Extent of Endoscopic Resection for Anterior Skull Base Tumors: An MRI-Based Volumetric Analysis

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J Neurol Surg B 2017;78:227–234.

Abstract

Objective To determine the volume of ventral skull base tumor removed following endoscopic endonasal (EEA) resection using MRI-based volumetric analysis and to evaluate the inter-rater reliability of such analysis.

Design Retrospective case series.

Setting Academic tertiary care hospital.

Participants EEA patients November 2012 to August 2015.

Main Outcome Measures Volumetric analysis of pre- and immediately postoperative MR imaging was performed independently by two investigators. The percentage of total tumor resected was evaluated according to resection goal and tumor type.

Results A total of 39 patients underwent resection. Intraclass correlation coefficients between the raters were 0.9988 for preoperative and 0.9819 for postoperative images. Tumors (and average percentage removed) included 17 nonsecreting pituitary adenomas (95.3%), 8 secreting pituitary adenomas (86.2%), 4 meningiomas (81.6%), 3 olfactory neuroblastomas (100%), 2 craniopharyngiomas (100%), 1 large B-cell lymphoma (90.5%), 1 germ cell neoplasm (48.3%), 1 benign fibrous connective tissue mass (93.4%), 1 epidermoid cyst (68.4%), and 1 chordoma (100%). For tumors treated with intent for gross total resection, $96.9 \pm 4.8\%$ was removed.

Conclusion EEAs achieved tumor resection rates of $\sim 97\%$ when total resection was attempted. The radiographic finding of residual tumor is of uncertain clinical significance. The volumetric analysis employed in this study demonstrated high inter-rater reliability and could facilitate further study.

Keywords

- ▶ endoscopic skull base surgery
- ▶ tumor volume
- ▶ endonasal
- ▶ extent of resection

Introduction

Tumors involving the anterior skull base remain an evolving therapeutic challenge. Classically approached via open craniofacial resection¹ or a subfrontal approach,² such tumors

have increasingly been accessed via entirely endoscopic, endonasal approaches (EEAs)^{3,4} in appropriately selected patients. Studies have suggested several potential benefits of endoscopic approaches, including decreased hospital stay and faster recovery⁵ with comparable complication rates and

received

June 9, 2016

accepted

October 24, 2016

published online

December 21, 2016

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Stuttgart · New York

DOI <https://doi.org/10.1055/s-0036-1597137>.
ISSN 2193-6331.

survival.⁵⁻⁸ Interest in EEAs is further fueled by improved operative visualization and the potential for superior functional and cosmetic outcomes.⁹

Regardless of approach, complete resection is often a central goal of surgical intervention. Despite early concerns regarding the oncologic acceptability of piecemeal rather than en bloc tumor resection utilized in EEAs,⁹ there is now broad consensus that the goal of complete resection, rather than the method of resection, should guide a surgeon's approach.^{10,11} As such, efforts are ongoing to continue to delineate indications, limitations, and techniques of entirely EEAs. However, there remain significant gaps in knowledge due in part to variations among different institutions' familiarity, surgical aggressiveness, and operative goals.^{7,12} Further study is required to help delineate the uses of EEAs, including studies reporting institutional success with gross total resection.

Volumetric calculations using MR imaging have been used elsewhere to assess tumor volume for a variety of tumors, both benign and malignant.¹³⁻¹⁶ However, despite advances in imaging, few studies have rigorously examined the utility of assessing extent of resection using pre- and postoperative imaging in an effort to objectify surgical outcomes. Such data are required to further delineate indications and limitations of EEAs for tumor resection. Furthermore, the limitations of such volumetric analyses have not been examined.

We evaluated the extent of resection of tumors approached via EEA technique at a single institution. A secondary aim of this study was to determine the validity of our method of volumetric calculation. We therefore report on patients who underwent EEA for resection of tumors affecting the anterior skull base.

Methods

Patients

Approval was obtained from the University of Wisconsin Institutional Review Board. Patients were identified using an institutional database of neurosurgical patients under the care of one of the authors (A.A.). All patients who underwent EEAs for management of tumors affecting the ventral skull base between November 2012 and August 2015 were included. Subjects of all ages were considered. Patients undergoing EEAs for treatment of other conditions (e.g., cerebrospinal fluid [CSF] leak repair, encephalocele management) were not included. Medical records were reviewed for patient demographic data, tumor histology, operative goals (gross total versus subtotal resection), dates of imaging and surgery, and radiographic records.

Volumetric Analysis

Tumor volumes were calculated using pre- and postoperative MR images. Volumetric analyses were performed using Vitrea Software (Vital Images Inc., Minnetonka, Minnesota, United States). Three-dimensional volumes were determined using a computer digitizer by manually delineating tumor borders on sequential image slices and calculating tumor volume based on slice thickness (►Fig. 1). Calculations were performed independently by two investigators. The optimal MR sequence for identification of tumor was determined by the

neuroradiologist (G.A.). For instances in which residual tumor was difficult to discern from postoperative change, volume tracings favored residual tumor volume in a conservative manner. Discrepancies were resolved by consensus. Time elapsed between preoperative imaging and surgery corresponded to either initial diagnostic imaging or surgical preparatory imaging (e.g., for image guidance software); postoperative imaging was obtained in the immediate postoperative period (postoperative days 0-2).

Surgical Approaches

Surgical approaches generally conformed to techniques described elsewhere^{9,17-21} and were performed endoscopically entirely via the endonasal corridor. Generally, approach was begun with bilateral maxillary antrostomies, unilateral or bilateral middle turbinectomies, bilateral complete ethmoidectomies, wide sphenoidotomies, and posterior septectomy. In most cases, a nasoseptal flap was elevated prior to drilling of the sphenoid rostrum.^{17,21} Extensive drilling of the skull base was performed to ensure that the dissection would not be limited by bone. In the case of pituitary adenomas, an extracapsular tumor dissection technique was employed.^{22,23} Reconstructive techniques varied based on tumor location and size, and generally involved multilayered closure variably using abdominal fat, fascia lata grafting, free mucosal grafts, and/or pedicled nasoseptal flap coverage. Lumbar drains were used for cases in which frank CSF was encountered during surgery, or in cases deemed high-risk for postoperative CSF leak.

Tumor Types

All tumors, both benign and malignant, affecting the ventral skull base were considered for inclusion.

Surgical Intent

Not all tumors were approached with intent for gross total resection; this is specified for each case. The percentage of total tumor resected was evaluated according to resection goal (total or subtotal resection) and tumor type. Examples of cases in which total resection was not a goal include cases of pituitary adenoma with extension lateral to the carotid artery. Also, cases in which the intraoperative pathologic interpretation revealed a process better treated with radiation (lymphoma); total resection was not attempted.

Statistical Analysis

Descriptive statistics are reported for percentage of tumor removed for each histologic subtype. Averages for pre- and postoperative volumes between the two raters were used when making these calculations. Intraclass correlation coefficients were calculated to evaluate inter-rater reliability for the pre- and postoperative measurements.

Results

Demographics

Thirty-nine patients were included (24 males and 15 females). Average age at the time of surgery was 50.1 ± 17.7 years (range 14-81 years) (►Table 1).

Table 1 Patient characteristics including surgical resection extent (total vs. subtotal), preoperative tumor volume, postoperative tumor volume, and percentage of tumor removed

Age	Histology	Goal	Pre (cc ³)	Post (cc ³)	% resected
54	Large B-cell lymphoma	Subtotal	15.2	1.5	90.5
68	Nonsecreting pituitary adenoma	Subtotal	13.2	0.6	95.6
49	Atypical meningioma	Subtotal	2.1	0.5	77.4
23	Germ cell neoplasm	Subtotal	11.3	5.9	48.3
50	Nonsecreting pituitary adenoma	Subtotal	13.6	1.7	87.6
56	Nonsecreting pituitary adenoma and meningioma	Subtotal	16.4	0.0	100.0
81	Epidermoid cyst	Subtotal	2.2	0.7	68.4
62	Atypical meningioma	Subtotal	46.5	23.6	49.1
75	Benign fibrous connective tissue	Subtotal	6.4	0.4	93.4
62	Nonsecreting pituitary adenoma	Subtotal	12.8	0.6	95.4
26	Prolactin-producing pituitary adenoma	Subtotal	21.2	13.4	36.7
53	ACTH-producing pituitary adenoma	Subtotal	31.6	7.1	77.6
68	Nonsecreting pituitary adenoma	Total	9.0	1.3	85.9
68	Nonsecreting pituitary adenoma	Total	9.7	0.1	98.5
63	Nonsecreting pituitary adenoma	Total	7.3	0.6	91.6
61	Nonsecreting pituitary adenoma	Total	3.8	0.0	100.0
52	Nonsecreting pituitary adenoma	Total	1.9	0.0	100.0
70	Nonsecreting pituitary adenoma	Total	9.5	0.6	94.0
29	ACTH-secreting pituitary adenoma	Total	4.1	0.1	96.6
32	GH-producing pituitary adenoma	Total	1.2	0.0	100.0
52	Atypical meningioma	Total	2.9	0.0	100.0
41	Prolactin-producing pituitary adenoma	Total	2.9	0.1	95.4
51	Nonsecreting pituitary adenoma	Total	23.2	2.3	90.2
62	Nonsecreting pituitary adenoma	Total	3.5	0.0	100.0
66	Nonsecreting pituitary adenoma	Total	36.7	0.9	97.6
32	Chordoma	Total	34.2	0.0	100.0
19	Craniopharyngioma	Total	4.4	0.0	100.0
34	GH- and prolactin-producing pituitary adenoma	Total	3.1	0.0	100.0
62	ACTH-producing pituitary adenoma	Total	7.1	1.2	83.2
66	Olfactory neuroblastoma	Total	20.6	0.0	100.0
44	Meningioma	Total	17.5	0.0	100.0
15	GH-producing pituitary adenoma	Total	1.6	0.0	100.0
31	Olfactory neuroblastoma	Total	11.8	0.0	100.0
37	Olfactory neuroblastoma	Total	0.3	0.0	100.0
52	Nonsecreting pituitary adenoma	Total	7.3	0.3	95.6
67	Nonsecreting pituitary adenoma	Total	12.7	0.1	99.5
53	Nonsecreting pituitary adenoma	Total	10.8	0.0	100.0
68	Nonsecreting pituitary adenoma	Total	8.6	0.9	89.0
14	Craniopharyngioma	Total	19.6	0.0	100.0

Tumor Types

Tumors included 17 nonsecreting pituitary adenomas, 8 secreting pituitary adenomas, 4 meningiomas, 3 olfactory neuroblastomas, 2 craniopharyngiomas, 1 epidermoid cyst, 1

chordoma, 1 large B-cell lymphoma, 1 germ cell neoplasm, and 1 benign fibrous tumor (→Table 1). Tumors affected diverse subsites; of the four meningiomas, three were olfactory groove meningiomas and one was a sellar/cavernous

Fig. 1 Volumetric analysis. Case example of a single slice tracing for preoperative (a) and postoperative (b) tumor volume for a patient with a nonsecreting pituitary adenoma. Three-dimensional volumes were determined using a computer digitizer by manually delineating tumor borders on sequential image slices and calculating tumor volume based on slice thickness.

lesion. Seven patients had undergone prior open approaches to tumors and thus underwent revision surgery through an EEA in the present analyses; in these cases, preoperative tumor volume was considered either residual volume or recurrent tumor volume. One patient was excluded due to the absence of postoperative imaging. One patient was excluded for rapid tumor growth resulting in larger tumor volume measured in the immediate postoperative period compared with preoperative imaging; calculation of extent of resection was therefore not possible for this patient.

Imaging

The MR sequence used for tumor volume calculation varied depending on tumor type and the subsites involved. Sequences were selected to optimize contrast between tumor and surrounding native tissue and to differentiate tumor from peritumoral edema (► **Table 2**). Inter-rater reliability between the two authors performing volumetric analyses was high, with intraclass correlation coefficients of 0.9988 for preoperative images and 0.9819 for postoperative images. Time elapsed between surgery and postoperative imaging was 1.3 ± 1.5 days.

Extent of Resection

Of the 39 tumors, 27 were approached with intent for complete resection. This included 13 of 17 nonsecreting pituitary adenomas, 6 of 8 secreting pituitary adenomas, 2 of 4 meningiomas, 3 of 3 olfactory neuroblastomas, 2 of 2 craniopharyngiomas, and 1 chordoma. Considering all tu-

mors, $90.7 \pm 15.5\%$ was resected. By tumor group, percentage removed was 95.3% for nonsecreting pituitary adenomas, 86.2% for secreting pituitary adenomas, 81.6% for meningiomas, 100% for olfactory neuroblastomas, 100% for craniopharyngiomas, 90.0% for the large B-cell lymphoma, 48.3% for the germ cell neoplasm, 93.4% for the benign fibrous connective tissue mass, 68.4% for the epidermoid cyst, and 100% for the chordoma.

For tumors treated with intent for gross total resection, $96.9 \pm 4.8\%$ was removed; this included 15 tumors for which 100% removal was achieved. By tumor type, the goal of gross total resection was met in 4 of 13 nonsecreting pituitary adenomas, 3 of 6 secreting pituitary adenomas, 2 of 2 meningiomas, 3 of 3 olfactory neuroblastomas, 2 of 2 craniopharyngiomas, and the chordoma.

Cases for which the goal of gross total resection was not met are presented in ► **Table 3**, including subsites involved as well as Knosp classification.²⁴

Discussion

EEAs are increasingly used to approach a variety of skull base pathologies. In appropriate cases, EEAs provide several advantages compared with open approaches, including minimization of brain retraction, improved visualization, avoidance of external incisions, bilateral access to midline tumors, and ease of access to certain anatomic locations.^{4,25} We report on our institution's rates of resection for a diverse series of tumors approached via EEA, using three-

Table 2 MRI sequence used for volumetric analysis

	Histology	MR sequence
1	Large B-cell lymphoma	T1-weighted gradient echo volume (BRAVO™)
2	Nonsecreting pituitary adenoma	T1-weighted gradient echo volume (BRAVO™)
3	Nonsecreting pituitary adenoma	T1-weighted postcontrast
4	Nonsecreting pituitary adenoma	T1-weighted gradient echo volume (BRAVO™)
5	Nonsecreting pituitary adenoma	T1-weighted postcontrast
6	Nonsecreting pituitary adenoma	T1-weighted gradient echo volume (BRAVO™)
7	Nonsecreting pituitary adenoma	T1-weighted gradient echo volume (BRAVO™)
8	Olfactory groove atypical meningioma, grade 2	T1-weighted gradient echo volume (BRAVO™)
9	Nonsecreting pituitary adenoma	T1-weighted gradient echo volume (BRAVO™)
10	ACTH-producing pituitary adenoma	T1-weighted gradient echo volume (BRAVO™)
11	Germ cell neoplasm	T1-weighted gradient echo volume (BRAVO™)
12	GH-producing pituitary adenoma	T1-weighted gradient echo volume (BRAVO™)
13	Craniopharyngioma	T2-weighted PROPELLER
14	ACTH-producing pituitary adenoma	T1-weighted postcontrast
15	Olfactory groove atypical meningioma, grade 2	T1-weighted gradient echo volume (BRAVO™)
16	Nonsecreting pituitary adenoma	T1-weighted postcontrast
17	Nonsecreting pituitary adenoma	T2-weighted, fat saturated
18	Prolactin-producing pituitary adenoma	T1-weighted gradient echo volume (BRAVO™)
19	Nonsecreting pituitary adenoma	T1-weighted gradient echo volume (BRAVO™)
20	Epidermoid cyst	T1-weighted postcontrast
21	Nonsecreting pituitary adenoma	T1-weighted postcontrast
22	Nonsecreting pituitary adenoma	T2-weighted PROPELLER
23	Chordoma	T2-weighted Cube-FLAIR
24	Craniopharyngioma	T1-weighted postcontrast
25	GH and prolactin-secreting pituitary adenoma	T1-weighted postcontrast
26	ACTH-producing pituitary adenoma	T1-weighted postcontrast
27	Sellar/cavernous atypical meningioma, grade 2	T1-weighted postcontrast, fat-saturated
28	Benign fibrous connective tissue	T1-weighted gradient echo volume (BRAVO™)
29	Olfactory neuroblastoma	T1-weighted MP RAGE
30	Olfactory groove transitional meningioma	T1-weighted postcontrast
31	GH-producing pituitary adenoma	T1-weighted postcontrast
32	Olfactory neuroblastoma	T1-weighted gradient echo volume (BRAVO™)
33	Olfactory neuroblastoma	T1-weighted gradient echo volume (BRAVO™)
34	Nonsecreting pituitary adenoma	T1-weighted postcontrast
35	Nonsecreting pituitary adenoma	T1-weighted postcontrast
36	Nonsecreting pituitary adenoma	T1-weighted postcontrast
37	Nonsecreting pituitary adenoma	T1-weighted postcontrast
38	Prolactin-secreting pituitary adenoma	T1-weighted gradient echo volume (BRAVO™)
39	Nonsecreting pituitary adenoma	T1-weighted postcontrast

Abbreviations: ACTH, adrenocorticotrophic hormone; cube-FLAIR, 3D fast-spin-echo sequence with inversion recovery preparation; FLAIR, fluid-attenuated inversion recovery imaging; GH, growth hormone; MP RAGE, magnetization-prepared 180 degrees radio-frequency pulses and rapid gradient-echo; PROPELLER, periodically rotated overlapping parallel lines with enhanced reconstruction technique. T1-weighted gradient echo volume (BRAVO™) (GE Healthcare, Buckinghamshire, United Kingdom).

Table 3 Tumors with unsuccessful gross total resection (volumes reported in cubic centimeters)

Histology	Pre (cc ³)	Post (cc ³)	Knosp classification	Critical structures involved
Nonsecreting pituitary adenoma	9.0	1.3	4	Invasion of right cavernous sinus, encasement of right cavernous internal carotid artery
Nonsecreting pituitary adenoma	9.7	0.1	2	Effacement of optic nerve
Nonsecreting pituitary adenoma	7.3	0.6	3	Invasion of bilateral cavernous sinuses
Nonsecreting pituitary adenoma	9.5	0.6	4	Invasion of left cavernous sinus; encasement of the cavernous, left supraclinoid internal carotid artery, right supraclinoid internal carotid artery, basilar artery, left superior cerebellar artery, right posterior communicating artery, and A1 segment of the right anterior communicating artery
Secreting pituitary adenoma	4.1	0.1	2	Displacement of optic chiasm, anterior communicating artery, and pituitary stalk; extension into the left cavernous sinus and upper clivus
Secreting pituitary adenoma	2.9	0.1	3	Extension into the left cavernous, abutment of left cavernous carotid artery
Nonsecreting pituitary adenoma	23.2	2.3	3	Obliteration of suprasellar cistern, effacement of optic nerve
Nonsecreting pituitary adenoma	36.7	0.9	3	Invasion of bilateral cavernous sinuses
Secreting pituitary adenoma	7.0	1.2	3	Effacement of optic chiasm, displacement of optic nerves, obliteration of prechiasmatic cistern, abutment of anterior communicating artery, abutment of distal basilar artery, P1 segment of posterior cerebral artery, proximal right superior cerebellar artery, and proximal right anterior inferior cerebellar artery, invasion of right cavernous sinus
Nonsecreting pituitary adenoma	7.3	0.3	3	Compression of optic chiasm and right optic nerve, encasement of right internal carotid artery, displacement of right A1 anterior cerebral and anterior communicating arteries, invasion of right cavernous sinus
Nonsecreting pituitary adenoma	12.7	0.1	3	Invasion of bilateral cavernous sinuses
Nonsecreting pituitary adenoma	8.6	0.9	4	Encasement of the left internal carotid artery and partial encasement of the right internal carotid artery

dimensional volumetric analyses of pre- and immediately postoperative MR imaging. Such volumetric analysis of radiographic imaging has been used elsewhere as a reliable method of evaluating extent of resection of tumors involving the anterior skull base,^{13–16} as gross total resection of many anterior skull base tumors is often a central oncologic goal of surgical resection. There remains, however, a paucity of published data on rates of gross total resection on tumors accessed via all surgical approaches including the EEA, and therefore a gap in our knowledge of how these tumors are currently managed, including what aspects of management could be targeted for future improvement. Furthermore, rigorous evaluation of the use of imaging in such assessment, including discussion of its limitations, has not to our knowledge been investigated.

Both pre- and postoperative imaging play integral roles in surgical decision making. The importance of appropriate patient selection for EEAs has been emphasized and is defined largely by tumor subsite involvement, invasion of critical structures, and consideration of tumor size. Furthermore, scrutiny of preoperative imaging helps define surgical intent, within the context of a surgeon's experience and institutional familiarity with a multidisciplinary endoscopic approach.⁷ The role of the neuroradiologist as a member of the multidisciplinary skull base team is therefore critical.²⁶

More recently, attention has begun to focus on a role of postoperative imaging in assessing not only outcomes, but the potential morbidity of operative approach. De Almeida and colleagues²⁵ recently evaluated postoperative changes in MRI with fluid-attenuated inversion recovery signal as a surrogate

for frontal lobe injury after resection of olfactory groove meningiomas. As technologies continue to advance, further radiographic opportunities for defining outcomes may emerge.

In our series, when the intent was for gross total tumor resection, ~97% of tumor volume was resected. When grouped by tumor type, this represents success in all tumors except pituitary adenomas, for which successful gross total resection was accomplished in 4 of 13 nonsecreting pituitary adenomas and 3 of 6 secreting pituitary adenomas. Pituitary adenomas represent the most common anterior skull base tumors and are likely the tumor mostly commonly approached via EEA at most institutions. Given their proximity to critical structures including the cavernous sinuses and internal carotid artery, complete resection can be challenging regardless of approach. Tumor resection can be further limited by the desire to maintain vascularized and functional native pituitary tissue as well as by the importance of maintaining adjacent vasculature supplying the optic chiasm. For functional tumors, the goal of resection, whether total or subtotal, is elimination of the associated endocrinopathy. Previous work has interrogated the challenges of pituitary tumor resection. Dehdashti and colleagues²⁷ reviewed 200 consecutive patients with pituitary adenoma who underwent purely endoscopic transsphenoidal resection of their lesions. The degree of gross total removal for tumors without cavernous sinus involvement was 96% and for intrasellar lesions was 98%; this compared favorably to tumors resected via the traditional microscopic procedure. Bohinski and colleagues²⁸ utilized intraoperative MRI in 29 consecutive patients with pituitary macroadenomas approached via transsphenoidal approach. The optimal endpoint (gross total resection for noninvasive tumors and debulking with optic chiasm decompression for invasive tumors) was achieved in only 34% upon initial surgical resection, the remaining 66% requiring further resection.

At our institution, less aggressive tumor resection is generally favored when there is concern for postoperative iatrogenic panhypopituitarism. The majority of tumors for which gross total resection failed involved critical structures (► **Table 3**).²⁴ This may have contributed to some cases of residual tumor in our series. Often some involution of tumor is expected over time secondary to devascularization, even when gross total resection is not possible. It is possible that in some cases residual tumor seen in our series will have resolved over time. Serial volumetric calculations over time following surgery would be required to more fully evaluate for this; however, this was out of the scope of the present study. As such, the clinical significance of residual tumor in all cases in our series is unknown.

While used in this study and others, the use of MR imaging to evaluate tumor volume has several inherent limitations. Particularly in the immediate postoperative period, peritumoral edema, parenchymal contusion, venous compromise, as well as reconstructive materials such as vascularized local tissue can limit clear delineation of residual tumor. Understanding the normal enhancing structures postoperatively such as the nasoseptal flap²⁹ is important in assessing for

postoperative extent of resection. In the present study, volume tracings favored residual tumor when there was question of residual tumor versus postoperative change; as such, our calculations of residual tumor volume may have conservatively overestimated rates of residual tumor in some cases. Furthermore, inherent variability in contrast phase during image acquisition, individual patient body habitus, normal neuroanatomic variability, and differences in operative technique introduce intrinsic differences when comparing MR images among patients. Despite these limitations, inter-rater reliability in our series was high. Coupling this type of analysis with the direct surgical experience will provide immediate feedback to surgical teams as they define the indications and limitations of EEAs compared with alternative surgical methods, and provides a baseline for patient observation or the planning of additional treatments.

Several aspects of this study warrant further investigation. While the timing of postoperative imaging was consistent in this study, generally on postoperative day 1, the timing of preoperative imaging was not controlled, and thus did not allow for control of potential tumor growth between imaging and surgery. Though clinically difficult to justify, a protocolized approach to the timing of imaging would be required to control for this confounder. Second, though volumetric analyses in our study were performed independently, true blinding was not possible given investigators' familiarity with specific cases and preemptive knowledge of the presence of residual tumor volume before completing volumetric analysis.

We report on our institution's rates of tumor resection after EEA, as visualized on pre- and postoperative MRI. EEA allowed for successful access to a diverse series of tumors with a high majority of tumor removed. A potential small volume of residual tumor in some patients is of uncertain clinical significance. Continued imaging surveillance is required to ascertain the true nature of this tissue and the impact (if any) on patient outcomes. The MRI-based volumetric analysis employed in this study demonstrated high inter-rater reliability for measuring radiographic evidence of tumor volume and could facilitate such a longitudinal study, as well as provide a baseline for clinical surveillance of patients.

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