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Utility of Early Postoperative DWI to Assess the Extent of Resection of Adult-Type World Health Organization Grade 2 and 3 Diffuse Gliomas

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ABSTRACT

BACKGROUND AND PURPOSE: World Health Organization (WHO) grade 2 and 3 diffuse gliomas account for approximately 5% of primary brain tumors. They are invasive and infiltrative tumors and have considerable morbidity, causing progressive neurologic deterioration. The mean survival time is <10 years from diagnosis. Surgical debulking represents first-line management. The extent of resection is associated with progression-free and overall survival. Radiologic assessment of the extent of resection is challenging. This can be underestimated on early postoperative MRI, meaning that accurate assessment may be achieved only on delayed follow-up imaging. We hypothesized that DWI may help facilitate more reliable estimates of the extent of resection on early postoperative MRI. This study aimed to assess the utility of DWI in early postoperative MRI to evaluate the extent of resection.

MATERIALS AND METHODS: A single-center observational cohort study was performed. All patients with histologically confirmed WHO grade 2 and 3 gliomas managed with surgical debulking between January 2015 and December 2020 were identified. Preoperative, early postoperative, and follow-up imaging were reviewed independently by 2 consultant neuroradiologists. The extent of resection was estimated with and without DWI sequences for each case.

RESULTS: Two hundred twenty-four patients with WHO grade 2 and 3 gliomas were managed with surgical debulking between 2015 and 2020. DWI was not performed on early postoperative MRI in 2 patients. With the use of DWI, the extent of resection was upgraded in 30% of cases (n = 66/222) and classified as "complete" or "supramaximal" in 58% of these patients (n = 38/66). In cases in which the extent of resection was upgraded with the use of DWI, signal abnormality was stable or reduced at follow-up in 78% (n = 49/63). In cases with worsening signal abnormality, 64% were deemed to be secondary to adjuvant radiation therapy (n = 9/14). Eight percent (n = 5/63) of patients with an increased estimated extent of resection using DWI demonstrated signal progression attributed to true disease progression at follow-up.

CONCLUSIONS: DWI is a helpful and reliable adjunct in differentiating residual tumor from marginal ischemia in early postoperative MRI in WHO grade 2 and 3 diffuse gliomas and increases the accuracy in assessing the extent of resection. It should be used routinely in these cases.

 $\textbf{ABBREVIATIONS:} \ EoR = extent \ of \ resection; \ IQR = interquartile \ range; \ WHO = World \ Health \ Organization$

World Health Organization (WHO) grade 2 and 3 adulttype diffuse gliomas (astrocytomas and oligodendrogliomas) are infiltrative and invasive brain tumors derived from supporting glial cells of the CNS. They make up approximately 5% of all primary brain tumors, with an estimated incidence of 1 per 100,000 population.^{2,3} Progressive neurologic decline secondary

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to continuous growth is followed by rapid deterioration following inevitable malignant transformation. The mean survival time is currently <10 years after diagnosis.^{4,5}

Treatment of astrocytomas and oligodendrogliomas is complex and nuanced. Cases are managed on an individualized basis. Diagnosis and management paradigms are continuously evolving. Molecular testing is supplanting traditional histologic analysis to establish diagnosis and guide management. Treatment may consist of surgery, radiation therapy, and/or chemotherapy. Previously, the role of surgery was considered controversial with a dearth of supporting high-level evidence. However, numerous recent studies support surgical debulking as first-line treatment, with an increased extent of resection (EoR) associated with significant

SUMMARY

PREVIOUS LITERATURE: Previous studies have highlighted challenges in accurately assessing the extent of resection in WHO grade 2 and 3 adult-type diffuse gliomas (astrocytomas and oligodendrogliomas). Challenges are primarily due to limitations of T2/FLAIR imaging. These sequences often overestimate residual tumor by failing to distinguish between true residual tumor and postsurgical changes. DWI helps improve differentiation. Its impact on the extent of resection assessment in postoperative imaging has not been validated.

KEY FINDINGS: DWI in early postoperative imaging significantly reduces overestimation of residual tumor, providing more accurate extent of resection assessment.

KNOWLEDGE ADVANCEMENT: This study highlights the importance of DWI in estimating the extent of resection in WHO grade 2 and 3 gliomas, facilitating more accurate assessment of residual tumor volume.

improvement in both progression-free and overall survival. ⁹⁻¹² EoR, therefore, represents an important prognostic marker following intervention.

EoR is estimated from postoperative MRI, with residual tumor represented by persistent hyperintensity on T2-weighted or FLAIR sequences.¹³ Early postoperative MRI is recommended ideally between 24 and 48 hours and within 72 hours after an operation in high-grade gliomas, 13-16 to avoid assessment for residual disease being confounded by nonspecific enhancement at the margins of the resection cavity. Various articles postulate that early postoperative imaging is vulnerable to overestimating residual tumor volume in low-grade gliomas, owing to signal abnormality due to postoperative edema and marginal ischemia/infarction resulting from surgical trauma. 17-19 However, interpreting the EoR on delayed follow-up imaging (ie, between 2 and 6 months postoperatively) also comes with difficulties, such as distinguishing residual tumor or disease progression from scarring, gliosis, encephalomalacia, and radiation-induced change. 17,18,20,21 Recommendations have only recently changed with the updated RANO 2.0 criteria, which now advise that postoperative MRI should be performed within 48 hours of surgery. 16

DWI may help address the susceptibility of overestimating residual disease on early postoperative MRI through distinguishing between infarcted tissue due to surgical trauma and arterial or venous ischemia, which markedly diffusion restricts, and residual tumor, which typically exhibits facilitated diffusion. ²² Accurate estimation of the EoR of WHO grade 2 and 3 diffuse gliomas on early postoperative imaging during delayed follow-up MRI may help establish accurate prognoses earlier and facilitate more expedient patient management. ²³ To the authors' knowledge, there has been only a single, small retrospective cohort study published to date specifically examining the utility of DWI in this setting. ²⁰ We aimed to address this paucity in the literature and more definitively define the role of DWI in assessing the EoR in early postoperative MRI following debulking of WHO grade 2 and 3 adult-type diffuse gliomas.

MATERIALS AND METHODS

Study Design and Patient Characteristics

A single-center, observational cohort study was performed following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement recommendations

for observational studies²⁴ (Online Supplemental Data). Ethics approval was obtained from the local institutional review board. An initial retrospective review of a prospectively maintained institutional histopathology database was performed. All patients with histologically confirmed WHO grade 2 (including diffuse astrocytoma and oligodendroglioma) and grade 3 (including anaplastic astrocytoma and anaplastic oligodendroglioma) gliomas managed surgically between January 2015 and December 2020 in accordance with the fourth edition of the WHO classification of CNS tumors²⁵ were recorded (noting that all cases would be classified as WHO grade 2 and 3 adult-type diffuse gliomas using the 5th edition of the WHO classification of CNS tumors²⁶). Established electronic medical records were searched to acquire patient demographics and treatment history. Patients undergoing both first debulking and repeat resections were included.

Preoperative, early postoperative, and first follow-up MRIs of all identified patients were accessed using a national integrated medical imaging system. Preoperative imaging findings were recorded, including tumor side, location, and size; involvement of eloquent brain; and the presence or absence of enhancement. Eloquent brain was defined as any area that, if injured, would result in a disabling neurologic deficit.²⁷

The EoR on early postoperative MRI was estimated independently by 2 senior neuroradiologists (each with >15 years of experience). The EoR was defined as being "supramaximal" (resection beyond the T2 FLAIR hyperintense tumor borders on preoperative imaging), "complete" (resection of 100% of T2 FLAIR hyperintense tumor), "near-total" (≥90% of T2 FLAIR hyperintense tumor), "subtotal" (40%–89% of T2 FLAIR hyperintense tumor), or "partial" (1%–39% of T2 FLAIR hyperintense tumor). These definitions follow the categories defined by Karschnia et al, 13 which are established from Class IV evidence from numerous studies published between 2006 and 2018.

An initial estimate was made by comparing the volume of signal abnormality between pre- and postoperative imaging on T2- and FLAIR-weighted sequences only. Imaging was subsequently re-reviewed during separate sessions to include DWI sequences on postoperative imaging (inclusive of b=1000 images and ADC maps), and a second estimate of the EoR was performed. Specifically, the presence or absence and extent of marked diffusion restriction in residual T2 FLAIR hyperintensity at the surgical cavity were recorded. Marked diffusion restriction

was defined as having ADC values of $<620 \times 10^{-6} \text{ mm}^2/\text{s}.^{28,29}$ 2D tumor measurement was performed in each case, in accordance with recommendations from updated RANO guidelines, ¹⁶ with the product of the maximal cross-sectional dimensions of T2 FLAIR signal abnormality used to determine the size of the tumor in each case. The estimated EoR was determined from visual assessment, and each case was assigned to 1 of the 5 categories defined by Karschnia et al. ¹³ All cases with a change in estimate between DWI blinded and nonblinded reviews were recorded. Cases with any discrepancy between estimates of EoR were resolved through a consensus discussion. Follow-up imaging was also reviewed for each case and regression, stability, or progression of signal abnormality and the presence of new enhancement were recorded.

Imaging Parameters

All studies were performed on 1.5T or 3T MR scanners. Scans at our institution were obtained on 1.5T Signa (GE Healthcare), 1.5T Magnetom Sola (Siemens), and 3T Magnetom Skyra (Siemens). Standard imaging protocols included T1-weighted, contrastenhanced T1-weighted, T2-weighted, T2 FLAIR, and DWI sequences with b-values of 0, 500, and 1000 s/mm² and corresponding ADC maps. Detailed acquisition parameters are provided in the Online Supplemental Data. It was not possible to acquire machine specifications or all imaging parameters for studies performed at external sites.

Statistical Analysis

Basic patient demographic data and treatment information (age, sex, date of surgery, age at diagnosis, age at the time of surgical debulking, and undergoing of chemotherapy or radiation therapy), histopathology (including the tumor grade and final integrated pathologic diagnosis), and imaging details (date of preoperative, early postoperative, and follow-up MRI scans; tumor characteristics on preoperative imaging; estimated debulking without and with DWI and progression; and stability or regression of signal abnormality on follow-up imaging) were recorded.

Analysis was performed in R Version 4.2.0 (http://www.r-project.org/). Summary statistics are reported as medians with interquartile ranges (IQRs) and frequency counts with percentages as appropriate. The relative frequency of radiologic estimates of complete-versus-incomplete resection were compared using simple hypothesis tests.

Logistic regression models were developed to examine the relationship among various factors hypothesized to potentially influence the extent of resection (EoR) on early postoperative imaging and the likelihood of a change in the EoR assessed by diffusion-weighted imaging (DWI) sequences. From these models, the odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Additionally, *P* values were provided for each regression coefficient, testing the null hypothesis that the coefficient of the variable in question was significantly different from zero. These factors included tumor grade, first debulking versus residual/recurrent tumor, side of the tumor, eloquent brain affected, and the presence of enhancement. A logistic regression model adjusted for postoperative MR with and without DWI and tumor volume was also fit to assess the influence of tumor size on the

estimated EoR. From this, the average marginal effect was reported³¹ for DWI-versus-non-DWI sequences, which represents the expected difference in the probability of estimated complete resection (including supramaximal resection) with and without DWI with the 95% CI.

RESULTS

During the study period, a total of 293 cases of WHO grade 2 and 3 tumors were recorded in our institutional histopathology database. Sixty-nine of these represented cases with only biopsies obtained and no surgical debulking. These were excluded from further analysis. The remaining 224 entries represented histologic diagnoses from samples acquired during surgical debulking. One hundred forty-seven of these were from patients undergoing their first debulking procedure, and 75 were from patients undergoing repeat surgery for residual or recurrent disease. DWI was not performed on early postoperative MRI in 2 patients who were subsequently excluded. Of the remaining 222 cases, 60% of patients were men (n = 134/222) and 40% were women (n = 88/222). The median age at time of diagnosis was 36 years (IQR, 28-47 years), and the median age at surgery was 37 years (IQR, 30-48.25 years). Most patients (69%) had a final integrated histopathologic diagnosis of oligodendroglioma (36%, n = 79/222) or diffuse astrocytoma (33%, n = 73/222). Nineteen percent of patients were diagnosed with anaplastic astrocytoma (n = 42/222); 10%, with anaplastic oligodendroglioma (n = 23/222); and 2%, with gemistocytic astrocytoma (n = 5/222). Of those with a diagnosis of gemistocytic astrocytoma, 3 cases were WHO grade 3 and 2 were WHO grade 2. In total, 66% of cases were WHO grade 2 tumors (n = 147/222) and 34% of cases were WHO grade 3 tumors (n = 75/222).

On preoperative imaging, 51% of tumors were right-sided (n = 114/222), 45% were left-sided (n = 100/222), and 4% were bilateral (n = 8/222). The frontal lobes were the most frequently affected site in 74% of cases (n = 165/222), followed by the temporal lobes, insula, and parietal lobes, which were affected in 29% (n = 65/222), 17% (n = 38/222), and 15% (n = 33/222), respectively. Mean tumor volume was 52.2 mL. Most patients' tumors were found to be confined to a single region (57%, n = 126/222). Tumors were found to involve >1 area in 43% of cases, with 2 areas being involved in 24% (n = 53/222), 3 areas being involved in 14% (n = 32/222), 4 areas being involved in 4% (n = 9/222), and 5 areas being involved in 1% of patients (n = 2/222). Fortysix percent (n = 102/222) of tumors were determined to involve eloquent brain. In 54% (n = 120/222) of cases, only non-eloquent brain was involved. Enhancement was seen in 21% (n = 47/222) of tumors, with 75% (n = 35/47) of these being confirmed to be anaplastic astrocytoma (36%, n = 17/47), anaplastic oligodendroglioma (30%, n = 14/47), or gemistocytic astrocytoma (9%, n = 14/47) 4/47) and 25% being diffuse astrocytoma (58%, n = 7/12) and oligodendroglioma (42%, n = 5/12). A detailed breakdown of patient demographics and imaging findings is provided in the Online Supplemental Data.

The median duration of the time between surgery and postoperative imaging was 2 days (IQR, 1–3 days). The median duration of time between surgery and delayed follow-up imaging was 181 days (IQR, 105–236 days). Resections were classified as

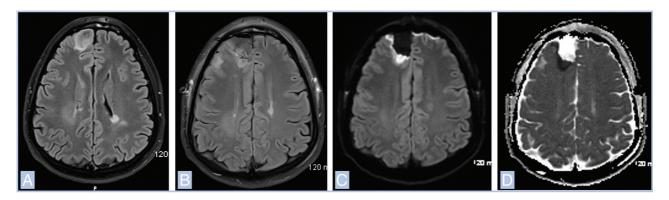


FIG 1. Right parasagittal frontal lobe mass in a 29-year-old man on axial FLAIR (*A*). Estimated EoR was supramaximal on postoperative FLAIR (*B*) and additional DWI sequences (*C*, *D*) did not change this estimate. However, DWI helps increase the confidence that the restricting abnormality posterior to the resection cavity is secondary to ischemia/contusion from surgery as opposed to residual tumor. Final integrated histopathologic diagnosis was diffuse astrocytoma, isocitrate dehydrogenase (*IDH*) mutant, *ATRX*-mutant, WHO grade 2 (4th edition of the WHO classification of CNS tumors, 2016).

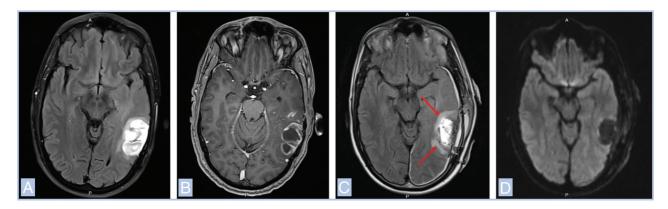


FIG 2. Lateral left temporal lobe mass in a 44-year-old man on axial FLAIR (A), with associated enhancement on postcontrast TI (B). Postoperative imaging demonstrates a residual FLAIR signal abnormality at the margins of the resection cavity (red arrows, C) without associated diffusion restriction (D). The EoR was estimated to be subtotal with and without DWI. Final integrated histopathologic diagnosis was anaplastic oligodendroglioma, IDH-mutant, ATRX wild-type, 1p19q co-deletion, WHO grade 3 (4th edition of the WHO classification of CNS tumors, 2016).

being supramaximal, complete, near-total, subtotal, partial, and biopsy-only. 13 Diffusion restriction was present at the margins of the resection cavity on postoperative MRI in 69% (n = 154/222) of cases and absent in 31% (n = 68/222). The presence of residual tumor appeared to be overestimated when assessed in the absence of DWI, with 86% of cases (n = 191/222) showing residual tumor compared with 70% (n = 156/222) when DWI sequences were included in the review (P < .001) (Online Supplemental Data). The use of DWI in addition to T2 and FLAIR sequences led to a change in the estimate of the EoR in 30% of cases (n =66/222), with an increase in the estimated EoR in all cases. The EoR was upgraded to complete or supramaximal in 58% (n =38/66). DWI did not lead to any change in the estimated EoR in 70% (n = 156/222) of cases (Figs 1 and 2). DWI was not performed in 2 cases (<1%). Eight patients were upgraded from an estimated partial resection before review with DWI sequences (7 subtotal and 1 complete). Thirty-two patients were upgraded from an estimated subtotal resection (21 near-total, 8 complete, 3 supramaximal). Twenty-two patients were upgraded from an estimated near-total resection (15 complete and 7 supramaximal). Four patients were upgraded from estimated complete resection to supramaximal.

The probability of a complete resection was 15% (95% CI, 8.5%-22.1%) higher when the EoR was estimated using DWI compared with estimates without DWI. The presence of enhancement appeared to decrease the likelihood of a change in the estimated EoR between assessment of early postoperative imaging with or without DWI (OR = 0.36; 95% CI, 0.14-0.8) (Fig 2). In the regression model adjusted for baseline tumor volume, the probability of complete resection across a range of tumor volumes was substantially increased when estimated with DWI (Fig 3). No other specific factor was identified to account for the discordance between the estimated EoR with and without DWI (Online Supplemental Data).

For cases in which DWI changed the estimated EoR, the volume of T2 FLAIR hyperintense abnormality was stable or had regressed on early postoperative MRI in 78% (n=49/63) of cases. Fourteen percent of cases had progression in signal abnormality attributed to adjuvant radiation therapy–related change (n=9/63) (Fig 4). An increase in signal abnormality attributed to disease progression was identified in 8% (n=5/63) (compared with 7% of the cases in which DWI did not increase the estimated EoR [n=11/151]). Three patients did not have delayed follow-up imaging available for review. Overall, in cases with an estimated

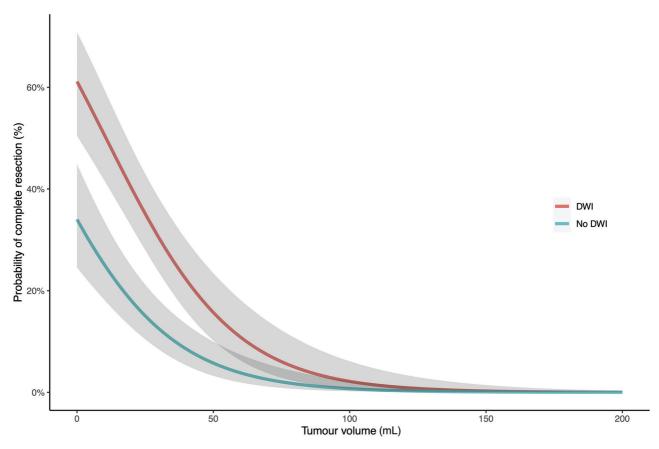


FIG 3. Probability of estimated complete resection for given tumor volumes with and without DWI.

EoR defined as complete or supramaximal with DWI, 89% (n = 58/65) had no evidence of disease progression on follow-up.

DISCUSSION

Radiologic assessment by MRI constitutes an essential pillar in the work-up of WHO grade 2 and 3 diffuse gliomas in both preand postoperative settings. In addition to the salient role it plays in the characterization of tumors before surgical intervention, imaging is also used postoperatively to delineate the estimated EoR, because studies have shown that the intraoperative assessment by a surgeon of the completeness of resection is comparatively unreliable.³² Increased EoR is a strong predictor of improved progression-free and overall survival^{33,34} and can also influence decisions regarding adjuvant therapy.³⁵ Thus, an accurate estimation of the EoR is imperative. In the setting of lower-grade gliomas, this is performed through volumetric assessment of the T2 FLAIR hyperintense abnormality associated with the tumor.¹³ Unfortunately, defining the EoR is particularly challenging in the early postoperative period, because aberrant T2 and FLAIR hyperintensity related to surgical trauma and/or arterial and venous ischemia confounds interpretation, with evidence to show that delayed follow-up imaging more closely correlates to long-term prognosis. 15,17,18 There is currently no established, evidence-based standard for timing of imaging after surgery. Delayed imaging can also cause diagnostic dilemmas, because factors such as postischemic encephalomalacia, gliosis, and radiation-induced change can pose challenges to

reliably estimating the EoR. ^{18,36} A more accurate EoR on early postoperative imaging within 72 hours may prompt earlier adjuvant treatment or repeat surgery. ³⁷

DWI helps to distinguish between surgical trauma, which markedly restricts diffusion, and residual tumor, which exhibits only mild restriction, if any (with ADC values typically at least 800×10^{-6} mm²/s).²² Thus, in the setting of WHO grade 2 and 3 diffuse gliomas, routine performance of DWI in early postoperative imaging helps reduce the subjectivity in the estimation of the EoR. Despite clear benefits, there is little published evidence to robustly support its use. The RANO working group recommend routine use of DWI in the assessment of enhancing tumors, but they do not explicitly mention its use when discussing WHO grade 2 and 3 diffuse gliomas. 15,16 Evidence-based recommendations from a recent expert consensus published by Karschnia et al¹³ do not allude to its use at all, and only comment on the interpretation of the volume of T2 FLAIR abnormality in the assessment of surgical debulking. A recently published study by Scherer et al²⁰ containing 43 patients hypothesized that DWI helps facilitate more accurate assessment of residual tumor within 72 hours of surgery. The authors retrospectively applied probabilistic segmentation of ADC maps in addition to assessment of T2 FLAIR hyperintense abnormality in a small patient cohort and found that this addition increased the precision in the estimated EoR. Our study aimed to address the relative paucity in the literature describing the applicability of DWI in early postoperative MRI and to add to the evidence base to support its use in this setting.

Our study reinforces the findings of Scherer et al²⁰ in a larger cohort of 222 patients. We found an apparent overestimation of residual tumor burden in the absence of DWI, with 86% of cases showing findings in keeping with residual tumor compared with 70% with the addition of DWI. Use of DWI changed the estimated EoR in almost 30% of cases and upgraded the extent of debulking to complete or supramaximal in 17% of the patients included in this study. In Fig 5, diffusion restriction at the margins of the resection cavity of a parasagittal right frontal mass upgraded the extent of resection from near-complete to

supramaximal. Figure 6 demonstrates restriction at the anterior and medial margins of a large mass in the left frontal lobe, which increased the estimated EoR from subtotal to complete resection. The overall probability of a complete surgical resection increased by 15% when DWI sequences were included. This tendency for DWI to help avoid overestimating residual tumor burden appears to be valid when delayed postoperative imaging is considered. Follow-up imaging was available for 98% of the patients included in the study, and in those cases in which DWI increased the estimated EoR, only 8% were found to have an increased volume in

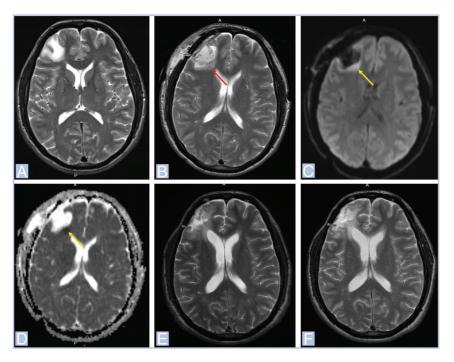


FIG 4. Right frontal lobe mass in a 42-year-old man on axial T2 (A). T2 hyperintensity at the posterior margin of the surgical resection cavity (*red arrow*, B) demonstrates corresponding diffusion restriction (*yellow arrows*, C and D). The estimated EoR was upgraded from subtotal to complete resection following the addition of DWI. Increased volume of signal abnormality around the resection cavity on repeat MR at 3 months postoperatively (E) was in keeping with radiation therapy—related change. Findings were stable on repeat imaging 6 months following this scan (F). Final integrated histopathologic diagnosis was anaplastic astrocytoma, *IDH*-mutant, *ATRX* wild-type, WHO grade 3 (4th edition of the WHO classification of CNS tumors, 2016).

T2 FLAIR signal abnormality attributed to disease progression. The influence of DWI sequences was uniform across several different factors that were hypothesized to possibly influence the estimated EoR in any given case, indicating that its addition to other sequences in early postoperative MRI consistently increases the estimated EoR. The benefit of DWI was lower in the setting of enhancing tumors (Online Supplemental Data). In many of these cases, the aim of surgical resection was to preferentially target the enhancing component of the tumor as opposed to the non-enhancing T2/FLAIR signal abnormality, which most likely explains these findings. The utility of DWI was not limited to its impact in changing the estimated EoR. In cases with no change in the estimation of resection extent, both reviewing neuroradiologists reported that the availability of DWI sequences increased their confidence in differentiating between postsurgical changes and residual disease. An example of this report is provided in Fig 1, which demonstrates diffusion restriction at the posterior aspect of the resection cavity of a parasagittal, right frontal mass, reinforcing

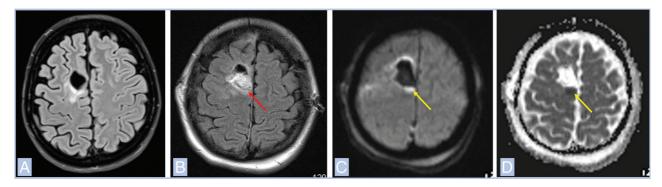


FIG 5. Recurrent parasagittal right frontal lobe lesion in a 21-year-old man on axial FLAIR (A). The initial EoR was >90% without DWI, with a thin rind of FLAIR signal abnormality anteriorly and a nodular focus posteriorly (red arrow) on postoperative FLAIR (β). Corresponding high signal on DWI and associated low ADC values (yellow arrows) at these sites (C and D) confirm that changes are in keeping with devitalized tissue. The subsequent estimate of EoR was upgraded to supramaximal. The final integrated histopathologic diagnosis was oligodendroglioma, IDH-mutant, 1p/19q co-deletion, WHO grade 2 (4th edition of the WHO classification of CNS tumors, 2016).

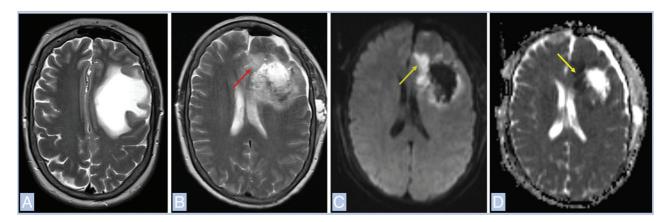


FIG 6. A large left frontal mass in a 50-year-old woman demonstrated on axial T2 (A). After debulking, the estimated EoR on postoperative imaging without DWI was 40%–90%, with an area of signal abnormality anteromedial to the surgical resection cavity (*red arrow*, *B*). Corresponding diffusion restriction at this site (*yellow arrows*, *C* and *D*) confirmed that changes were secondary to surgical trauma. The EoR was subsequently upgraded to complete excision. The final integrated histopathologic diagnosis was oligodendroglioma, *IDH*-mutant, 1p/19q co-deletion, WHO grade 2 (4th edition of the WHO classification of CNS tumors, 2016).

the opinion of reviewers that FLAIR hyperintense abnormality at this site was in keeping with postoperative ischemia.

Limitations of this study include its retrospective nature and single-center design. However, our institution is a national neurosurgical center with a large catchment area. Other inherent biases are also acknowledged, such as the inclusion of external MRI scanners, which may lack uniformity in imaging protocols. Both primary and recurrent tumor resections were included in the analysis, possibly contributing to the variability in the collected data. There was also inhomogeneity regarding the timing of obtaining the first follow-up MRI. The end point of statistical analysis in this study was also limited to the first delayed follow-up MRI for each patient. Thus, long-term survival analysis could not be performed in the validation of DWI as an adjunct to other MRI sequences.

The results of this study show that DWI, in addition to T2 and FLAIR sequences, serves as a useful and reliable adjunct in assessing the extent of resection of WHO grade 2 and 3 astrocytomas and oligodendrogliomas by helping to address the tendency of early postoperative MRI to overestimate residual tumor burden in this setting. As management for these tumors continues to develop and evolve, the optimal timing of adjuvant radiation therapy remains unclear. In indicated cases, early postoperative radiation therapy has been shown to increase the time to progression compared with delayed treatment.²³ Given that the findings on postoperative imaging may influence treatment decisions, earlier accurate estimates of residual tumor may become an important factor in future treatment paradigms. Therefore, incorporating the interpretation of DWI into the analysis paradigm for determining the EoR should be standard practice in all postoperative patients with WHO grade 2 and 3 adult-type diffuse gliomas.

CONCLUSIONS

We hypothesized that DWI may help facilitate more reliable estimates of the EoR on early postoperative MRI following surgical debulking of WHO grade 2 and 3 adult-type diffuse gliomas, and the results of this study demonstrate that its addition to T2- and FLAIR-weighted sequences is associated with a significant change

in the estimates of the EoR in these cases. DWI assists in differentiating residual tumor from postoperative ischemia/infarction, increasing the accuracy in the assessment of the extent of surgical debulking. Findings from early postoperative MRI can also be used to aid in differentiating disease progression from scarring, encephalomalacia, and radiation-induced changes on subsequent follow-up imaging. The increased EoR of WHO grade 2 and 3 astrocytomas and oligodendrogliomas is associated with increased progression-free and overall survival. Postoperative image findings after surgical debulking may influence future treatment and its timing for patients. Thus, an accurate estimation of the EoR in postoperative imaging is important, and our study shows that DWI increases the accuracy of EoR estimates.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

REFERENCES

- Ostrom QT, Price M, Neff C, et al. CBTRUS Statistical Report: primary brain and other central nervous system tumors diagnosed in the United States in 2016–2020. Neuro Oncol 2023;25:1–99 Medline
- Bauchet L. Epidemiology of Low-Grade Gliomas. In: Duffau H, ed. Diffuse Low-Grade Gliomas in Adults: Berlin, Heidelberg: Springer-Verlag; 2017:13–53
- Munkvold BR, Solheim O, Bartek J, et al. Variations in the management of diffuse low-grade gliomas: a Scandinavian multicenter study. Neurooncol Pract 2021;8:706–17 CrossRef Medline
- Duffau H, Taillandier L. New concepts in the management of diffuse low-grade glioma: proposal of a multistage and individualised therapeutic approach. Neuro Oncol 2015;17:332–42 CrossRef Medline
- Wessels PH, Weber WE, Raven G, et al. Supratentorial grade II astrocytoma: biological features and clinical course. Lancet Neurol 2003;2:395–403 CrossRef
- Komori T. Update of the 2021 WHO Classification of Tumors of the Central Nervous System: adult diffuse gliomas. Brain Tumor Pathol 2023;40:1–3 CrossRef Medline
- Brar K, Hachem LD, Badhiwala JH, et al. Management of diffuse low-grade glioma: the renaissance of robust evidence. Front Oncol 2020;10:575658 CrossRef Medline
- Weller M, van den Bent M, Tonn JC, et al. European Association for Neuro-Oncology (EANO) guideline on the diagnosis and treatment

- of adult astrocytic and oligodendroglial gliomas. Lancet Oncol 2017;18:315–29 CrossRef Medline
- Scherer M, Ahmeti H, Roder C, et al. Surgery for diffuse WHO grade II gliomas: volumetric analysis of a multicenter retrospective cohort from the German study group for intraoperative magnetic resonance imaging. Neurosurgery 2019;86:E64-74 CrossRef Medline
- Molinaro AM, Hervey-Jumper S, Morshed RA, et al. Association of maximal extent of resection of contrast-enhanced and noncontrast-enhanced tumor with survival within molecular subgroups of patients with newly diagnosed glioblastoma. JAMA Oncol 2020; 6:495-503 CrossRef Medline
- Hervey-Jumper SL, Zhang Y, Philips JJ, et al. Interactive effects of molecular, therapeutic, and patient factors on outcome of diffuse low-grade glioma. J Clin Oncol 2023;41:2029–42 CrossRef Medline
- Wijnenga MM, French PJ, Dubbink HJ, et al. The impact of surgery in molecularly defined low-grade glioma: an integraded clinical, radiological, and molecular analysis. Neuro Oncol 2018;20:103–12 CrossRef Medline
- 13. Karschnia P, Vogelbaum MA, van den Bent M, et al. Evidence-based recommendations on categories for extent of resection in diffuse glioma. *Eur J Cancer* 2021;149:23–33 CrossRef Medline
- Ruiz-Garcia H, Middlebrooks EH, Trifiletti DM, et al. The extent of resection in gliomas-evidence-based recommendations on methodological aspects of research design. World Neurosurg 2022;161: 382–95.e3 CrossRef Medline
- 15. Vogelbaum MA, Jost S, Aghi MK, et al. Application of novel response/progression measures for surgically delivered therapies for gliomas: Response Assessment in Neuro-Oncology (RANO) Working Group. Neurosurgy 2011;70:234–43 CrossRef Medline
- Wen PY, van den Bent M, Youssef G, et al. RANO 2.0: update to the Response Assessment in Neuro-Oncology criteria for high- and low-grade gliomas in adults. J Clin Oncol 2023;41:5187–99 CrossRef Medline
- 17. Belhawi SM, Hoefnagels FW, Baaijen JC, et al. Early postoperative MRI overestimates residual tumour after resection of gliomas with no or minimal enhancement. Eur Radiol 2011;21:1526–34 CrossRef Medline
- 18. Bette S, Kaesmacher J, Huber T, et al. Value of early postoperative FLAIR volume dynamic in glioma with no or minimal enhancement. World Neurosurg 2016;91:548–59.e1 CrossRef Medline
- Coburger J, Merkel A, Scherer M, et al. Low-grade glioma surgery in intraoperative magnetic resonance imaging: results of a multicenter retrospective assessment of the German study group for intraoperative magnetic resonance imaging. Neurosurgy 2016;78:775–86 CrossRef Medline
- Scherer M, Jungk C, Götz M, et al. Early postoperative delineation of residual tumor after low-grade glioma resection by probabilistic quantification of diffusion-weighted imaging. J Neurosurgy 2019;130:2016–24 CrossRef Medline
- Smith JS, Chang EF, Lamborn KR, et al. Role of extent of resection in the long-term outcome of low-grade hemispheric gliomas. J Clin Oncol 2008:26:1338–45 CrossRef Medline

- Hilario A, Ramos A, Perez-Nuñez A, et al. The added value of apparent diffusion coefficient to cerebral blood volume in the preoperative grading of diffuse gliomas. AJNR Am J Neuroradiol 2012;33: 701–07 CrossRef Medline
- Dhawan S, Patil CG, Chen C, et al. Early versus delayed postoperative radiotherapy for treatment of low-grade gliomas. Cochrane Database Syst Rev 2020;20:CD009229 2 CrossRef Medline
- 24. von Elm E, Altman DG, Egger M, et al; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008;61:344–49 CrossRef Medline
- Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 2016;131:803–20 CrossRef Medline
- Louis DN, Perry A, Wesseling P, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol 2021;23:1231–51 CrossRef Medline
- Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurgy 1986;65:476–83 CrossRef Medline
- Purushotham A, Campbell BC, Straka M, et al. Apparent diffusion coefficient threshold for delineation of ischemic core. Int J Stroke 2013;10:348–53 CrossRef Medline
- Warach S, Gaa J, Siewert B, et al. Acute human stroke studied by whole brain echo planar diffusion-weighted magnetic resonance imaging. Ann Neurol 1995;37:231–41 CrossRef Medline
- 30. The R CoreTeam. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing; 2022
- Norton EC, Dowd BE, Maciejewski ML. Marginal effects: quantifying the effect of changes in risk factors in logistic regression models. JAMA 2019;321:1304–05 CrossRef Medline
- Shaw EG, Berkey B, Coons SW, et al. Recurrence following neurosurgeon-determined gross-total resection of adult supratentorial low-grade glioma: results of a prospective clinical trial. J Neurosurg 2008;109:835–41 CrossRef Medline
- 33. Ius T, Isola M, Budai R, et al. Low-grade glioma surgery in eloquent areas: volumetric analysis of extent of resection and its impact on overall survival: a single-institution experience in 190 patients. *J Neurosurg* 2012;117:1039–52 CrossRef Medline
- 34. Jakola AS, Myrmel KS, Kloster R, et al. Comparison of a strategy favoring early surgical resection vs a strategy favoring watchful waiting in low-grade gliomas. *JAMA* 2012;308:1881–88 CrossRef Medline
- 35. Elsheikh M, Bridgman E, Lavrador JP, et al. Association of extent of resection and functional outcomes in diffuse low-grade glioma: systematic review and meta-analysis. *J Neurooncol* 2022;160:717–24 CrossRef Medline
- Smith JS, Cha S, Mayo MC, et al. Serial diffusion-weighted magnetic resonance imaging in cases of glioma: distinguishing tumor recurrence from postresection injury. J Neurosurg 2005;103:428–38 CrossRef Medline
- 37. Chammas M, Saadeh F, Maaliki M, et al. **Therapeutic interventions** in adult low-grade gliomas. *J Clin Neurol* 2019;15:1–8 CrossRef Medline