convergence.

HGG, both IDHmt and IDHwt, were reported as the most commonly reirradiated tumour types, consistent with previous surveys and clinical experience, this being also supported by published guidelines [2]. Our respondents echoed this preference, with fractionated stereotactic and intensity-modulated techniques being the most widely used approaches. Overall, systemic therapy was reserved almost exclusively for malignant gliomas, particularly in high-grade subtypes, aligning with established treatment paradigms and ongoing research into combined modality approaches [2,10,15,16]. Reirradiation of lower-grade gliomas, ependymomas, medulloblastomas, meningiomas and other benign tumours was reported less frequently, likely reflecting limited clinical evidence and increased concern about long-term toxicity [8,9,17]. Nevertheless, selected centres reported offering reirradiation for these indications based on individual assessment. In meningiomas, reirradiation was more frequently reported for grade 2–3 tumours, a pattern that corresponds with emerging data suggesting favourable local control and acceptable toxicity when using fractionated SRT with strict dosimetric constraints. However, practices remain non-uniform, with significant variability in timing, technique, and dose prescription, underscoring the need for further standardization [8,13,18–20].

Tumour-specific trends in target volume delineation were also evident. Tumour types where edema and/or post-operative cavities are more often included in the target volumes tend to have larger GTV-to-CTV margins, likely reflecting greater clinical uncertainty or aggressiveness. Conversely, more well-defined, or indolent tumours tend to have less inclusion and smaller margins. However, this is a trend rather than a strict linear correlation. This variability may be explained in part by differing institutional philosophies, imaging interpretation standards, and risk tolerance. This should be interpreted with caution, as current evidence and expert guidelines generally recommend keeping the GTV as small as possible and avoiding systematic inclusion of peritumoral edema, which does not necessarily represent active tumour tissue. Instead, target delineation should focus on contrast-enhancing or FLAIR-suspicious areas. Similarly, the relatively large CTV margins reported by some centres deviate from contemporary practice, where highly conformal approaches and image-guided verification aim to minimize margins to reduce normal tissue exposure [8,9,21,22].

A key finding in our study was the lack of consensus on the minimum interval required between radiotherapy courses. While many centres reported a preference for an interval of at least 6–12 months, thresholds varied considerably, and some decisions were based on tumour type or recurrence dynamics rather than fixed cut-offs. Overall, the most frequently cited limits across OARs reflect cautious cumulative thresholds in line with literature on reirradiation tolerance, although inter-institutional variability remains notable. Some reported cumulative constraints appeared overly permissive- for example, optic pathway limits above 100–108 Gy EQD2- which clearly exceed the tolerance reported in clinical series and guidelines. Likewise, constraints for structures such as the hippocampus varied widely, despite the absence of robust evidence supporting hippocampal sparing in the reirradiation or even primary setting when tumour coverage would be compromised. These observations further reflect the absence of robust data defining safe cumulative dose thresholds for many OARs and emphasize the need for harmonized, evidence-based dose constraints in the reirradiation context. Further studies integrating detailed data on concurrent medication use (including corticosteroids) and long-term toxicity follow-up are needed to complement these practice-pattern insights and better define safe cumulative dose thresholds [13,15,23].

Barriers to reirradiation identified by respondents included concerns about toxicity, lack of guidelines, and insufficient data to support decision-making, which appear to be more influential than logistical constraints. Lack of standardized guidelines limited prospective data, and potential uncertainty were mentioned, particularly for non-glioma tumour types, concerns that are in line with those expressed in other reports [3,15,16,23].

This study is subject to several limitations. The open dissemination and voluntary nature of the survey preclude the calculation of a response rate and may introduce self-selection bias, favouring centres with greater interest or expertise in reirradiation. Additionally, while the data provide valuable insight into practice patterns, clinical outcomes and dosimetric details were not assessed, limiting our ability to evaluate treatment efficacy or toxicity.

Despite these limitations, this work provides a valuable evaluation of reirradiation practices across Europe and highlights key areas requiring harmonization. Future efforts should focus on developing consensus protocols, integrating normal tissue recovery modelling, and promoting prospective data collection through registries and trials [23,24]. Such initiatives are essential to improve safety and standardize care for patients undergoing reirradiation for recurrent brain tumours.

CRediT authorship contribution statement

Andrada Turcas: Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Raphael Bodensohn:** Conceptualization. **Elena Clerici:** Conceptualization. **Isacco Desideri:** Conceptualization. **Felix Ehret:** Writing – review & editing, Conceptualization. **Nils Gleim:** Formal analysis, Conceptualization. **Harat Maciej:** Conceptualization. **Pierina Navarria:** Conceptualization. **Aoife Williamson:** Conceptualization. **Jonas Willmann:** Writing – review & editing, Conceptualization. **Nicolaus Andratschke:** Writing – review & editing, Conceptualization. **Giuseppe Minniti:** Writing – review & editing, Supervision, Conceptualization. **Maximilian Niyazi:** Writing – review & editing, Supervision, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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