Amar S. Shah, MD, MPHS[‡*]
Alexander T. Yahanda, MS[‡*]
Peter T. Sylvester, MD[‡]
John Evans, RN[‡]
Gavin P. Dunn, MD, PhD[‡]
Randy L. Jensen, MD, PhD[§]
John Honeycutt, MD[¶]
Daniel P. Cahill, MD, PhD[‖]
Garnette R. Sutherland, MD[#]
Mark Oswood, MD, PhD[**‡‡]
Mitesh Shah, MD[§§]
Steven R. Abram, MD[¶¶]
Keith M. Rich, MD[‡]
Joshua L. Dowling, MD[‡]
Eric C. Leuthardt, MD, PhD[‡]
Ralph G. Dacey, MD[‡]
Albert H. Kim, MD, PhD[‡]
Gregory J. Zipfel, MD[‡]
David D. Limbrick, Jr, MD, PhD[‡]
Matthew D. Smyth, MD[‡]
Jeffrey Leonard, MD[‖‖]
Michael R. Chicoine, MD[‡]

[‡]Washington University School of Medicine, St. Louis, Missouri; [§]Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah; [¶]Cook Children's Hospital, Fort Worth, Texas; [‖]Massachusetts General Hospital, Boston, Massachusetts; [#]University of Calgary, Calgary, Canada; [**]University of Minnesota, Minneapolis, Minnesota; [‡‡]Allina Health, Minneapolis, Minnesota; [§§]Goodman Campbell and Indiana University, Indianapolis, Indiana; [¶¶]St. Thomas Hospital, Nashville, Tennessee; [‖‖]Department of Neurosurgery, Nationwide Children's Hospital, Columbus, Ohio

*Amar S. Shah and Alexander T. Yahanda contributed equally to this work.

Correspondence:
Michael R. Chicoine, MD,
Department of Neurosurgery,
Washington University School of Medicine,
660 S Euclid Ave,
St. Louis, MO 63110, USA.
Email: chicoinem@wudosis.wustl.edu

Received, May 31, 2019.
Accepted, May 24, 2020.

Using Histopathology to Assess the Reliability of Intraoperative Magnetic Resonance Imaging in Guiding Additional Brain Tumor Resection: A Multicenter Study

BACKGROUND: Intraoperative magnetic resonance imaging (iMRI) is a powerful tool for guiding brain tumor resections, provided that it accurately discerns residual tumor.

OBJECTIVE: To use histopathology to assess how reliably iMRI may discern additional tumor for a variety of tumor types, independent of the indications for iMRI.

METHODS: A multicenter database was used to calculate the odds of additional resection during the same surgical session for grade I to IV gliomas and pituitary adenomas. The reliability of iMRI for identifying residual tumor was assessed using histopathology of tissue resected after iMRI.

RESULTS: Gliomas (904/1517 cases, 59.6%) were more likely than pituitary adenomas (176/515, 34.2%) to receive additional resection after iMRI ($P < .001$), but these tumors were equally likely to have additional tissue sent for histopathology (398/904, 44.4% vs 66/176, 37.5%; $P = .11$). Tissue samples were available for resections after iMRI for 464 cases, with 415 (89.4%) positive for tumor. Additional resections after iMRI for gliomas (361/398, 90.7%) were more likely to yield additional tumor compared to pituitary adenomas (54/66, 81.8%) ($P = .03$). There were no significant differences in resection after iMRI yielding histopathologically positive tumor between grade I (58/65 cases, 89.2%; referent), grade II (82/92, 89.1%) ($P = .98$), grade III (72/81, 88.9%) ($P = .95$), or grade IV gliomas (149/160, 93.1%) ($P = .33$). Additional resection for previously resected tumors (122/135 cases, 90.4%) was equally likely to yield histopathologically confirmed tumor compared to newly-diagnosed tumors (293/329, 89.0%) ($P = .83$).

CONCLUSION: Histopathological analysis of tissue resected after use of iMRI for grade I to IV gliomas and pituitary adenomas demonstrates that iMRI is highly reliable for identifying residual tumor.

KEY WORDS: iMRI, Glioma, Pituitary, Resection, Histopathology, Intraoperative MRI, Pituitary adenoma, Tumor, Additional resection

Neurosurgery 0:1–11, 2020 DOI:10.1093/neuros/nyaa338 www.neurosurgery-online.com

Intraoperative magnetic resonance imaging (iMRI) has been shown to improve maximal safe resection of a variety of brain tumor types in adults and children, including low-grade gliomas (LGG), high-grade gliomas (HGG), pituitary adenomas, and other histopathologies.[1-19] Previously published reports indicate that up to 70% of patients may undergo additional tumor resection under the same anesthesia session after use of iMRI,[20]

ABBREVIATIONS: CI, confidence interval; **EOR,** extent of resection; **GBM,** glioblastoma; **GTR,** gross-total resections; **HGG,** high-grade gliomas; **IDH,** isocitrate dehydrogenase; **I-MiND,** IMRIS Multicenter iMRI Neurosurgery Database; **iMRI,** intraoperative magnetic resonance imaging; **LGG,** low-grade gliomas; **NOS,** not otherwise specified; **OR,** odd ratio; **OS,** overall survival; **PFS,** progression-free survival; **PPV,** positive predictive value; **T,** Tesla; **WHO,** World Health Organization

Neurosurgery Speaks! Audio abstracts available for this article at www.neurosurgery-online.com.
Supplemental digital content is available for this article at www.neurosurgery-online.com.

which can potentially improve extent of resection (EOR), overall survival (OS), and progression-free survival (PFS). Few studies have correlated iMRI findings with the histopathological analysis of specimens acquired after iMRI,[21-26] and the limited data that are available from small series largely applies to glioblastoma (GBM) (Table 1). Even for GBM, the sensitivity of iMRI in accurately identifying tumor is not consistently characterized. For instance, Hesselmann and colleagues[25] showed that histopathology of specimens collected from 50 GBM resections after the use of iMRI identified tumor in 43 cases (86%), whereas Coburger et al[24] showed that the sensitivity of iMRI in identifying residual tumor as confirmed by histopathology for 34 GBM resections was 41%.

The reliability of iMRI in identifying "true" residual tumor remains incompletely understood. Certain studies place the sensitivity of iMRI for GBM between 50% and 67%.[22,23] For LGG surgery, a study of 13 cases with 30 biopsy samples found that iMRI had a sensitivity of 83% (identified residual tumor in areas in which biopsies were positive for tumor) and specificity of 67% (did not identify tumor in areas in which biopsies were negative for tumor) for identifying residual tumor as confirmed by histopathology.[21] Defining the reliability of iMRI for the detection of residual tumor is of significant importance, as the process by which surgeons assess residual tumor and the need for additional resection after iMRI remains ill defined.[20]

The present study analyzed data from a large multicenter cohort of patients who underwent surgical resection of brain tumors, focusing on the most common types of brain tumors for which iMRI was used (grade I to IV gliomas and pituitary adenomas). The aim of this study was to discern the reliability with which iMRI may identify residual tumor for these tumor types, independent of the indications for use of iMRI or the intended EOR. It also assessed the positive predictive value (PPV) of iMRI.

METHODS

I-MiND Database and Variables

The IMRIS Multicenter iMRI Neurosurgery Database (I-MiND) is a REDCap[27]-mixed retrospective/prospective registry containing over 7000 patients who underwent brain surgery for tumors or other conditions with or without iMRI. This voluntary database includes 9 North American neurosurgical institutions. Data entry into this registry is performed by clinical research coordinators at each site and is periodically audited. Patients were added to the database on the sole condition of having surgery for a brain tumor or other conditions and were not added based on any particular outcome, pathology, or imaging criteria. The database was queried to identify patients who had additional resections performed during the same case after completion of iMRI. Institutional review board approval was received at all participating sites. No patient consent was necessary, as all data were retrospectively analyzed and deidentified. For the purposes of this study, because outcomes, EOR, goals of surgery, or the impact of iMRI on survival were not assessed, and because the only inclusion criteria was whether the patient had undergone surgery for a brain tumor, selection bias in the data should have been minimal. Surgeries were conducted between 2007 and 2019.

Data collected included tumor histopathology, incidence, location, number of iMRI scans performed, number of times additional resection was performed after iMRI, reasons that further resections were not pursued, and whether the additional tissue resected after the iMRI was collected for histopathology evaluation. The most common groups of tumors for which iMRI was used were World Health Organization (WHO) grade I to IV gliomas, mixed neuronal-glial tumors (dysembryoplastic neuroepithelial tumor and ganglioglioma), and pituitary adenomas (Figure 1). Tumors were classified as best as possible according to WHO 2016 guidelines,[28] though this was not possible in all instances given the year in which the tumor was diagnosed and availability of retrospective genetic and histopathological data. Incidence was characterized as newly diagnosed or previously resected. For analyses, mixed neuronal-glial tumors were considered part of the glioma cohort.

iMRI and Additional Resection

Surgical resection, preoperative imaging, and postoperative histopathological workup were performed as was standard at each participating institution (ie, there was no central protocol for imaging or pathological workup of resected tissue). After initial resection, iMRI scans were performed using a movable 1.5 Tesla (T) or 3.0 T magnet (IMRIS, Minnetonka, Minnesota) depending on the institution at the surgeon's discretion. Additional resection was pursued if residual tumor was suggested by iMRI and the surgeon deemed further resection to be appropriate. The number of instances of iMRI use was recorded. Additional resection was labeled "yes" only if additional tissue was removed. If the surgeon returned to the operating field but did not remove additional tissue, the rationale for not pursuing additional resection was described as no evidence of residual disease, risk to brain structures, risk to vascular structures, inaccessible residual, or other. The reliability of iMRI was assessed by reviewing histopathological reports for confirmation of tumor in tissue samples from cases when the surgeon chose to send new specimens from additional resections performed after iMRI. Whether additionally resected tumor after iMRI was sent for independent pathology was at the surgeon's discretion and did not occur for all additional resections.

Statistical Analysis

Statistical analyses were performed by 2 authors in collaboration with colleagues from the Division of Biostatistics at the host institution. Analyses were performed using SAS edition 9.4 (SAS Institute, Cary, North Carolina). Two-sample *t*-tests were used to compare continuous variables. Logistic regression and frequency table analyses were performed to calculate odds of iMRI use, additional resection, and positive histopathology based on tumor type and tumor incidence. Maximum likelihood estimates were used to assess differences between groups. A P-value $< .05$ was considered statistically significant.

RESULTS

A total of 2032 patients with gliomas or pituitary adenomas whose cases utilized iMRI were identified. Of these, additional resection after iMRI was performed in 1080 cases (53.1%) (Figure 1). A total of 111 patients underwent a second iMRI, 15 a third, and 5 a fourth, with 38, 8, and 2 additional resections, respectively, performed after each iMRI study was completed. HGG were the most common pathology (Table 2). Isocitrate

TABLE 1. Summary of Previous Studies Reporting Histopathological Confirmation After iMRI

Author and year (ref)	Other adjuncts	Methods	MRI strength	# Cases	Disease pathology	Sensitivity	Specificity	PPV	NPV
Coburger 2014[24]	5-ALA	Initial resection under white light followed by 5-ALA and iMRI (T1 with Gd-GTPA). Areas corresponding to fluorescence and contrast enhancement after initial resection marked; biopsies taken from these sites to assess for histopathological evidence of residual tumor.	1.5 T	42	GBM (n = 34), metastases (n = 8)	41% (GBM), 75% (mets)	70% (GBM), 80% (mets)	67% (GBM), 86% (mets)	70% (GBM), 80% (mets)
Coburger 2015[21, c]	cioUS, lioUS	Resection until presumed GTR. cioUS, lioUS, iMRI (T2 and FLAIR sequences). Navigated biopsies taken from all marked areas and "control" areas.	1.5 T	13 cases (30 samples)	LGG (6 astrocytoma [14 bx], oligodendroglioma [6], 4 oligoastrocytoma [10])	83%	67%	91%	50%
Hauser 2016[26]	5-ALA	Pre-op iMRI (T1w + C). Resection performed until all 5-ALA fluorescent tissue removed. iMRI with contrast performed in areas with enhancement marked for navigated resection.	0.15 T	10 cases (28 samples)	GBM	NR[b]	NR[b]	64%	NR[b]
Coburger 2017[22]	5-ALA, cioUS	Initial resection under white light followed by iMRI (T1 with and without Gd-GTPA, T2, and FLAIR), 5-ALA, and intraoperative ultrasound. Biopsies taken from areas corresponding to potential residual tumor seen by each imaging modality.	1.5 T	33	GBM	50%	100%	n/a	n/a
Heßelmann 2017[25]	None	Patients received iMRI scan (T1 with and without Gd-GTPA, T2, FLAIR, DWI) after initial resection. Additional resection was performed for residual contrast-enhancing tumor seen on iMRI.	1.5 T	68	GBM	95%	69.50%	86%	88%
Pala 2018[23]	5-ALA, met-PET	Pre-op met-PET. Resection until presumed GTR; 5-ALA (12 cases; 42 samples) and iMRI (T1w + C [Gd-DTPA], T2w, FLAIR, PWI, DWI; 18 cases, 59 samples) performed. Suspicious lesions marked for navigated biopsies as per previous study.[24]	1.5 T (Gd-DTPA)	18 cases (59 samples)	GBM	50%	n/a[a]	NR[a]	NR[a]
[a]Pala 2018 (second iMRI arm)[23]	5-ALA, met-PET	(Same as above)	1.5 T (PWI)	18 cases (59 samples)	GBM	67%	n/a[a]	NR[a]	NR[a]

Sn = sensitivity, Sp = specificity, PPV = positive predictive value, NPV = negative predictive value. 5-ALA = 5-aminolevulinic acid, cioUS = conventional intraoperative ultrasound, DWI = diffusion-weighted images, Gd-DTPA = gadolinium-DTPA, iMRI = intraoperative MRI, lioUS = linear intraoperative ultrasound, met-PET = 11C-methionine positron emission tomography, FLAIR = fluid-attenuated inversion recovery, PWI = perfusion-weighted images, GBM = glioblastoma. LGG = low-grade glioma. NR = not reported.

[a]In Pala et al,[23] only 1 sample of 59 taken was negative so sensitivity could not be calculated. Frequencies were not reported so PPV and NPV were unable to be calculated.

[b]In Hauser et al,[26] no biopsies were taken from control regions. Thus, sensitivity, specificity, and NPV could not be determined.

[c]In the study by Coburger et al, 2015[21], values for 5-ALA were as follows: n = 117. Sn = .81, Sp = .43, PPV = .96, and NPV = .125.

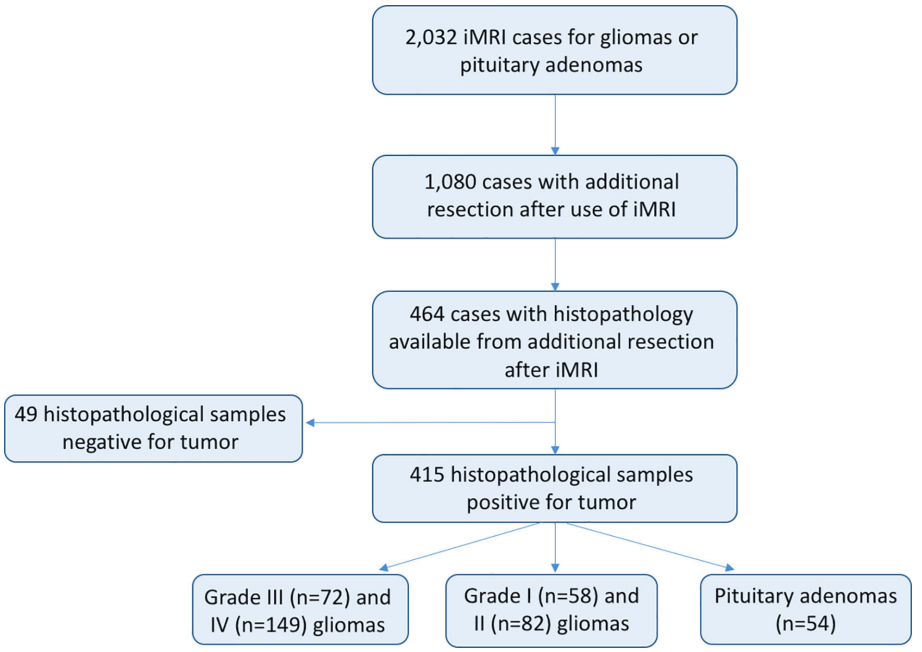

FIGURE 1. *Flowchart showing the number of cases at various stages of data selection during the analyses.*

TABLE 2. Frequency of iMRI-Guided Resection, Tissue Specimen Availability, Pathology Results, and Reported Reasons for No iMRI-Guided Resection For All Diagnoses

		Glioma				
	All cases	WHO I	WHO II	WHO III	WHO IV	Pituitary adenoma
All iMRI cases, # (%)	2032 (100)	388 (19.09)	307 (15.1)	268 (13.18)	554 (27.26)	515 (25.34)
iMRI-guided resection	1080 (53.14)	192 (49.48)	201 (65.47)	169 (63.05)	342 (61.73)	176 (34.17)
Tissue not obtained post-iMRI	616 (57.03)	127 (66.14)	109 (54.22)	88 (52.07)	182 (53.21)	110 (62.5)
Tissue obtained post-iMRI	464 (42.96)	65 (33.85)	92 (45.77)	81 (47.92)	160 (46.78)	66 (37.5)
Pathology positive	415 (89.43)	58 (89.23)	82 (89.13)	72 (88.88)	149 (93.12)	54 (81.81)
Pathology negative	49 (10.56)	7 (10.76)	10 (10.86)	9 (11.11)	11 (6.87)	12 (18.18)
No iMRI-guided resection	952 (46.85)	196 (50.51)	106 (34.52)	99 (36.94)	212 (38.26)	339 (65.82)
No residual	707 (74.26)	174 (88.77)	76 (71.69)	69 (69.69)	148 (69.81)	240 (70.79)
Residual inaccessible	245 (25.73)	22 (11.22)	30 (28.3)	30 (30.3)	64 (30.18)	99 (29.2)

WHO = World Health Organization.

All iMRI case percentages (top row) are based on total iMRI cases. Percentages for all other table rows based on the count within each category. Glioma cases were more likely to receive iMRI-guided resection, but equally likely as pituitary adenomas to have post-iMRI-resected tissue sent for histopathological analysis. Gliomas were more likely to yield pathologically confirmed residual tumor after use of iMRI.

Exclusions: Cases were excluded if WHO grade unavailable for glioma cases (26), iMRI-guided resection was not performed due to poor image quality (4), reason for performance of iMRI was not available (51), and iMRI was obtained for quality assurance purposes only (43).

dehydrogenase (IDH) status information was found for 683 patients (271 mutated [39.7%] and 412 wild-type [60.3%]).

Use of iMRI and Additional Resection

Among the 2032 tumor patients with EOR data, 469 received gross-total resections (GTR), and those GTR patients more often underwent additional resection after iMRI (272/469 cases, 58%) compared to patients who received subtotal/near total resections (611/1191, 51.3%) ($P = .01$; odd ratio, OR 1.31 [1.06, 1.63]). However, when stratifying by tumor type, this relationship between iMRI and GTR only remained significant for pituitary tumors (82 GTR of 167 cases, 49.1%) ($P < .001$; OR 2.68 [1.79, 4.0]). Gliomas (904 additional resections of 1517 cases, 59.6%)

TABLE 3. Univariate Logistic Regression Analyses Predicting the Likelihood of iMRI-Guided Resection (Left) and Post-iMRI Sample Histopathological Positivity (Right) for Glioma and Pituitary Adenoma Cases

	iMRI-guided resection				Post-iMRI sample pathology positive			
Covariates impacting resection	n	# (%)	Univariate OR (95% CI)	Multivariate OR (95% CI)	n	# (%)	Univariate OR (95% CI)	Multivariate OR (95% CI)
Diagnosis	2032	1080 (53.14)			464	415 (89.43)		
Pituitary adenoma	515	176 (34.17)	Ref	ref	66	54 (81.81)	ref	ref
Glioma	1517	904 (59.59)	2.84 (2.31-3.5)**	2.97 (2.36-3.74)**	398	361 (90.7)	2.17 (1.07-4.42)*	1.75 (0.76-4.02)
EOR	1660	883 (53.19)			397	355 (89.42)		
Near/subtotal	1191	611 (51.3)	Ref	ref	295	264 (89.49)	ref	ref
Gross total	469	272 (57.99)	1.31 (1.06-1.63)*	1.52 (1.21-1.9)**	102	91 (89.21)	1.03 (0.48-2.06)	1.09 (0.51-2.31)
Tumor incidence	2032	1080 (53.14)			464	415 (89.43)		
New diagnosis	1469	757 (51.53)	Ref	ref	329	293 (89.05)	ref	ref
Prior resection	562	323 (57.47)	1.27 (1.05-1.55)*	1.02 (0.81-1.27)	135	122 (90.37)	1.07 (0.56-2.06)	1.11 (0.53-2.32)

= Number of positive cases, *$P < .05$, **$P < .01$, 95% CI = 95% confidence interval, N = total number of cases, NA = not able to compute, OR (odds ratio), ref = reference. Odds ratios (OR) and 95% confidence intervals (CI) for covariates are listed.

were more likely than pituitary adenomas (176/515 cases, 34.2%) to receive additional resection after iMRI ($P < .001$). Gliomas were as likely as pituitary adenomas to have additional tissue sent for histopathology (398 samples sent of 904 cases, 44% vs 54/196, 37.5%) ($P = .11$) (Table 2). For gliomas, additional resection after iMRI was most common for grade II gliomas (201/307 cases, 65.5%). Grade II ($P < .001$; OR 1.94 [1.42, 2.63]), grade III (169/268 cases, 63.0%) ($P = .001$; OR 1.74 [1.27, 2.40]), and grade IV gliomas (342/554 cases, 61.7%) ($P < .001$; OR 1.65 [1.27, 2.14]) underwent additional resection more frequently compared to grade I gliomas (192/388 cases, 49.5%) (referent). When analyzing all tumor types together, of the 562 cases that underwent surgery for previously resected tumors, 57.5% (323/562) had additional resection after iMRI, compared to 51.5% (757/1469) for newly diagnosed tumors ($P = .02$; OR 1.27 [1.05, 1.55]) (Table 3).

Regarding specific glioma subtypes, as compared to astrocytomas (301/499 cases, 60.3%; referent), ependymomas (33/80, 41.2%) ($P = .008$; OR 0.52 [0.32, 0.84]) and other grade I/II gliomas (111/222, 50%) ($P = .03$; OR 0.71 [0.53, 0.97]) were less likely to receive iMRI-guided additional resection, whereas oligodendrogliomas (127/178, 71.3%) ($P = .03$; OR 1.46 [1.04, 2.06]) were more likely to receive additional resection (Table 4). GBMs (327/523, 62.5%) ($P = .46$; OR 1.09 [0.86-1.38]) were as likely to receive additional resection as astrocytomas. A full breakdown of iMRI-guided cases for all gliomas can be seen in Table 5. For pituitary adenomas, tumors exhibiting parasellar invasion (140/340, 41.2%) were more likely to receive additional resection after iMRI compared to those that did not (31/158, 19.6%) ($P < .001$; OR 2.87 [1.83, 4.49]). Pituitary adenomas were also more likely to receive additional resection after iMRI as size increased, particularly above 30 mm (48/104, 46.1%) ($P < .001$; OR 5.63 (2.33, 13.63]) (Table 6).

A multivariate analysis of all 2032 cases that involved an iMRI scan demonstrated that glioma diagnosis ($P < .001$) and GTR (<.001) were associated with having undergone additional resection after iMRI. For gliomas specifically, WHO grades II and III were more likely to receive additional resection after iMRI (compared to grade I; *P*-values < .001), but grade IV, tumor incidence, and EOR were not significant. For pituitary tumors, GTR ($P = .001$) and tumor size ≥10 mm ($P = .008$) were associated with having undergone iMRI. Tumor incidence, secretory status, and parasellar extension were not significantly associated with iMRI use. No variables were significantly associated with increased odds of tissue resected after iMRI being positive for tumor except functional pituitary adenoma status. The full list of variables analyzed may be seen in Tables 3-6.

Reliability of Additional Resection

Independent histopathological specimens acquired from resections performed after iMRI were available for 464 cases, of which 415 (89.4%) were positive for tumor. Gliomas (361/398, 90.7%) were more likely to have positive pathology after iMRI-guided additional resection compared to pituitary adenomas (54/66, 81.8%) ($P = .03$) (Table 3). GBM was the glioma diagnosis most likely to have positive histopathology after additional resection (149/160 cases, 93.1%) ($P = .03$; OR 2.33 [1.06, 5.11]) (Table 4). There were no significant differences in the likelihood of positive histopathology from specimens after iMRI among grade I (58/65 cases, 89.2%; referent), grade II (82/92, 89.1%) ($P = .98$; OR 0.99 [0.36, 2.75]), grade III (72/81, 88.9%) ($P = .95$; OR 0.97 [0.34, 2.75]), or grade IV gliomas (149/160, 93.1%) ($P = .33$; OR 1.64 [0.60, 4.42]) (Table 4). For pituitary

TABLE 4. Univariate and Multivariate Logistic Regression Analyses Predicting the Likelihood of iMRI-Guided Resection (Left) and Post-iMRI Sample Histopathological Positivity (Right) for Glioma Cases

	iMRI-guided resection				Post-iMRI sample pathology positive			
Covariates impacting glioma resection	**n**	**# (%)**	**Univariate OR (95% CI)**	**Multivariate OR (95% CI)**	**n**	**# (%)**	**Univariate OR (95% CI)**	**Multivariate OR (95% CI)**
EOR	1210	726 (60.0)			340	307 (90.3)		
Near/subtotal	908	536 (59.0)	ref	ref	266	239 (89.84)	ref	ref
Gross total	302	190 (62.9)	1.2 (0.9-1.5)	0.9 (0.7-1.3)	74	68 (91.9)	1.3 (0.5-3.3)	1.2 (0.5-3.1)
Tumor incidence	1516	904 (59.6)			398	361 (90.7)		
New diagnosis	1052	622 (59.1)	ref	ref	274	247 (90.1)	ref	ref
Prior resection	464	282 (60.8)	1.1 (0.9-1.3)	0.9 (0.7-1.2)	124	114 (91.9)	1.1 (0.5-2.4)	1.2 (0.5-2.8)
WHO grade	1517	904 (59.6)			398	361 (90.7)		
Grade I	388	192 (49.5)	ref	ref	65	58 (89.2)	ref	ref
Grade II	307	201 (65.5)	1.9 (1.4-2.6)**	2.2 (1.5-3.3)**	92	82 (89.1)	1.0 (0.4-2.8)	1.5 (0.5-4.6)
Grade III	268	169 (63.0)	1.7 (1.3-2.4)**	2.8 (1.7-4.4)**	81	72 (88.9)	1.0 (0.3-2.8)	1.4 (0.5-4.0)
Grade IV	554	342 (61.7)	1.6 (1.3-2.1)**	1.3 (0.4-4.3)	160	149 (93.1)	1.6 (0.6-4.4)	2.1 (0.7-5.8)
IDH-1 status	683	432 (63.3)			207	193 (93.2)		
Mutated	271	190 (70.1)	ref	ref	89	84 (94.4)	ref	ref
Non-mutated	412	242 (58.7)	0.6 (0.4-0.8)**	–	118	109 (92.4)	1.4 (0.5-4.3)	–
Glioma subtype	1517	904 (59.6)			398	361 (90.7)		
Astrocytoma	366	211 (57.7)	ref	ref	80	68 (85.0)	ref	ref
Ependymoma	80	33 (41.3)	0.5 (0.3-0.8)**	0.3 (0.2-0.6)**	12	12 (100)	–	–
GBM	529	332 (62.8)	1.2 (0.9-1.6)	1.6 (0.5-5.2)	154	143 (92.9)	2.3 (1.0-5.5)	–
Oligodendroglioma	178	127 (71.3)	1.8 (1.2-2.7)*	1.4 (0.9-2.4)	71	65 (91.5)	1.9 (0.7-5.4)	–
Other high grade	90	51 (56.7)	0.9 (0.6-1.5)	0.6 (0.3-1.2)	24	22 (91.7)	1.9 (0.4-9.4)	–
Other low grade	274	150 (54.7)	0.9 (0.6-1.2)	1.0 (0.7-1.5)	57	51 (89.5)	1.5 (0.5-4.3)	–

= number of positive cases, $^{*}P < .05$, $^{**}P < .01$, 95% CI = 95% confidence interval, N = total number of cases, NA = not able to compute, OR (odds ratio), ref = reference. Odds ratios (OR) and 95% confidence intervals (CI) for covariates are listed. Astrocytoma involves grade I to III astrocytomas. Other HGG include glioma NOS (74), gliosarcoma (14), and pleomorphic xanthroastrocytoma (2). Other low-grade gliomas include angiocentric (3), DNET (59), ganglioglioma (82), glioma NOS (115), and pleomorphic xanthroastrocytoma (15). WHO grade II to IV gliomas were more likely to receive iMRI-guided resection than grade I gliomas. Compared to astrocytomas, oligodendrogliomas were more likely to receive iMRI-guided resection, and ependymomas, other low-grade gliomas, and other HGG were less likely.

adenomas, no factors were associated with increased odds of additionally resected tissue being positive for tumor, including size and parasellar extension (Table 6). All 66 pituitary cases with additional pathology were performed using an endoscopic endonasal approach.

Additional resection after iMRI for previously resected tumors (122/135 cases, 90.4%) was not more likely to yield histopathologically confirmed tumor compared to newly-diagnosed tumors (293/329, 89.0%) ($P = .83$; OR = 1.07 [0.56, 2.06]). Of 49 (10.6%) cases in which pathology from additional resections after iMRI did not show tumor on histopathological testing, 20 were grades III or IV, 17 were grades I or II, and 12 were pituitary adenomas. In total, 36 of 49 cases were newly diagnosed tumors (11 grades III and IV, 16 grades I and II, and 9 pituitary adenomas) and 13 (9 grades III and IV, 1 grade II, and 3 pituitary adenomas) had prior resection. No significant trends were noted for these 49 cases. Detailed imaging and pathology reports were available for 34/49 cases. In 28 of the 34 instances (82%), GTR was presumed before iMRI scans were performed. The iMRI findings were "accurate" in 4 cases (the iMRI scan was correctly interpreted as having no residual), "equivocal" in 10 cases (scan was interpreted as containing suspicious regions that may have represented either surgical changes or residual tumor), and "misleading" in 20 cases (scan was incorrectly interpreted as having areas that were very likely residual tumor) (Figure 2). Over half (19 of 34, 55.9%) of these cases revealed normal brain tissue, 9 showed reactive changes or radiation necrosis, 3 showed hematoma, and 2 showed scattered atypical cells. Six cases were recurrent lesions that had received prior radiation; pathology for these lesions revealed reactive changes or radiation necrosis. No common characteristics were found linking cases with "misleading" iMRI findings. Two case illustrations of instances when iMRI was misleading have been published as Supplemental Digital Content (**Text**, **Supplemental Digital Content 1** and **Figures**, **Supplemental Digital Content 2-5**).

TABLE 5. Detailed Breakdown of iMRI-Guided Resections by Glioma Histopathological Diagnosis and Grade

Glioma diagnosis	iMRI cases	iMRI-guided resection	Post-iMRI sample	Post-iMRI samples pathology positive (% of samples)	Post-iMRI samples pathology positive (% of cases)
WHO grade I					
Angiocentric	3	1 (33.3%)	1 (100%)	1 (100%)	1 (33.3%)
Astrocytoma, pilocytic	199	101 (50.7%)	31 (30.6%)	26 (74.2%)	26 (13%)
Astro, SEGA	12	4 (33.3%)	1 (25%)	0 (0%)	0 (0%)
DNET	59	36 (61%)	9 (25%)	9 (90%)	9 (15.2%)
Ganglioglioma	82	38 (46.3%)	12 (31.5%)	11 (91.6%)	11 (13.4%)
Glioma NOS	33	11 (33.3%)	8 (72.7%)	8 (100%)	8 (24.2%)
Subependymoma	4	1 (25%)	1 (100%)	1 (100%)	1 (25%)
WHO Grade II					
Astrocytoma, diffuse	61	42 (68.8%)	16 (38%)	14 (87.5%)	14 (22.9%)
IDH mutated	23	14 (60.9%)	6 (42.9%)	6 (100%)	6 (26.1%)
IDH wild-type	13	10 (76.9%)	4 (40%)	3 (75%)	3 (23.1%)
IDH data unavailable	25	18 (72%)	6 (33.3%)	5 (83.3%)	5 (20%)
Ependymoma	34	15 (44.1%)	5 (33.3%)	5 (100%)	5 (14.7%)
Glioma NOS	82	56 (68.2%)	26 (46.4%)	21 (80.7%)	21 (25.6%)
Oligodendroglioma	113	81 (71.6%)	46 (56.7%)	43 (93.4%)	43 (38%)
PXA	15	8 (53.3%)	1 (12.5%)	1 (100%)	1 (6.6%)
WHO Grade III					
Astrocytoma, anaplastic	94	64 (68%)	32 (50%)	28 (87.5%)	28 (29.7%)
IDH mutated	51	36 (70.6%)	17 (47.2%)	13 (76.5%)	13 (25.5%)
IDH wild-type	19	12 (63.2%)	9 (75%)	9 (100%)	9 (47.4%)
IDH data unavailable	24	16 (66.7%)	6 (37.5%)	6 (100%)	6 (25%)
Ependymoma, anaplastic	42	17 (40.4%)	6 (35.2%)	6 (100%)	6 (14.2%)
Glioma NOS, anaplastic	66	42 (63.6%)	19 (45.2%)	17 (89.4%)	17 (25.7%)
Oligodendroglioma, anaplastic	65	46 (70.7%)	25 (54.3%)	22 (88%)	22 (33.8%)
PXA, anaplastic	2	1 (50%)	0 (0%)	0 (0%)	0 (0%)
WHO Grade IV					
GBM	529	332 (62.8%)	154 (46.4%)	143 (92.9%)	143 (27%)
IDH mutated	50	32 (64%)	16 (50%)	16 (100%)	16 (32%)
IDH wild-type	284	169 (59.5%)	75 (44.4%)	69 (92%)	69 (24.3%)
IDH data unavailable	195	131 (67.2%)	63 (48.1%)	58 (92.1%)	58 (29.7%)
Glioma NOS	8	4 (50%)	3 (75%)	3 (100%)	3 (37.5%)
Gliosarcoma	14	4 (28.5%)	2 (50%)	2 (100%)	2 (14.2%)
Total	1517	904	398	361	361

IDH = isocitrate dehydrogenase, NET = desmoplastic neuroepithelial tumor, NOS = not otherwise specified, PXA = pleomorphic xanthroastrocytoma, SEGA = subependymal giant cell astrocytoma.

DISCUSSION

Key Results

Maximal safe resection of many types of benign and malignant brain tumors may lead to increased OS and PFS.[7,29-38] The use of iMRI has been shown to be a beneficial method by which surgeons may achieve more extensive EOR for a variety of tumor types,[4,7,8,11,30,39-41] but few studies analyze the histopathology of additional tissue that was removed after iMRI.[21-26] Unlike most prior investigations, the goal of this study was not to examine the impact of iMRI on EOR or survival or the impact of EOR on outcomes. Rather, this study analyzed a large multicenter database to better elucidate the reliability with which iMRI could enable additional tumor resection for common groups of tumors (gliomas grades I to IV and pituitary adenomas), irrespective of the surgeon's indication for the use of iMRI or the intended EOR. For 464 surgeries that had tissue available from additional resections performed after iMRI, tumor was confirmed by histopathology in 415 cases (89.4%). This current study is the largest of its kind to date to provide histopathological assessment of the additional tissue resected after iMRI to determine the reliability of this surgical adjunct in identifying residual tumor. It furthermore provides data on iMRI's reliability across a large cohort of surgeons who may be employing this imaging modality in heterogeneous ways.

Interpretation

The rate of additional tumor resection after iMRI has varied across previously published studies for different tumor

TABLE 6. Univariate Logistic Regression Analyses Predicting the Likelihood of iMRI-Guided Resection (Left) and Post-iMRI Sample Histopathological Positivity (Right) for Pituitary Adenoma Cases

Covariates impacting pituitary adenoma resection	iMRI-guided resection				Post-iMRI sample pathology positive			
	N	# (%)	Univariate OR (95% CI)	Multivariate OR (95% CI)	n	# (%)	Univariate OR (95% CI)	Multivariate OR (95% CI)
EOR	450	157 (34.88)			57	48 (84.21)		
Near/subtotal	283	75 (26.5)	Ref	ref	29	25 (86.2)	ref	ref
Gross total	167	82 (49.1)	2.68 (1.79-4)**	2.24 (1.38-3.65)**	28	23 (82.14)	0.74 (0.18-3.08)	0.81 (0.13-4.8)
Tumor incidence	515	176 (34.17)			66	54 (81.81)		
New diagnosis	417	135 (32.37)	Ref	ref	55	46 (83.63)	ref	ref
Prior resection	98	41 (41.83)	1.5 (0.96-2.36)	1.48 (0.8-2.74)	11	8 (72.72)	0.52 (0.17-2.36)	0.17 (0.01-2.52)
Secretory status	476	165 (34.66)			63	51 (80.95)		
Non-functional	299	113 (37.79)	ref	ref	40	35 (87.5)	ref	ref
Functional	177	52 (29.37)	0.69 (0.46-1.02)	0.61 (0.35-1.04)	23	16 (69.56)	0.33 (0.09-1.19)	0.08 (0-0.79)*
Tumor extension	498	171 (34.33)			65	53 (81.53)		
None	158	31 (19.62)	ref	ref	13	9 (69.23)	ref	ref
Parasellar	340	140 (41.17)	2.87 (1.83-4.49)**	1.65 (0.89-3.04)	52	44 (84.61)	2.4 (0.6-9.9)	2.14 (0.32-14.31)
Tumor size (ref: <10 mm)	430	152 (35.34)			59	47 (79.66)		
<10 mm	53	7 (13.2)	ref	ref	2	2 (100)	ref	ref
10-30 mm	273	97 (35.53)	3.62 (1.58-8.33)**	4.2 (1.44-12.23)**	39	29 (74.35)	ref	ref
>30 mm	104	48 (46.15)	5.63 (2.33-13.63)**	4.95 (1.54-15.86)**	18	16 (88.88)	2.58 (0.5-13.22)	2.49 (0.22-28.29

Gross-total resection, prior resection, parasellar extension, and macroadenoma status were associated with performance of additional resection after iMRI. Odds ratios (OR) and 95% confidence intervals (CI) for covariates are listed.

= number of positive cases, *$P < .05$, **$P < .01$, 95% CI = 95% confidence interval, N = total number of cases, NA = not able to compute, OR (odds ratio).

types.[7,21,22,26,42] In our study, additional resection after iMRI was pursued in 53.1% of all cases, and the frequency of additional resections after iMRI differed among grade I (49.5%), grade II (65.5%), grade III (63%), and grade IV (61.7%) gliomas and pituitary adenomas (34.2%). Some of these additional resection rates for individual tumor types are lower than what has been reported. For instance, Scherer et al,[20] in a study of 224 glioma resections using iMRI, found that additional resection was performed in 70% of cases. A study of pituitary adenomas demonstrated additional resection rates after iMRI of 47% and 13% in microscopic and endoscopic surgeries, respectively.[43] Sylvester et al[7] showed an additional resection rate after iMRI of 35.9% for 156 pituitary adenomas cases, and Serra et al[44] reported additional resection rate after iMRI in 53% of cases, regardless of intended EOR. One possible explanation for some of the variation in the current study compared to prior studies is that the current study characterized additional resection as a function of all patients who received iMRI, whereas other studies limit this proportion to those in which residual disease is noted.

The ability of iMRI to identify residual tumor and guide the surgeon to reliable additional resection after iMRI was 89% to 93% as confirmed by histopathology across grade I to IV gliomas and pituitary adenomas analyzed in our investigation. This value is higher than PPVs reported in the literature (Table 1).[21-26] However, our study found that no residual disease was noted on iMRI in 74.2% of instances in which additional resection was not pursued after iMRI. Although a high PPV may be expected for particularly invasive pathologies such as grade II to IV gliomas, this was consistent for grade I gliomas and pituitary adenomas as well. Our study did not identify unique characteristics of tumors for which additional tissue resected after iMRI failed to yield residual tumor on histopathological evaluation. Review of the histopathology from these cases with negative pathology showed that normal tissue was most commonly reported. Prior to completion of iMRI, a presumed GTR was achieved in 28/34 cases with negative pathology after iMRI, though the iMRI scan itself was misleading in 59% of negative histopathology cases and equivocal in another 29%. No unifying explanation could be identified in cases with negative pathology to explain why there was negative histopathology of this resected tissue after iMRI.

That some histopathology of tissue resected after iMRI did not reveal tumor could have been due to images misleading surgeons to believe that there was residual tumor when there was not. Alternatively, the iMRI study may, in fact, have identified residual tumor, but the surgeon may not have been able to accurately localize that tumor for further resection, or the specimen sent for histopathological assessment was not totally representative of the tissue that was removed (sampling error). Tissue shifts and other surgical phenomena may impact accuracy when trying to identify residual tumor. Integration of the images acquired from the iMRI study into a surgical navigation tool can improve the reliability of identifying residual tumor but may not completely resolve inaccuracies.

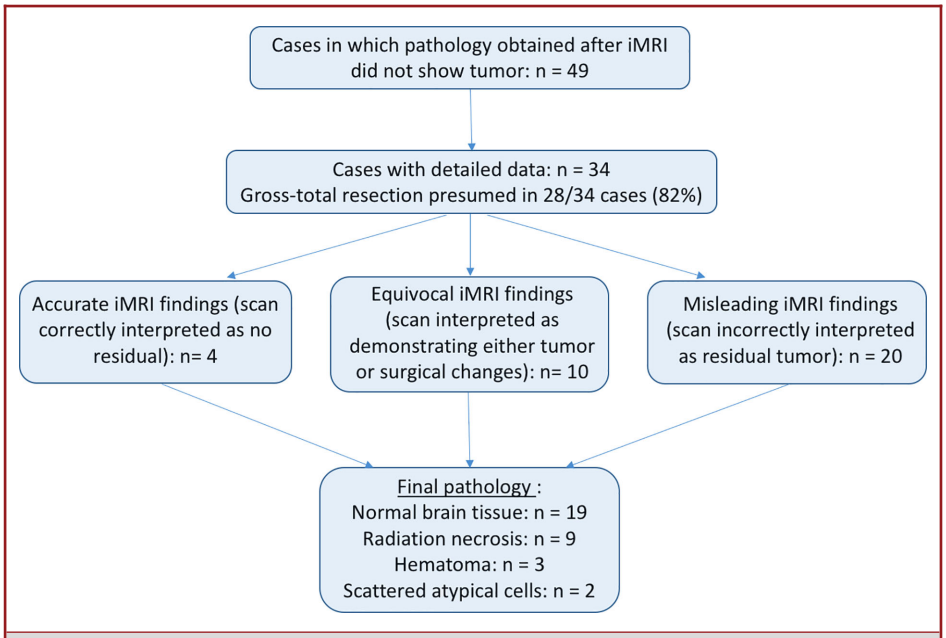

FIGURE 2. *Flowchart demonstrating characteristics of cases in which additional resection undertaken after iMRI did not demonstrate residual tumor.*

Generalizability

The fact that iMRI is so consistent at identifying additional tumor across different types of tumors is an important finding. This current study is the first to demonstrate this accuracy on such a broad scale, and the fact that we use a multicenter cohort makes these data more generalizable to tumor resection patients than for prior studies. Regardless of the likelihood of pursuing additional resection, this study demonstrates that iMRI may have a role as an important tool to help increase EOR. Of course, when considering a surgeon's decision to use iMRI, it could be hard to discern if additional tumor resected after iMRI was due to the surgeon's inability to identify residual tumor after an aggressive initial attempt at GTR or whether a surgeon was initially operating more conservatively because they knew that iMRI was going to be used later. That said, characterizing the aggressiveness or caution that surgeons may display during initial resection was outside of the scope of this study, which did not quantify the impact of iMRI on the ultimate EOR.

Limitations

This study has its limitations. The data were collected retrospectively, and only 43% of additional resection cases after iMRI had available histopathology. Given the time of diagnosis and the available genetic information, classification of tumors according to most current standards was not always possible, which may complicate strict comparisons between different tumors and grades and resulted in a subset of 189 tumors classified as "glioma not otherwise specified" (NOS). However, for all these NOS specimens, a WHO grade was assigned by a pathologist. Furthermore, though the database is periodically audited by research coordinators and researchers at each respective site, an audit of all the data and viewing of all images was not performed by a central core of reviewers. The EOR (eg, GTR) that was intended preoperatively by a surgeon was not available. It is also possible that different imaging benchmarks were used by surgeons to define the amount of tissue that would be resected (eg, some surgeons may have used the contrast-enhancing portions, whereas others may have used T2/FLAIR signal for malignant gliomas). There are potential biases in the study because tissue specimens from the additional resections performed after iMRI were sent for histopathological evaluation in only a portion of the cases, according to surgeons' preferences and habits, and without a clear-cut protocol (although, as mentioned in the Methods section, overall selection bias should be low). Residual tumor was determined by final, not intraoperative, pathology, so discrepancies could not be determined between the 2. Based on how the data were collected, only true positive rates and false positive rates could be assessed—sensitivity and specificity of iMRI could not be determined, nor could instances when iMRI was interpreted as GTR but there actually was residual tumor present. There was a possible bias concerning specificity because we did not have true or false negative results for pathology after iMRI. Finally, a future study of differences between 1.5 T and 3.0 T iMRI would be a valuable study, as this database did not allow for discerning differences in magnet strength among all cases.

CONCLUSION

The use of iMRI during resection of grade I to IV gliomas and pituitary adenomas is highly reliable for the identification of residual tumor, as confirmed in this large multicenter cohort analysis of histopathological specimens acquired from resections performed after completion of iMRI.

Disclosures

Dr Chicoine received funding from IMRIS Inc for an unrestricted educational grant to support an iMRI database and outcomes analysis project, the IMRIS Muliticenter iMRI Neurosurgery Database (I-MiND). The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article. Dr Chicoine received funding from The Head for the Cure Foundation and Mrs Carol Rossfeld and The Alex & Alice Aboussie Family Charitable Foundation. REDCap^{TM} database supported by Clinical and Translational Science Award (CTSA) Grant [UL1 TR000448] and Siteman Comprehensive Cancer Center and NCI Cancer Center Support Grant P30 CA091842.

REFERENCES

1. Coburger J, Nabavi A, König R, Wirtz CR, Pala A. Contemporary use of intraoperative imaging in glioma surgery: a survey among EANS members. *Clin Neurol Neurosurg*. 2017;163:133-141 (doi:10.1016/j.clineuro.2017.10.033).
2. Chicoine MR, Lim CCH, Evans JA, et al. Implementation and preliminary clinical experience with the use of ceiling mounted mobile high field intraoperative magnetic resonance imaging between two operating rooms. *Acta Neurochir (Wien)*. 2011;109:97-102 (doi:10.1007/978-3-211-99651-5_15).
3. Liang D, Schulder M. The role of intraoperative magnetic resonance imaging in glioma surgery. *Surg Neurol Int*. 2012;3(5):320.
4. Nimsky C, Fujita A, Ganslandt O, Von Keller B, Fahlbusch R. Volumetric assessment of glioma removal by intraoperative high-field magnetic resonance imaging. *Neurosurgery*. 2004;55(2):358-371.
5. Nimsky C, Ganslandt O, Buchfelder M, Fahlbusch R. Intraoperative visualization for resection of gliomas: the role of functional neuronavigation and intraoperative 1.5 t MRI. *Neurol Res*. 2006;28(5):482-487.
6. Roder C, Breitkopf M, Bisdas S, et al. Beneficial impact of high-field intraoperative magnetic resonance imaging on the efficacy of pediatric low-grade glioma surgery. *Neurosurg Focus*. 2016;40(3):E13.
7. Sylvester PT, Evans JA, Zipfel GJ, et al. Combined high-field intraoperative magnetic resonance imaging and endoscopy increase extent of resection and progression-free survival for pituitary adenomas. *Pituitary*. 2015;18(1):72-85.
8. Kuhnt D, Becker A, Ganslandt O, Bauer M, Buchfelder M, Nimsky C. Correlation of the extent of tumor volume resection and patient survival in surgery of glioblastoma multiforme with high-field intraoperative MRI guidance. *Neuro-oncol*. 2011;13(12):1339-1348.
9. Maldaun MVC, Khawja SN, Levine NB, et al. Awake craniotomy for gliomas in a high-field intraoperative magnetic resonance imaging suite: analysis of 42 cases. *J Neurosurg*. 2014;121(4):810-817.
10. Napolitano M, Vaz G, Lawson TM, et al. Glioblastoma surgery with and without intraoperative MRI at 3.0T. *Neurochirurgie*. 2014;60(4):143-150.
11. Senft C, Franz K, Blasel S, et al. Influence of iMRI-guidance on the extent of resection and survival of patients with glioblastoma multiforme. *Technol Cancer Res Treat*. 2010;9(4):339-346.
12. Shah MN, Leonard JR, Inder G, et al. Intraoperative magnetic resonance imaging to reduce the rate of early reoperation for lesion resection in pediatric neurosurgery. *J Neurosurg Pediatr*. 2012;9(3):259-264.
13. Karsy M, Akbari SH, Limbrick D, et al. Evaluation of pediatric glioma outcomes using intraoperative MRI: a multicenter cohort study. *J Neurooncol*. 2019;143(2):271-280.
14. Choudhri XAF, Klimo P, Auschwitz TS, Whitehead MT, Boop FA. 3T intraoperative MRI for management of pediatric CNS neoplasms. *Am J Neuroradiol*. 2014;35(12):2382-2387.
15. Hatiboglu MA, Weinberg JS, Suki D, et al. Impact of intraoperative high-field magnetic resonance imaging guidance on glioma surgery. *Neurosurgery*. 2009;64(6):1073-1081.
16. Haydon DH, Chicoine MR, Dacey RG Jr. The impact of high-field-strength intraoperative magnetic resonance imaging on brain tumor management. *Neurosurgery*. 2013;60(SUPPL 1):92-97.
17. Kremer P, Tronnier V, Steiner HH, et al. Intraoperative MRI for interventional neurosurgical procedures and tumor resection control in children. *Childs Nerv Syst*. 2006;22(7):674-678.
18. Kuhnt D, Ganslandt O, Schlaffer SM, Buchfelder M, Nimsky C. Quantification of glioma removal by intraoperative high-field magnetic resonance imaging: an update. *Neurosurgery*. 2011;69(4):852-863.
19. Leuthardt EC, Lim CCH, Shah MN, et al. Use of movable high-field-strength intraoperative magnetic resonance imaging with awake craniotomies for resection of gliomas: preliminary experience. *Neurosurgery*. 2011;69(1):194-206.
20. Scherer M, Jungk C, Younsi A, Kickingereder P, Müller S, Unterberg A. Factors triggering an additional resection and determining residual tumor volume on intraoperative MRI: analysis from a prospective single-center registry of supratentorial gliomas. *Neurosurg Focus*. 2016;40(3):E4.
21. Coburger J, Scheuerle A, Thal DR, et al. Linear array ultrasound in low-grade glioma surgery: histology-based assessment of accuracy in comparison to conventional intraoperative ultrasound and intraoperative MRI. *Acta Neurochir (Wien)*. 2015;157(2):195-206.
22. Coburger J, Scheuerle A, Pala A, Thal D, Wirtz CR, König R. Histopathological insights on imaging results of intraoperative magnetic resonance imaging, 5-Aminolevulinic acid, and intraoperative ultrasound in glioblastoma surgery. *Neurosurgery*. 2017;81(1):165-174.
23. Pala A, Reske SN, Eberhardt N, et al. Diagnostic accuracy of intraoperative perfusion-weighted MRI and 5-aminolevulinic acid in relation to contrast-enhanced intraoperative MRI and ^{11}C-methionine positron emission tomography in resection of glioblastoma: a prospective study. *Neurosurg Rev*. 2019;42(2):471-479.
24. Coburger J, Scheuerle A, Wirtz CR, et al. Tumor detection with 5-aminolevulinic acid fluorescence and Gd-DTPA-enhanced intraoperative MRI at the border of contrast-enhancing lesions: a prospective study based on histopathological assessment. *Neurosurg Focus*. 2014;36(2):E3.
25. Hesselmann V, Mager AK, Goetz C, et al. Accuracy of high-field intraoperative MRI in the detectability of residual tumor in glioma grade IV resections. *Rofo*. 2017;189(6):519-526.
26. Hauser SB, Kockro RA, Actor B, Sarnthein J, Bernays R-L. Combining 5-ALA fluorescence and intraoperative MRI in glioblastoma surgery. *Neurosurgery*. 2016;78(4):475-483.
27. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) – A metadata driven methodology and workflow process for providing translational research informatict support. *J Biomed Inform*. 2009;42(2):377-381.
28. 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(6):803-820.
29. Vuorinen V, Hinkka S, Färkkilä M, Jääskeläinen J. Debulking or biopsy of malignant glioma in elderly people – A randomised study. *Acta Neurochir (Wien)*. 2003;145(1):5-10.
30. Zhang Z, Yang K, Xia Y, Meng X, Yu X. High-field intraoperative magnetic resonance imaging increases extent of resection and progression-free survival for nonfunctioning pituitary adenomas. *World Neurosurg*. 2019;127:e925-e931 (doi:10.1016/j.wneu.2019.04.001).
31. Brown TJ, Brennan MC, Li M, et al. Association of the extent of resection with survival in glioblastoma. *JAMA Oncol*. 2016;2(11):1460-1469.
32. Li YM, Suki D, Hess K, Sawaya R. The influence of maximum safe resection of glioblastoma on survival in 1229 patients: Can we do better than gross-total resection? *J Neurosurg*. 2016;124(4):977-988.
33. Sanai N, Polley MY, McDermott MW, Parsa AT, Berger MS. An extent of resection threshold for newly diagnosed glioblastomas. *J Neurosurg*. 2011;115(1):3-8.
34. Trifiletti DM, Alonso C, Grover S, Fadul CE, Sheehan JP, Showalter TN. Prognostic implications of extent of resection in glioblastoma: analysis from a large database. *World Neurosurg*. 2017;103:330-340 (doi:10.1016/j.wneu.2017.04.035).

35. Chaichana KL, McGirt MJ, Laterra J, Olivi A, Quiñones-Hinojosa A. Recurrence and malignant degeneration after resection of adult hemispheric low-grade gliomas. *J Neurosurg*. 2010;112(1):10-17.
36. McGirt MJ, Chaichana KL, Attenello FJ, et al. Extent of surgical resection is independently associated with survival in patients with hemispheric infiltrating low-grade gliomas. *Neurosurgery*. 2008;63(4):700-708.
37. 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(8):1338-1345.
38. Snyder LA, Wolf AB, Oppenlander ME, et al. The impact of extent of resection on malignant transformation of pure oligodendrogliomas. *J Neurosurg*. 2014;120(2):309-314.
39. Li P, Qian R, Niu C, Fu X. Impact of intraoperative MRI-guided resection on resection and survival in patient with gliomas: a meta-analysis. *Curr Med Res Opin*. 2017;33(4):621-630.
40. Senft C, Franz K, Ulrich CT, et al. Low field intraoperative MRI-guided surgery of gliomas: a single center experience. *Clin Neurol Neurosurg*. 2010;112(3):237-243.
41. Kubben PL, ter Meulen KJ, Schijns O, ter Laak-Poort MP, van Overbeeke JJ, van Santbrink H. Intraoperative MRI-guided resection of glioblastoma multiforme: a systematic review. *Lancet Oncol*. 2011;12(11):1062-1070.
42. Akbari SH, Sylvester PT, Kulwin C, et al. Initial experience using intraoperative magnetic resonance imaging during a trans-sulcal tubular retractor approach for the resection of deep-seated brain tumors: a case series. *Oper Neurosurg*. 2019;16(3):292-301.
43. Pala A, Brand C, Kapapa T, et al. The value of intraoperative and early postoperative magnetic resonance imaging in low-grade glioma surgery: a retrospective study. *World Neurosurg*. 2016;102:144-150.
44. Serra C, Burkhardt JK, Esposito G, et al. Pituitary surgery and volumetric assessment of extent of resection: a paradigm shift in the use of intraoperative magnetic resonance imaging. *Neurosurg Focus*. 2016;40(3):E17.

Neurosurgery Speaks! *Audio abstracts available for this article at www.neurosurgery-online.com.*

Supplemental digital content *is available for this article at www.neurosurgery-online.com.*

Supplemental Digital Content 1. Text. Supplemental descriptions of 2 cases in which iMRI studies were misleading and led to additional resection that was negative for residual tumor on histopathology.

Supplemental Digital Content 2. Figure. Axial T1-, **A**, and T2-weighted, **B**, preoperative MRI images demonstrating a left frontoparietal glioblastoma.

Supplemental Digital Content 3. Figure. Axial intraoperative T1-weighted MRI studies with contrast that were read as demonstrating residual tumor in the inferomedial, **A**, (red arrow) and posterior superior, **B**, (red arrow) aspects of the resection bed.

Supplemental Digital Content 4. Figure. Axial T1-, **A**, and T2-weighted, **B**, preoperative MRI images demonstrating a left temporal grade II astrocytoma.

Supplemental Digital Content 5. Figure. Axial intraoperative T2-weighted MRI studies that were read as demonstrating residual tumor in the superomedial, **A**, (red arrow) and posterior inferior, **B**, (red arrow) aspects of the resection bed.

COMMENTS

This multi-institutional retrospective study describes their combined experience with iMRI to aid the resection of gliomas and pituitary adenomas. One of the key findings was that gliomas were more likely than pituitary adenomas to undergo additional resection based on iMRI findings. Accordingly, additional resection resulted in a tumor diagnosis more frequently in gliomas than adenomas. Interestingly, after additional resection, there was no difference in histology-proven tumor yield amongst the four grades of glioma. This work is timely as the use of iMRI continues to expand and a nice example of a multi-institutional collaborative effort yielding more impactful results then would have been possible with a single-institutional study.

Eric M. Thompson
Durham, North Carolina

The authors of this large multicenter, retrospective study found an association with residual tumor as seen on intraoperative MRI and histopathologic findings. Both gliomas and pituitary adenomas were included in this study. It was found that tumor tissue, confirmed by histopathology, was seen in the vast majority, 89.4%, of additional resections after intraoperative MRI inspection. Overall, this study confirms the reliability of iMRI in identifying residual tumor. Provision of other information would have improved the applicability of this study. For instance, it was observed that additional resection after iMRI was performed in 59.6% of glioma cases. It would have been useful to know the surgeon's goal for surgery, ie, gross total resection or subtotal resection. Also, we need to know if the surgeons were intentionally less aggressive knowing they would be using iMRI, thus skewing toward more conservative resections and yielding a higher percentage of residual tumor found on histopathology of post-iMRI samples.

Alexa Bodman
Jeffrey Olson
Atlanta, Georgia