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Surgical Management of Deep-Seated Metastatic Brain Tumors Using Minimally Invasive Approaches

Kelly Gassie[1] Keila Alvarado-Estrada[1] Perry Bechtle[1] Kaisorn L. Chaichana[1]

[1] Department of Neurosurgery, Mayo Clinic, Jacksonville, Florida, United States

Address for correspondence Kaisorn L. Chaichana, MD, Department of Neurosurgery, Mayo Clinic, 4500 San Pablo Road South, Jacksonville, FL 32224, United States (e-mail: chaichana.kaisorn@mayo.edu).

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Abstract

Background and Study Aims/Objective Metastatic brain tumors are the most common type of adult brain tumors. Treatment involves surgery and/or radiation therapy. Surgery is typically reserved for patients with good neurologic function, solitary and accessible lesions, symptomatic lesions, and/or those with good systemic control of their primary cancer. Deep-seated lesions, however, are typically treated with palliative options including radiation and medical therapies. We summarize our personal experience with minimally invasive surgical approaches for these deep-seated metastatic brain tumors using tubular retractors with exoscopic visualization.

Material and Methods Patients with deep-seated metastatic brain tumors who were operated on from January 2016 to December 2017 by the senior author were collected prospectively. "Deep seated" was defined as any subcortical location below the deepest adjacent sulcus in close proximity to the basal ganglia and/or thalamus. "Minimally invasive" was defined as the use of tubular retractors with exoscopic visualization.

Results A total of 15 consecutive patients with an average $\pm$ standard deviation age of 63 $\pm$ 12 years underwent surgical resection of a deep-seated metastasis. The tumor was located in the centrum semiovale in seven (47%) (3 corticospinal tract, 2 superior longitudinal fasciculus, 1 visual tract, 1 inferior frontal occipital fasciculus), basal ganglia in three (20%), thalamus in two (13%), and cerebellum in three (20%). Median percentage resection was 100% (interquartile range:100–100%), and, following surgery, seven (47%), seven (47%), and one (7%) had an improved, stable, and worse Karnofsky Performance Score, respectively. No patients had notable local complications including stroke, infection, hemorrhage, and/or seizure. All patients underwent postoperative stereotactic radiosurgery.

Conclusion This minimally invasive approach can be used to achieve extensive resection with minimal morbidity for arguably the highest risk metastatic brain tumors.

Keywords

- deep seated
- exoscope
- metastatic brain tumors
- minimally invasive approaches
- tubular retractors

Introduction

Metastatic brain tumors are the most common central nervous system tumors in adults.[1–5] The most common primary tumors include the lung, breast, kidney, skin, and gastrointestinal systems.[1–5] The treatment of this disease involves some combination of surgery and/or radiation therapy.[1–5] Surgery is typically reserved for patients with good neurologic function, solitary and accessible lesions, symptomatic lesions, and/or those with good systemic control of their primary cancer.[2,3,6,7]

A subset of patients with metastatic brain cancer develop deep-seated lesions within critical white matter tracts, basal ganglia, and/or thalamic structures.[2,3,6,7] These lesions are typically treated with stereotactic radiosurgery (SRS) because

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of the potentially increased risk of surgical morbidity associated with accessing and resecting them.[6,7] SRS, unlike surgery, does not improve mass effect, is less effective for larger lesions, is associated with a delayed treatment effect, and does not provide tissue for diagnosis and molecular analyses.[6,7] However, minimally invasive approaches may decrease the morbidity associated with conventional surgical approaches for these deep-seated lesions.[8–14] The use of this approach was primarily limited to studies combining metastatic brain tumors with other pathology.[10,15,16] In this study, we summarize our personal experience with these approaches for deep-seated metastatic brain tumors.

Material and Methods

Patient Selection

Before the start of this study, institutional review board approval was obtained to collect patient data prospectively. All patients who were operated on by the senior author were identified prospectively, and patient information and outcomes were collected. From January 2016 to December 2017, 15 consecutive patients were operated on for a single deep-seated metastatic brain lesion using minimally invasive approaches. "Deep seated" was defined as any subcortical location below the deepest adjacent sulcus in close proximity to the basal ganglia and/or thalamus. "Minimally invasive" was defined as the use of tubular retractors with exoscopic visualization, as previously described.[8,10–12] The variables that were prospectively collected included age, sex, tumor location, pre- and postoperative neurologic function, Karnofsky Performance Score (KPS), pre- and postoperative tumor volume, and length of hospital stay.

General Treatment Strategy

The surgical goal for each case was gross total resection without neurologic deficit. The patients with deep-seated lesions who were typically offered surgery were those with solitary and/or symptomatic lesions with significant size ($>$ 2.5 cm) and mass effect with good recursive partitioning analysis (RPA) scores (class 1–2).[2] In cases where patients presented with RPA class 3 (KPS $<$ 70), surgery was offered when lesions caused significant mass effect and/or neurologic deficits. Patients with lesions, especially deep seated ones $\leq$ 2.5 cm, were typically offered radiation therapy to minimize the potential morbidity associated with surgical intervention unless there was significant mass effect and symptoms associated with the lesion. Minimally invasive approaches were chosen when the lesions were deep seated below the adjacent sulcus in eloquent regions including critical white matter projection and association tracts, basal ganglia, and/or thalamus.

The surgical approach was previously described.[10–12] Patients who were offered surgery with the use of minimally invasive approaches typically underwent high-resolution magnetic resonance imaging (MRI) with and without contrast and diffusion tensor imaging within 48 hours of surgery (►**Figs. 1** and **2**). The planned surgical approach was chosen based on minimizing morbidity to eloquent cortical and subcortical structures. The patient was taken to the operating room on the day of surgery and induced and intubated per routine. After intubation, the patient's head was fixated in a Mayfield skull clamp. If possible, the head was kept neutral to maintain orientation. Under stereotactic guidance, a small 3-cm skin incision was then made overlying the planned trajectory, followed by a $\sim$ 2-cm craniotomy. The craniotomy was centered on the desired sulcus, thus allowing for a transsulcal, parafascicular approach to minimize potential injury to adjacent eloquent cortical and subcortical areas.

After the craniotomy, the dura was opened in a cruciate fashion. The sulcus was then opened sharply under exoscopic visualization and magnification (0- or 90-degree exoscope; Vitom, Karl Storz, El Segundo, California, United States). After the sulcus was opened to its depth, a preselected tubular retractor (NICO BrainPath, Indianapolis, Indiana, United States) was then passed to the superficial surface of the lesion with the aid of stereotactic navigation guidance. For smaller and/or deeper lesions, ultrasound (Hitachi Aloka, Wallingford, Connecticut, United States) was used to help with trajectory planning and lesion targeting. Once the superficial aspect of the lesion was reached, the tubular retractor was either held manually or fixated with a Leyla retractor system (B. Braun Medical Inc., Bethlehem, Pennsylvania, United States).

A pseudo en bloc resection was then performed involving internal debulking with the use of a combination of tumor forceps, suction, tissue-biting device (Myriad, NICO) and/or bipolar cautery, followed by delivering the capsule of the tumor circumferentially in one piece. During internal debulking, the tumor cells were confined to the tubular retractor that was docked onto the tumor surface to minimize potential disseminated disease. In cases of larger tumors, the tubular retractor was manipulated and toggled to access the entire tumor. After resection, the retractor was withdrawn, and the dura, bone, and skin were closed in standard fashion. A postoperative MRI was done within 48 hours. The patient then underwent postoperative stereotactic radiosurgery within 3 weeks of the surgery, with the radiation focused on the resection cavity.

Results

Fifteen consecutive patients underwent surgical resection of a deep-seated metastatic brain tumor during the reviewed period (►**Table 1**). The average $\pm$ standard deviation age was 63 ± 12 years. Seven (47%) were female. Tumors were located in the centrum semiovale in seven (47%), basal ganglia in three (20%), thalamus in two (13%), and cerebellum in three (20%). Among the lesions located in the centrum semiovale, three involved the corticospinal tract, two the superior longitudinal fasciculus, one the visual tract, and one the inferior frontal occipital fasciculus. The median preoperative KPS was 60 (IQR: 50–90). The most common presenting symptoms were headaches in seven (47%), confusion/mental status changes in 6 (40%), weakness in five (33%), and seizures in two (13%). The primary tumor was

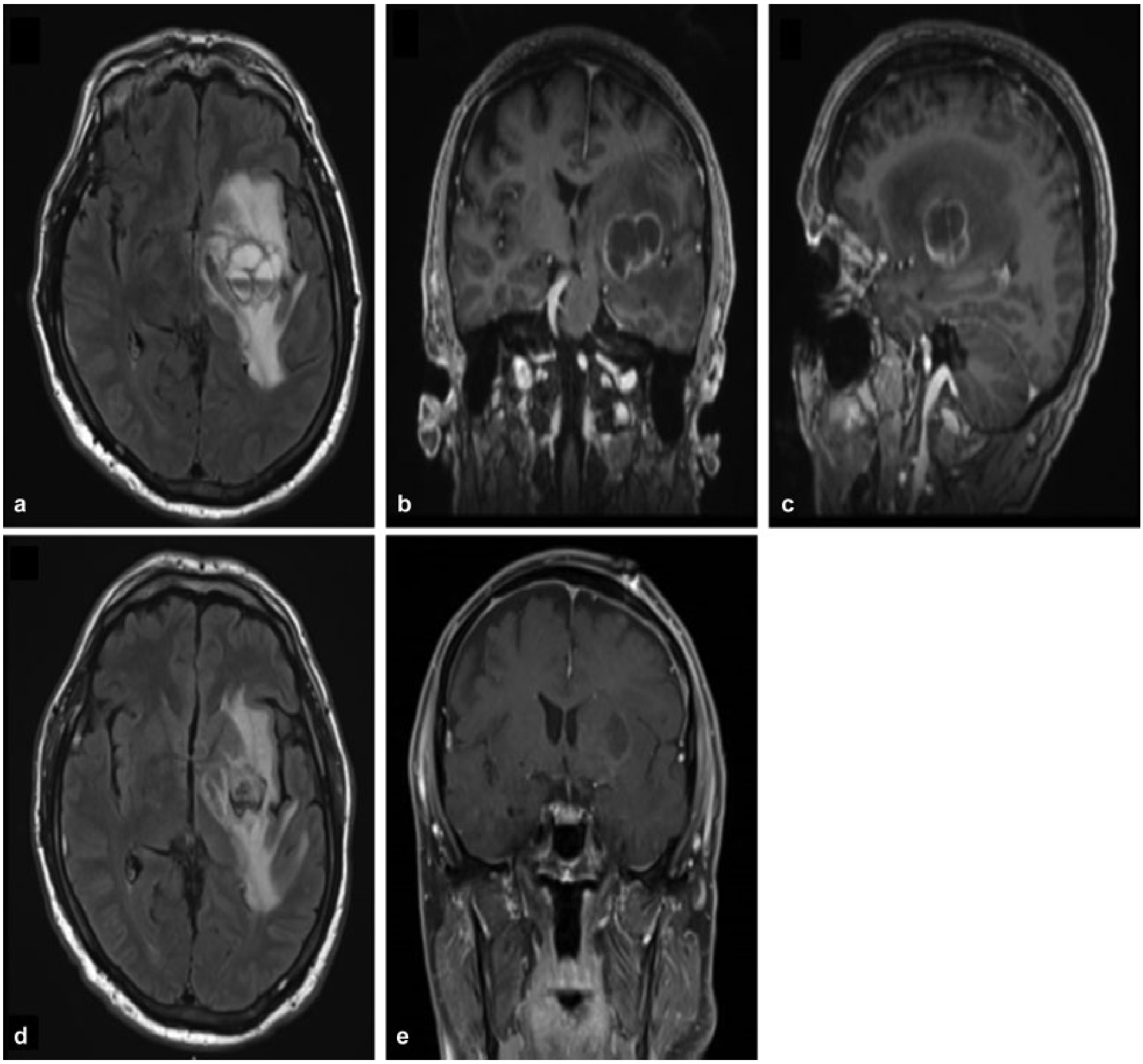

Fig. 1 Left basal ganglia non–small cell lung cancer metastasis. This 49-year-old male patient presented with headaches and confusion, and he underwent gross total resection using minimally invasive techniques through a left frontal trans-sulcal approach. Preoperative (**a**) axial T2-weighted fluid-attenuated inversion recovery (FLAIR) and (**b**) coronal and (**c**) sagittal T1-weighted magnetic resonance imaging (MRI) with contrast. Postoperative (**d**) axial T2-weighted FLAIR and (**e**) coronal T1-weighted MRI with contrast.

a non–small cell lung cancer in eight (53%), bladder cancer in in two (13%), gastrointestinal cancer in one (7%), melanoma in one (7%), renal cell cancer in one (7%), and small cell lung cancer in one (7%). For the patient with the small cell lung cancer, biopsy of the lung lesion revealed mixed adenoma and small cell carcinoma.

The median percentage tumor resection was 100% (IQR: 100–100%). Only one patient underwent subtotal resection due to a decline in motor-evoked potentials during the case. Following surgery, the median KPS was 80 (IQR: 70–90); seven (47%) had improved KPS, seven (47%) had stable KPS, and one (7%) had worse KPS. The patient with worse KPS had worsened leg weakness secondary to involvement in the internal capsule of the thalamic lesion. However, at the postoperative visit, the leg weakness had nearly resolved. No patients had notable postoperative hemorrhages, strokes, seizures, wound infections, and/or other local complications. One (7%) had a new postoperative deep vein thrombosis requiring anticoagulation. The median length of stay following surgery was 2 days (IQR: 2–3.5 days). All patients underwent postoperative SRS. The median follow-up time was 6 months (IQR: 2–12 months). No patients had carcinomatosis as of most recent follow-up.

Discussion

In this prospective consecutive case series, 15 patients with deep-seated metastatic brain tumors involving eloquent cortical and subcortical structures underwent resection using a minimally invasive approach consisting of tubular

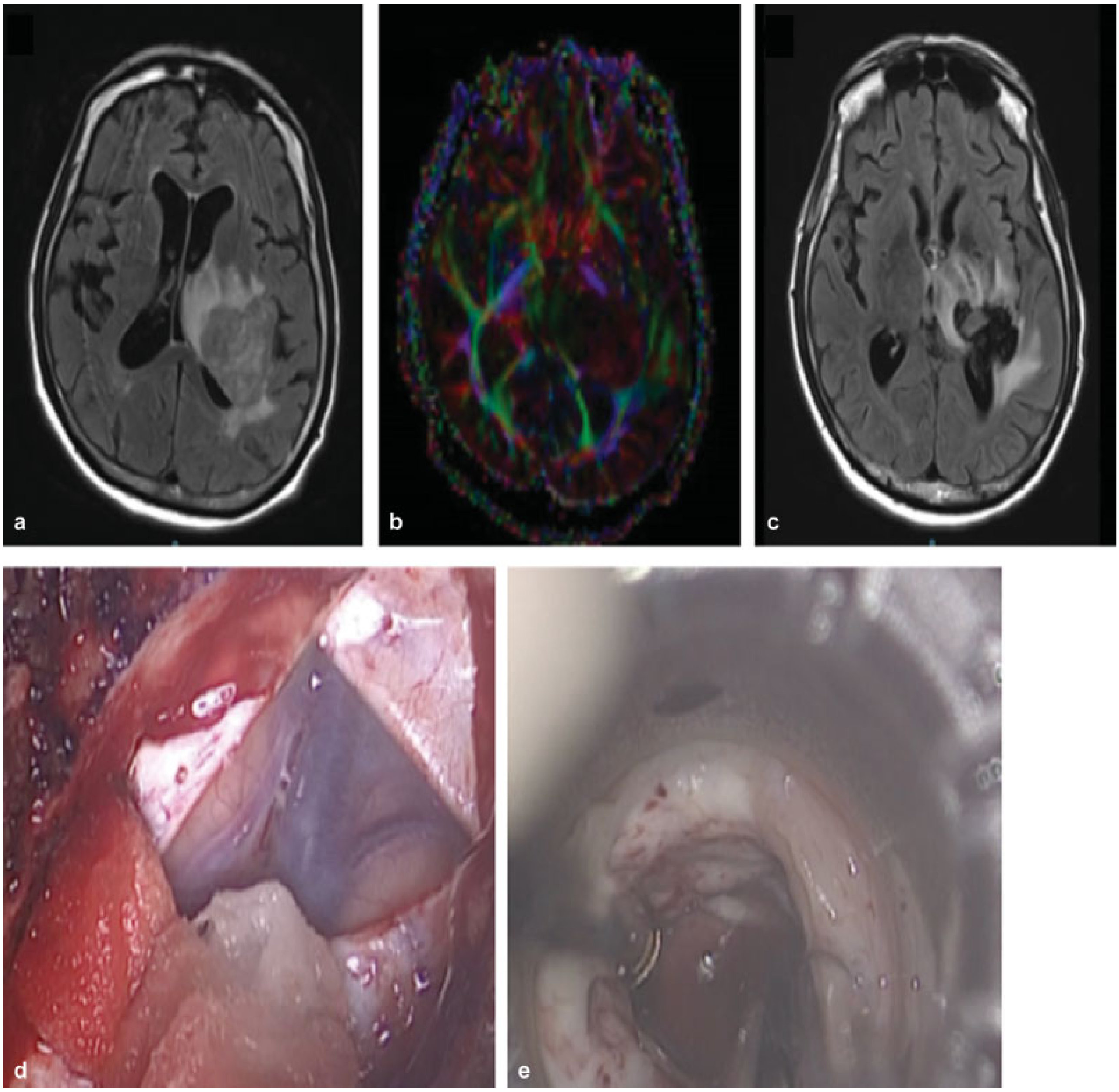

Fig. 2 Left thalamic non-small lung metastasis. This 64-year-old man presented with right hemiparesis and underwent gross total resection using minimally invasive techniques through a left superior parietal trans-sulcal approach. Preoperative (**a**) T2-weighted fluid-attenuated inversion recovery (FLAIR) and (**b**) axial diffusion tensor imaging; (**c**) postoperative T2-weighted FLAIR with motion artifact; (**d**) intraoperative view through the exoscope, and (**e**) the view through the tubular retractor after gross total resection of the lesion.

retractors and exoscopic visualization. Although the lesions in this series were in eloquent or deep-seated locations, 14 (93%) had improved or stable neurologic function after surgery; 14 (93%) underwent gross total resection. No significant local complications including strokes, hemorrhages, and infections occurred, and all patients were functional enough to undergo postoperative SRS. This is the largest individual case series evaluating the use of this approach for deep-seated metastatic brain tumors.

There are $\sim$ 200,000 new metastatic brain tumor cases in the United States each year, which is $\sim$ 10 times more prevalent than gliomas.[1–5] Approximately 30 to 70% of patients with primary cancers develop metastatic brain tumors.[1–5] This number is expected to rise as more patients develop primary cancers, imaging technology becomes more widely available, and the lack of progress continues in finding ways to prevent cancers from metastasizing to the brain.[1–5] When patients develop metastatic brain tumors, the treatment typically involves some combination of surgery and/or radiation therapy.[1–5] This management is partially dictated by their RPA class, consisting of age, KPS, primary tumor control, and the presence of systemic disease.[1–5] Patients in RPA class I (age $<$ 65 years, KPS $\geq$ 70, controlled primary cancer, and no extracranial metastases) and many in class II (age $>$ 65 years, KPS $\geq$ 70, uncontrolled primary cancer and/or extracranial metastases) are typically offered surgery

Table 1 Patients who underwent resection of deep-seated brain metastasis using minimally invasive approaches and techniques

Patient no.	Location	Presenting symptoms	Pathology	Resection, %	Preop versus postop KPS	Length of hospital stay, d
1	Centrum semiovale (SLF)	Seizures	GI	100	Stable	5
2	Centrum semiovale (visual tract)	Seizures	NSCLC	100	Stable	4
3	Basal ganglia	Headaches, personality change	NSCLC	100	Stable	5
4	Cerebellar hemisphere	Confusion	Renal cell	100	Improved	2
5	Cerebellar vermis	Lethargy	NSCLC	100	Improved	2
6	Centrum semiovale (SLF)	Headaches	SCLC	100	Stable	3
7	Thalamus	Headaches, weakness	NSCLC	100	Worsened	2
8	Centrum semiovale (CST)	Headaches, weakness	NSCLC	100	Improved	2
9	Basal ganglia	Headaches, confusion	Bladder	100	Improved	2
10	Cerebellar vermis	Headaches, confusion	Salivary	100	Stable	2
11	Centrum semiovale (CST)	Weakness	NSCLC	95.7	Stable	2
12	Centrum semiovale (IFOF)	Headaches	Melanoma	100	Stable	2
13	Basal ganglia	Lethargy	NSCLC	100	Improved	2
14	Thalamus	Weakness	NSCLC	100	Improved	4
15	Centrum semiovale (CST)	Weakness	Bladder cancer	100	improved	3

Abbreviations: CTS, corticospinal tract; GI, gastrointestinal; IFOF, inferior frontal occipital fasciculus; NSCLC, non–small cell lung cancer; SCLC, small cell lung cancer; SLF, superior longitudinal fasciculus.

if their lesion is of significant size causing mass effect is surgically accessible and causing symptoms.[1–5] Most surgeons define accessibility as superficially located.[1–5] For patients with lesions not meeting these criteria, they are typically offered nonsurgical and/or palliative options including radiation and/or steroid therapy.[1–5]

Deep-seated lesions are surgically challenging and therefore typically treated with palliative options because of their relative inaccessibility.[10–12] Moreover, these deep-seated lesions are typically associated with significant mass effect and/or neurologic deficit because they are near the confluence of the ventricular system (i.e., third ventricle), condensed white matter tracts (i.e., internal capsule), and eloquent gray matter nuclei in close proximity to each other (i.e., basal ganglia and thalamus), and therefore they usually present with a poor KPS as was the case in this series. The conventional approach for managing deep-seated brain tumors is to perform a standard needle biopsy to obtain tissue for diagnosis when diagnosis is unclear, followed by radiation therapy.[1–5] This is because the standard surgical approach involves a large craniotomy, extensive white matter dissection, and then resection, associated with significant morbidity.[9,10,12] Because most metastatic brain tumors undergo postoperative radiation therapy, the risk of neurologic injury can delay radiation therapy.[1–5] Therefore, to minimize potential morbidity with these high-risk deep-seated lesions, most surgeons do not pursue surgical resection.[1–5] This withholding of surgical resection means the potential benefits of surgery cannot be realized that include surgical debulking to make adjuvant therapy more effective, relief of mass effect, symptomatic improvement, and/or more tissue for molecular analyses.[10,12]

Minimally invasive approaches are being used for a variety of intracranial lesions.[8,10–12,14,16–19] Tubular retractors have been used for decades.[8,10–12,14,16–19] In the 1980s, Kelly used metal tubes of different sizes attached to the stereotactic frame to access thalamic tumors with the aid of computer-assisted resection.[13,20] These early channel-based retractors were then developed into transparent ovular retractors with inner stylets to resect pathology in deep-seated locations that included intraventricular lesions such as colloid cysts, high-grade gliomas, and abscesses, among others.[17,18] These larger retractors were typically limited to transcortical approaches through noneloquent cortical regions such as the anterior frontal lobe.[13,16–18,21] Circular instead of ovular retractors were then developed that allowed transsulcal access, and therefore approaches could be used in eloquent cortical regions.[10–12,14] These circular retractors were initially used to access deep-seated intracranial hemorrhages involving the basal ganglia, insula, and thalamus,[14] and later applied for excisional biopsies and resections of deep-seated gliomas[10–12] and intraventricular lesions.[19] The application of this technique in a strictly metastatic brain tumor population is limited.[8,16]

Previous studies using minimally invasive approaches for metastatic brain tumors are few and limited.[15,16,22] Hong and colleagues demonstrated the use of minimally invasive methods for 20 patients with deep-seated lesions; 8 had metastatic brain tumors.[16] Day described the same approach in 49 patients; 23 had gliomas, 20 had metastatic tumors, and 6 had intracranial hemorrhages.[15] In this study, five (10%) had a new deficit, one had a stroke (2%), and one (2%) died.[10,16] More recently, Bakhsheshian and colleagues demonstrated the use of this approach for metastatic brain tumors for 25 patients from six centers over a 6-year period. Gross total resection was achieved in 80%, with one patient each (4% each) developing new weakness and a deep vein thrombosis.[8]

This is the first study that focuses on a single surgeon's use of a minimally invasive approach for deep-seated metastatic brain tumors. This is important because the management and surgical approach for these lesions differ than other pathology including gliomas, abscesses, and demyelinating disorders, among others. This study also studies the application of this approach via a transsulcal route to minimize potential injury to eloquent cortical and subcortical tracts. Prior studies primarily used a transcortical route.[13,16,18,21] Lastly, this study also used the most modern optics with exoscopic visualization to maximize optics and ergonomics, whereas other earlier studies used primarily microscopic visualization.[13,16,18,21] The exoscope is similar to an endoscope, but instead of being inside the body cavity, it hovers outside of the body similar to a microscope. The advantages of an exoscope, as compared with a microscope, is that it provides greater magnification, has wider focal lengths, and offers better ergonomics. Nonetheless, the surgeries in this series could have been done with a microscope without the advantages just described.

This study, however, has some limitations. The metastatic lesions in this study are diverse and therefore not applicable to one type.[3] It is well known that the lesion's consistency varies with the primary pathology.[3] Moreover, the number in this study limits its generalizability even though this is the largest single surgeon's experience in the literature. A significant portion of patients in this study presented with a poor KPS, and therefore RPA class 3 was likely because of the deep-seated location of their brain metastases and therefore represents the poorest prognostic subset of patients with metastatic brain cancer. Additionally, the use of tubular retractors is limited to deep-seated locations below the sulcal boundaries in eloquent locations. It does not apply to more superficial lesions and those located in noneloquent areas. Nevertheless, we believe this study documents the applicability of this approach to metastatic tumors arguably in the most dangerous locations by being deep in the brain in eloquent locations involving critical gray matter structures and white matter tracts.

Conclusions

A subset of metastatic brain tumors occurs in deep-seated locations. Historically patients with these lesions were only offered palliative options including stereotactic needle biopsy, radiation therapy, and medical therapy because aggressive surgical resection was associated with significant morbidity. We demonstrate in the largest single surgeon's experience the use of tubular retractors via transsulcal approaches to deep-seated metastatic brain tumors with exoscopic visualization. This approach can be used to achieve extensive resection with minimal morbidity for arguably the highest risk metastatic brain tumors.

Conflict of Interest
Kaisorn L. Chaichana is a course instructor for NICO BrainPath. The other authors have declared no conflicts of interest for this article.

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