

Complications of stereotactic biopsy of lesions in the sellar region, pineal gland, and brainstem

A retrospective, single-center study

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Abstract

Stereotactic biopsy (STB) is commonly used in the pathological diagnosis of intracranial lesions. The associated complication and mortality rates are low, but few reports with large sample sizes have assessed the complications of STB for lesions in the brain midline.

To evaluate the complications of STB of lesions in the sellar region, pineal region, and brainstem.

This was a retrospective analysis of patients who underwent STB of lesions in the sellar region, pineal region, and brainstem at the Neurosurgery Department, Sixth Medical Center, PLA General Hospital, China, between January 2015 and December 2017. The rates of and possible reasons for surgical complications (including bleeding) and mortality were analyzed.

A total of 145 patients underwent STB of midline brain lesions, including 16 (11.0%) in the sellar region, 18 (12.4%) in the pineal region, and 111 (76.6%) in the brainstem. Successful biopsy of the sellar region, pineal region, and brainstem was achieved in 16/16 (100%), 18/18 (100%), and 107/111 (96.4%) patients, respectively. There were no complications following STB of lesion in the sellar or pineal regions. Complications occurred in 17/111 patients (15.3%) during/after brainstem biopsy, three of whom died (2.7%). The main clinical manifestations were facioplegia, facial pain, changes in blood pressure and heart rate, and difficulty breathing.

STB of lesions in the sellar region, pineal region, and brainstem had a high success rate, but mortality was 2.7%. The occurrence of complications (15.3%) was closely related to the anatomical and functional characteristics of the region biopsied.

Abbreviations: CNS = central nervous system, STB = stereotactic biopsy.

Keywords: biopsy, brain stem, complication, pineal gland, postoperative, sella turcica, stereotactic techniques

1. Introduction

Stereotactic biopsy (STB) using three-dimensional positioning technology is an important method used to obtain histopathological specimens from specific parts of the brain. STB is playing an increasingly important role in the diagnosis of central nervous system (CNS) diseases for two main reasons. First, although imaging techniques have improved rapidly in recent years, many

brain lesions still require a pathological diagnosis because they have similar imaging manifestations. For example, studies have found that a combination of different imaging techniques correctly diagnosed brain diseases in only 63% to 73% of cases.^[1,2] Second, a precise molecular pathological diagnosis is important to predict prognosis and guide accurate treatment. For example, previous investigations found that the 1-year survival rates were 80% and 49%, respectively, for low- and high-grade brainstem gliomas and 93% and 42%, respectively, for low- and high-grade diffuse brainstem gliomas.^[3,4] Furthermore, advances in molecular pathology techniques have led to a new era in the pathological classification of brain tumors. For example, genetic abnormalities such as 1p/19q co-deletion and mutations in isocitrate dehydrogenase and histone H3-K27M are closely related to the prognosis of patients with glioma.^[5] Therefore, obtaining pathological specimens is often an important prerequisite for predicting prognosis and implementing the appropriate treatment strategy.

STB is a reasonably straightforward procedure with advantages over traditional craniotomy that include accurate positioning, minimal trauma and high rate of positive diagnosis. Kongkham et al reviewed more than 100 cases of STB in the literature and found an average disability rate of 4.9% (0.4–17.2%) and a mortality rate of 0–3.3%.^[6] Can et al summarized the results of 512 cases of CT-guided STB and found that the diagnosis rate was 96.7%, with complications in 10 patients (1.6%) and 2 cases of death (0.4%).^[7] Hamisch et al reported permanent and transient neurological deficit rates of 0.7% and

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5.8%, respectively, following STB in 269 patients <18 years old, and no patients died.^[8] In our previous study of 550 patients who underwent STB of brain lesions, the diagnosis rate was 96.6%, bleeding occurred in 13 cases (2.4%) after biopsy, epilepsy occurred in 7 cases (1.2%) during surgery, transient neurological dysfunction manifested in 23 cases (4.2%), and there were no deaths.^[9] Furthermore, STB in elderly patients (≥ 70 years old), many of whom had comorbidities or were receiving anticoagulant medication, was associated with a technical success rate of 99.6%, a pathological diagnosis rate of 97.0%, a transient morbidity rate of 8.3%, a permanent morbidity rate of 3.5% and a mortality rate of 0.4%.^[10] The above data support STB as the first-choice method for obtaining intracranial pathological specimens.

Nevertheless, it is more challenging to biopsy specimens from the deep part of the midline brain, such as the sellar region, pineal region, and brainstem, than from the superficial part. The sellar region is located in the central part of the middle cranial fossa and includes important structures such as the sella turcica, sphenoid sinus, pituitary, cavernous sinus, internal carotid artery, optic nerve, and hypothalamus. The most common clinical symptoms of lesions in this part of the brain are due to compression of surrounding structures and dysfunction of the hypothalamic-pituitary axis. STB often uses the transfrontal approach, which can avoid the surrounding normal structures, although a nasal transsphenoidal approach can also be utilized for biopsy of the sellar region. Only a few case reports have described the biopsy of simple space-occupying lesions in the sellar region. For example, Frighetto et al reported the biopsy of parasellar lesions in 4 patients using the trans-oval foramen approach.^[11]

The pineal gland is located at the top of the diencephalon, and the upper and posterior parts are surrounded by large veins such as the great cerebral vein of Galen and internal cerebral veins, which narrows the window for safe puncture. Compression of a lesion at this site during biopsy can precipitate acute obstructive hydrocephalus, which is a clinical emergency. For example, Quick-Weller et al reported that 6 of 14 patients (42.8%) required postoperative extraventricular drainage to relieve obstructive hydrocephalus after biopsy of the pineal region.^[12]

The brainstem consists of three parts: the midbrain, pons, and medulla. STB of the brainstem generally adopts a transfrontal or transcerebellar approach, depending on the lesion site. Dellaretti et al^[13] compared the complications and diagnosis rates of the transfrontal and transcerebellar approaches and found no significant differences between them. Because the brainstem is an area with the most dense distribution of cerebral nuclei, the risk of complications after STB is higher than that for the sellar or pineal regions. Quick-Weller et al retrospectively reviewed 26 patients who underwent STB of brainstem lesions and found a diagnosis rate of 100%, a surgery-related complication rate of 19.2% and a mortality rate of 3.8%.^[2] Kickingereeder et al performed a meta-analysis of 38 studies including 1480 brainstem biopsies and determined a diagnostic success rate of 96.2%, a complication rate of 7.8%, a permanent disability rate of 1.7% and a mortality rate of 0.9%.^[14]

The aim of this study was to retrospectively review data for patients at our hospital in order to evaluate the diagnosis rate and complications of STB for lesions in the sellar region, pineal region, and brainstem. Furthermore, possible factors influencing the diagnosis rate and complication rate were analyzed.

2. Methods

2.1. Study design and participants

This was a retrospective analysis of consecutive patients who underwent STB at the Department of Neurosurgery, Sixth Medical Center, PLA General Hospital, Beijing, China between January 2015 and December 2017. The inclusion criteria were:

1. imaging examinations identified a space-occupying lesion in the brain;
2. the nature of the lesion was unknown;
3. STB was indicated as a necessary investigation after discussion in the department;
4. the lesion was limited to the sellar region, pineal region, or brainstem and was considered amenable to biopsy;
5. preoperative examinations revealed no surgical contraindications; and
6. the patient and relatives consented to STB.

The exclusion criteria were:

1. additional lesions in other regions of the brain;
2. poor general clinical condition, abnormal blood coagulation or other factors that precluded the use of local anesthesia or general anesthesia; and
3. STB was refused by the patient and relatives.

The study was approved by the Ethics Committee of the Sixth Medical Center. Informed consent for inclusion in the analysis was waived because the study was retrospective.

2.2. STB

In order to maximize the accuracy and safety of the positioning, most patients underwent framed biopsy under local anesthesia. First, the frame of the orientation device was installed, the target was located around the center of the frame, and the positioning plate was placed on the frame (or base ring). A frameless stereotactic-guided biopsy was performed under general anesthesia for patients who could not cooperate with a framed biopsy under local anesthesia. On the day of surgery, markers were placed according to the site of tissue sampling. Metal plates were used as markers for CT scanning, and lipid balls were used for MRI. The markers covered the target lesions and were arranged in a spatially staggered manner so that the three points were not in one plane. CT and MRI scanning and positioning were performed. The imaging data were transmitted to the workstation of the Aero-tech stereotactic surgery planning system. The biopsy target, cranial entry point and biopsy trajectory were designed according to the lesion sites, sizes and shapes determined from three-dimensional imaging. CT or MRI images were used to guide biopsy in all cases. The tissue sampling approach was appropriately designed after three-dimensional reconstruction of the lesions by the computer-assisted stereotactic surgery planning software. The location of skull drilling was determined by the location of the lesions. For lesions in the sellar region, drilling was generally carried out 3 cm from the sagittal suture and in front of the coronal suture (Fig. 1). Drilling at the parietal lobe was usually adopted for lesions in the pineal region (Fig. 2). If the brainstem lesion was located in the midbrain, a transfrontal approach was used with the patient supine: the hole was drilled 1 to 2 cm behind the coronal suture and 3 cm from the midline to ensure that the approach was parallel to the longitudinal axis of the brainstem

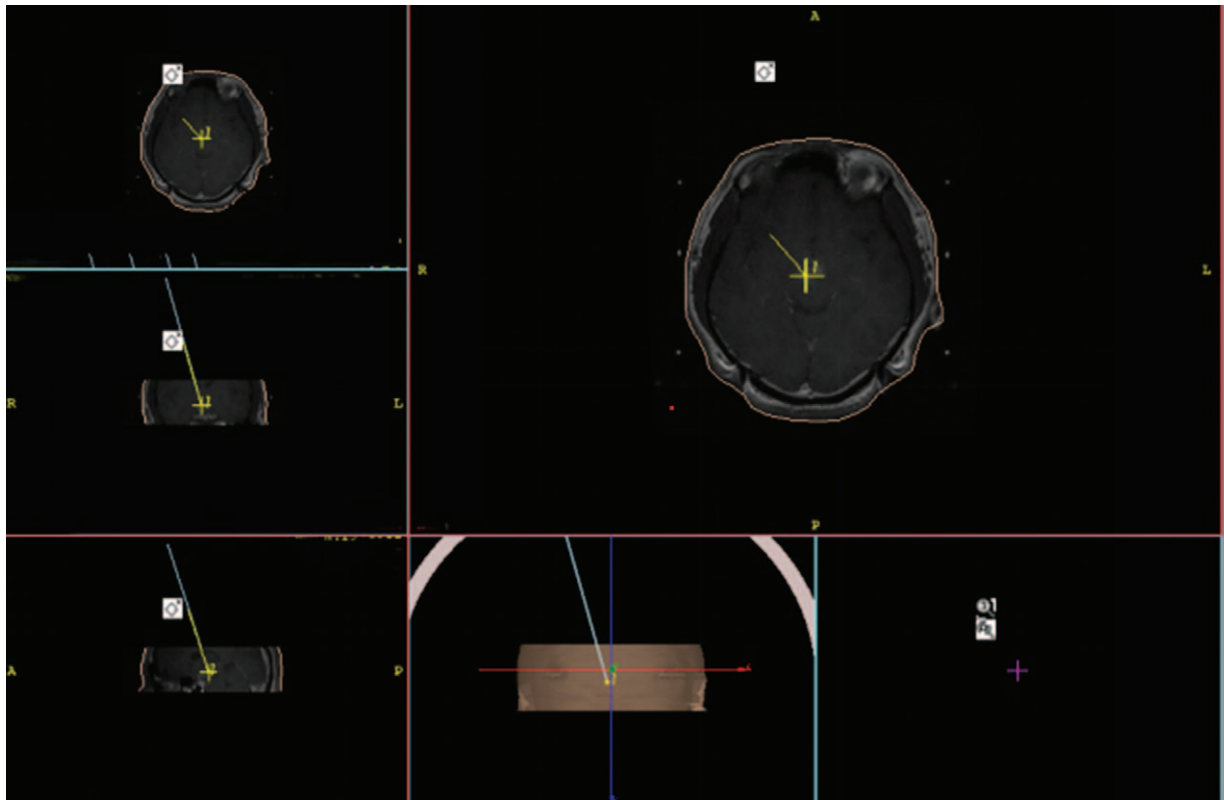


Figure 1. Planning the approach for stereotactic biopsy of a lesion in the sellar region. Generally, drilling was carried out 3 cm from the sagittal suture and in front of the coronal suture.

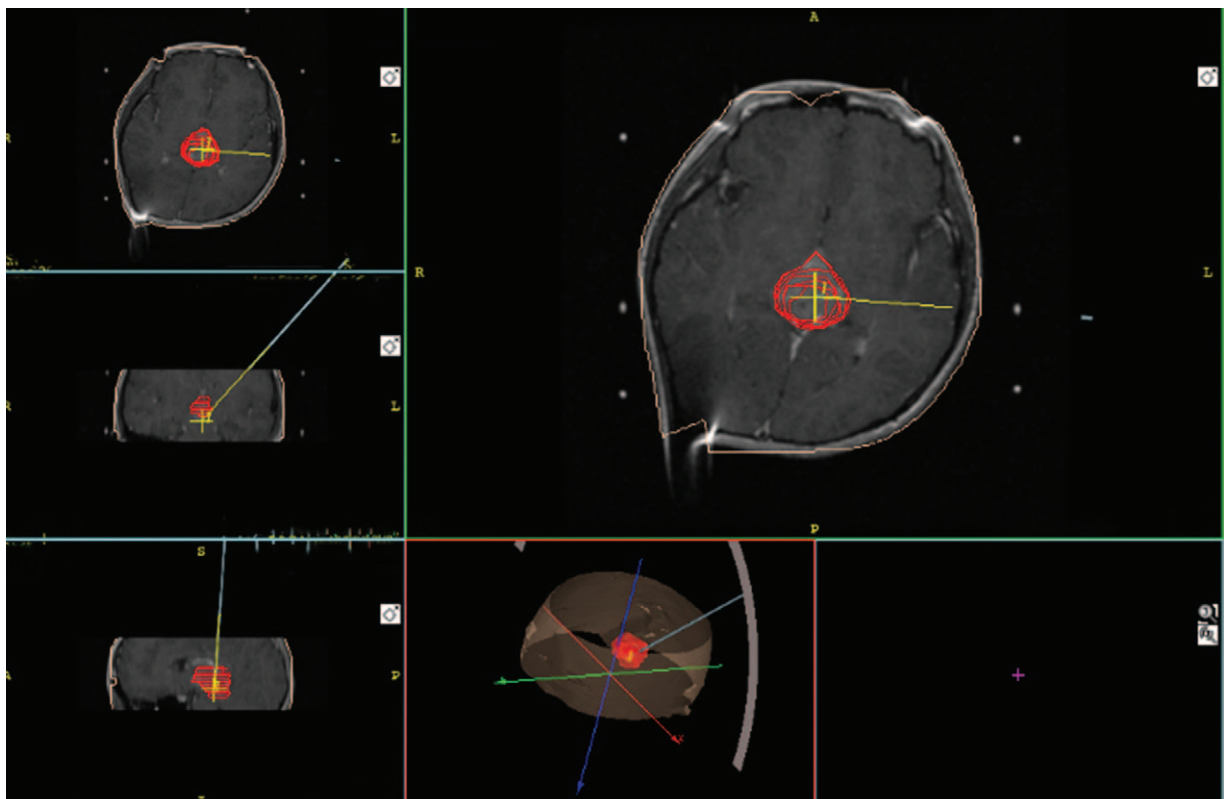


Figure 2. Planning the approach for stereotactic biopsy of a lesion in the pineal region. Generally, drilling was performed at the parietal lobe.

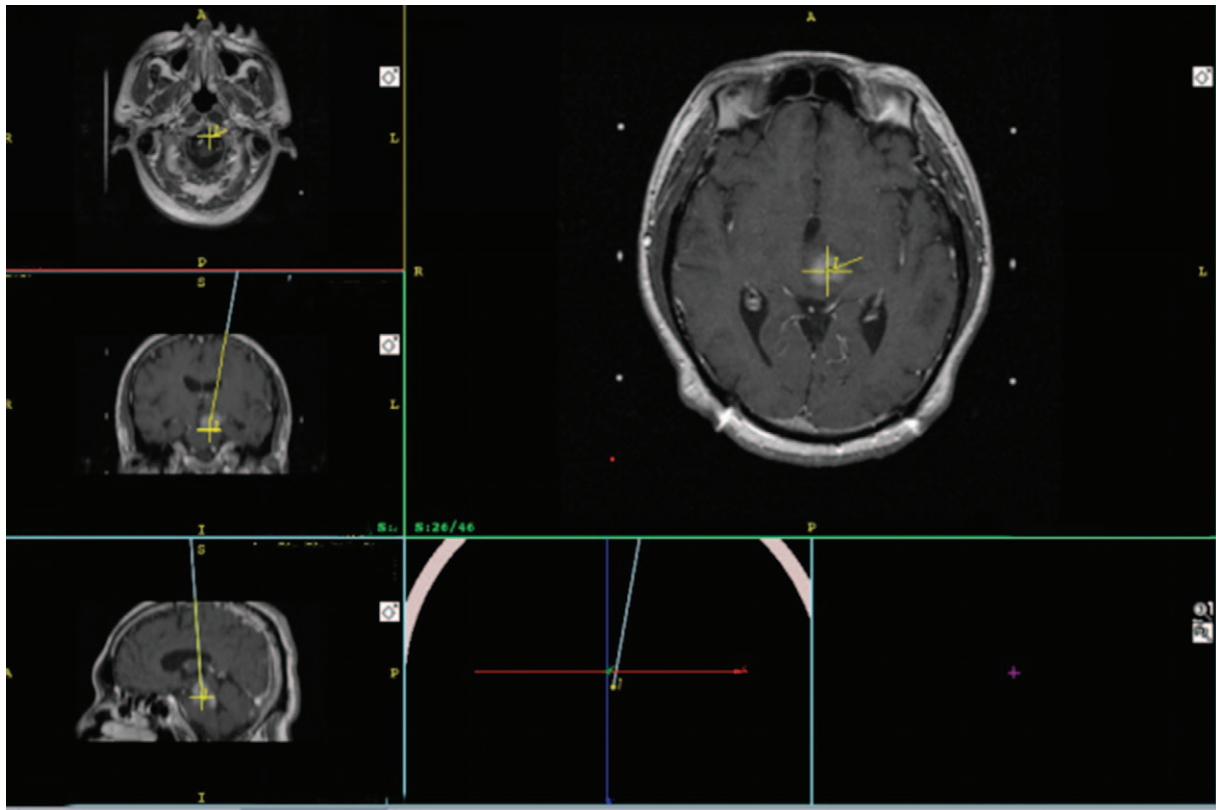


Figure 3. Planning the approach for stereotactic biopsy of a lesion in the midbrain. Generally, a transfrontal approach was used with the patient supine. The hole was drilled 1 to 2 cm behind the coronal suture and 3 cm from the midline to ensure that the approach was parallel to the longitudinal axis of the brainstem.

(Fig. 3). For lesions in the pons and medulla, a transcerebellar posterior cranial fossa approach was generally used with the patient in a seated position: the hole was drilled 3 to 5 cm below the external occipital protuberance and 5 cm from the midline (Fig. 4). All STBs were performed by experienced surgeons with ≥ 3 years of experience of stereotactic clinical work.

2.3. Clinical characteristics and main outcome measures

The following demographic and clinical characteristics were extracted from the medical records: gender, age, clinical symptoms, biopsy results, surgery-related complications, and surgery-related mortality. The main outcomes analyzed were diagnosis rate, incidence of complications and surgery-related mortality.

2.4. Statistical analysis

All data were analyzed using SPSS 19.0 (IBM Corp., Armonk, NY). Data are presented as mean \pm standard deviation or n (%), as appropriate. The chi-squared test was used for statistical comparisons between groups. $P < .05$ was considered statistically significant.

3. Results

3.1. Demographic and clinical characteristics of the study participants

A total of 145 patients (82 males, 56.6%) aged 32.9 ± 20.0 years (range, 3–78 years) were included in the analysis. The mean

disease course was 6.5 ± 11.5 months (range, 0–84 months). The lesion was located in the brainstem in 111 patients (76.6%), the pineal region in 18 patients (12.4%) and the sellar region in 16 patients (11.0%). The demographic and clinical characteristics of the patients stratified by the location of the lesion (sellar region, pineal region, or brainstem) are shown in Table 1.

3.2. Biopsy methods

STB was performed with a frame under local anesthesia in 141 of the 145 patients (97.2%) and without a frame under general anesthesia in 4 patients (2.8%), all of whom were children (aged 3, 5, 5, and 8 years, respectively). Five patients (3.5%) were fitted with a ventriculoperitoneal shunt prior to STB due to hydrocephalus, including three patients with pineal region lesions and two patients with brainstem lesions.

3.3. Biopsy results

A confirmed pathological diagnosis was obtained in all 16 patients with lesions in the sellar region (i.e., a diagnosis rate of 100%). There were seven cases of germ cell tumors (43.8%), two cases of glioblastoma (12.5%), 2 cases of anaplastic astrocytoma (12.5%), two cases of Langerhans cell histiocytosis (12.5%), one case of metastatic tumor (6.3%), one case of diffuse large B-cell lymphoma (6.3%), and one case of CNS vasculitis (6.3%).

A diagnosis rate of 100% was also achieved for the 18 patients with lesions in the pineal region. There were nine cases of germ cell tumors (50.0%), three cases of anaplastic astrocytoma (16.7%), two cases of pineoblastoma (11.1%), one case of

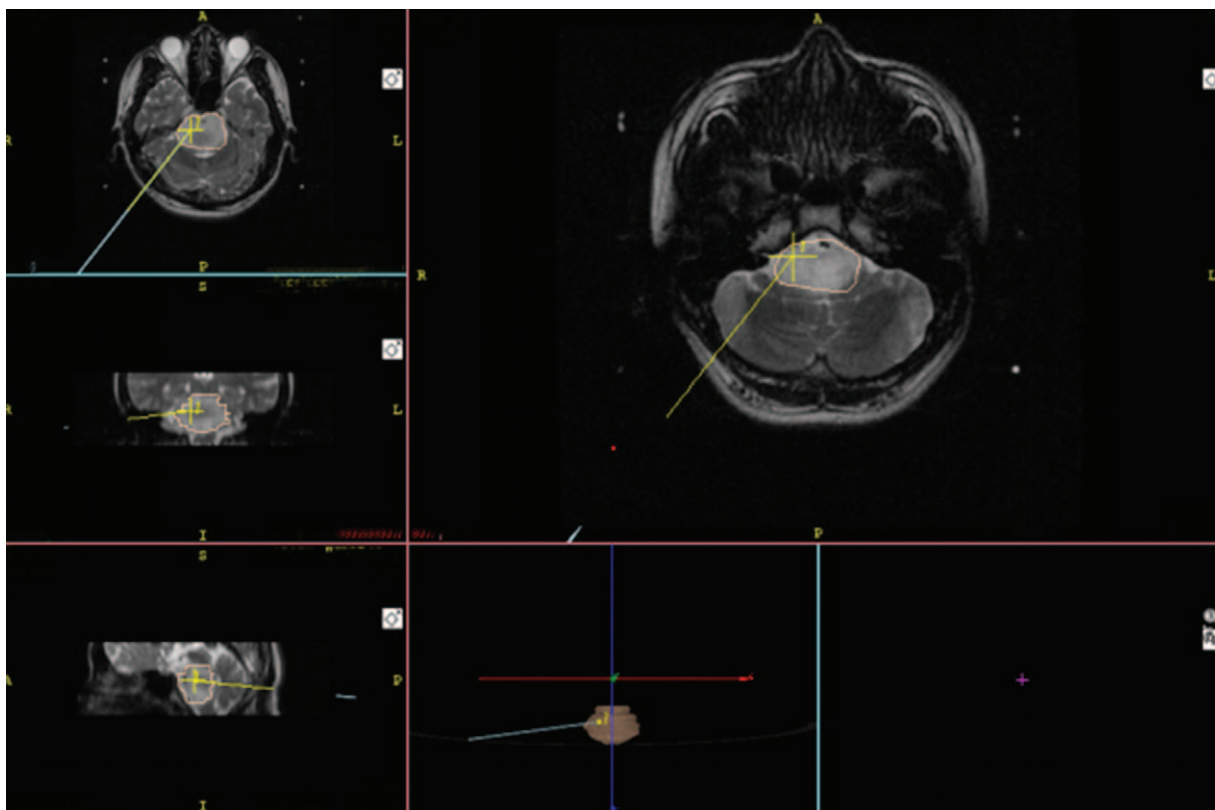


Figure 4. Planning the approach for stereotactic biopsy of a lesion in the pons or medulla. Generally, a transcerebellar posterior cranial fossa approach was used with the patient in a seated position. The hole was drilled 3 to 5cm below the external occipital protuberance and 5cm from the midline.

Table 1
Demographic and clinical characteristics of the study participants.

Characteristic	Sellar region (n = 16)	Brainstem (n = 111)	Pineal region (n = 18)
Gender			
Male	11 (68.8%)	58 (52.2%)	12 (66.7%)
Female	5 (31.3%)	53 (47.8%)	6 (33.3%)
Age (years), mean ± SD	33.7 ± 20.6	32.7 ± 20.1	33.9 ± 20.4
Age (years), range	10–73	3–78	11–68
Disease course (months), mean ± SD	8.9 ± 15.1	6.2 ± 11.3	5.7 ± 8.8
Disease course (months), range	0.5–60	0.17–84	0–30
Symptoms			
Headache/dizziness	5 (31.3%)	39 (35.1%)	9 (50.0%)
Diplopia	0 (0%)	20 (18.0%)	6 (33.3%)
Tinnitus	0 (0%)	0 (0%)	1 (5.6%)
Memory loss	0 (0%)	0 (0%)	1 (5.6%)
Unstable walking	0 (0%)	28 (25.2%)	1 (5.6%)
Polydipsia/polyuria	4 (25.0%)	0 (0%)	1 (5.6%)
Limb weakness	0 (0%)	34 (30.6%)	1 (5.6%)
Somnolence	3 (18.8%)	0 (0%)	0 (0%)
Visual disturbance	5 (31.3%)	0 (0%)	0 (0%)
Amenorrhea	1 (6.3%)	0 (0%)	0 (0%)
Limb muscle spasm	1 (6.3%)	0 (0%)	0 (0%)
Dysphagia/hoarseness	0 (0%)	16 (14.4%)	0 (0%)
Facial numbness	0 (0%)	9 (8.1%)	0 (0%)
Strabismus	0 (0%)	5 (4.5%)	0 (0%)
None	0 (0%)	3 (2.7%)	1 (5.6%)

Data are presented as n (%) unless otherwise stated. SD=standard deviation.

glioblastoma (5.6%), one case of choriocarcinoma (5.6%), 1 case of metastatic tumor (5.6%), and one case of diffuse large B-cell lymphoma (5.6%).

STB was successful in 106 of the 111 patients with brainstem lesions (96.4%), whereas pathological specimens could not be obtained from the remaining four patients (3.6%). Among the 106 confirmed diagnoses, there were 43 cases of diffuse astrocytoma (40.6%), 22 cases of anaplastic astrocytoma (20.8%), 8 cases of diffuse midline glioma (7.6%), 8 cases of low grade glioma (7.6%), 7 cases of glioblastoma (6.6%), 5 cases of diffuse large B-cell lymphoma (4.7%), 2 cases of T-cell lymphoma (1.9%), 2 cases of gliocyte hyperplasia (1.9%), 1 case of high-grade glioma (0.9%), 1 case of glioma (0.9%), 1 case of metastatic tumor (0.9%), 1 case of epidermoid cyst (0.9%), 1 case of a demyelinating lesion (0.9%), 1 case of reactive tissue hyperplasia after radiotherapy (0.9%), 1 case of an inflammatory lesion (0.9%), 1 case of amyloidosis (0.9%), 1 case of necrosis (0.9%), and 1 case of normal brain tissue (0.9%).

3.4. Surgical complications

Neurological complications occurred during or after biopsy in 17 of the 111 patients who underwent brainstem biopsy (15.3%), and three of these patients died (2.7%). The main clinical manifestations of the complications were facioplegia, facial pain, changes in blood pressure and heart rate, and difficulty breathing (see Table 2 for details). No neurological complications occurred in patients who underwent STB of lesions in the pineal region or sellar region.

Table 2
Complications of stereotactic biopsy of brainstem lesions.

No.	Gender	Age	Lesion position	Anesthesia method	Puncture approach	Clinical symptoms	Pathology diagnosis	Complications
1	Female	62 years	Pons	Local anesthesia	Trans-occipital	Insomnia and headache for 4 months, left limb weakness for >2 months	NA	The lesion was hard in texture. No specimen obtained. Headache during surgery was relieved after surgery
2	Male	27 years	Pons	Local anesthesia	Trans-occipital	Intermittent diplopia for 1 year, left limb weakness for >6 months	NA	Nausea and vomiting occurred after the target was reached, so surgery was terminated
3	Female	11 years	Pons	Local anesthesia	Trans-occipital	Dizziness, headache and left limb weakness for 1 month	NA	The head moved after the target was reached, and the patient was unable to cooperate, so surgery was terminated
4	Male	50 years	Pons	Local anesthesia	Trans-occipital	Dizziness and unstable walking for 2 years	Anaplastic astrocytoma	Facial paralysis and facial numbness occurred after surgery
5	Male	7 years	Pons	Local anesthesia	Trans-occipital	Leukemia for >1 year, space-occupying lesion in brainstem found after 10 months	Low grade glioma	Left facial paralysis occurred after surgery
6	Male	8 years	Pons	Local anesthesia	Trans-occipital	Left eye esotropia for 3 months, unstable walking for 1 month	Diffuse astrocytoma	Facial pain occurred during surgery, and facial paralysis worsened after surgery
7	Female	11 years	Pons	Local anesthesia	Trans-occipital	Right facial paralysis for 2 months	Anaplastic astrocytoma	Facial pain occurred during surgery but gradually subsided after surgery
8	Female	29 years	Pons	Local anesthesia	Trans-occipital	Headache and left limb paralysis for 2 years, diplopia for 7 months	Diffuse astrocytoma	Facial paralysis and facial numbness after surgery
9	Female	43 years	Pons	Local anesthesia	Trans-occipital	Swallowing difficulty for >6 months, diplopia for 4 months	Anaplastic astrocytoma	Nausea and vomiting occurred the day after surgery, but the symptoms improved after treatment
10	Female	42 years	Pons	Local anesthesia	Trans-occipital	Dizziness and nausea for 3 months, left tinnitus for 2 weeks	Diffuse astrocytoma	Vomiting and dizziness occurred during surgery
11	Female	61 years	Pons	Local anesthesia	Trans-occipital	Dizziness for 1 month, nausea for 2 weeks	Lymphoma	Headache, dizziness and vomiting occurred during surgery, but the symptoms improved after treatment
12	Male	37 years	Pons	Local anesthesia	Trans-occipital	Dysarthria for 2 months	Diffuse astrocytoma	Blood pressure and heart rate increased and breathing was difficult during surgery
13	Male	5 years	Pons	General anesthesia	Trans-frontal	Unstable walking for 3 months	Gliocyte hyperplasia	Cardiac arrest occurred during surgery, but the patient was successfully resuscitated
14	Female	57 years	Pons	Local anesthesia	Trans-occipital	Unstable walking and blurred vision progressively worsening over 4 years, alalia for 1 year	Diffuse astrocytoma	Cardiac arrest occurred 3 days after surgery, but the patient was successfully resuscitated
15	Male	35 years	Pons	Local anesthesia	Trans-occipital	Unstable walking for 1 week	Glioblastoma	Intraoperative hemorrhage into the ventricle resulted in coma, and the patient died 21 days after surgery
16	Male	8 years	Pons	Local anesthesia	Trans-occipital	Limited movement of the left eye for 4 months	Anaplastic astrocytoma	The surgical area showed gradual swelling, and the patient died 18 days after surgery
17	Female	17 years	Pons	Local anesthesia	Trans-frontal	Blurred vision for 3 months	Anaplastic astrocytoma	The patient died due to cerebral hernia 3 days after surgery

3.5. Factors associated with STB-related complications

Patients with and without complications related to brainstem biopsy showed no significant differences in age, gender, or puncture approach (Table 3).

4. Discussion

Notable findings of this single-center retrospective analysis were that STB yielded a pathological diagnosis in all patients with lesions in the sellar or pineal regions and about 96% of patients

Table 3
Analysis of factors potentially associated with complications of brainstem biopsy.

Factor	No complications	With complications	P
Age			.94
≤18 years	31 (33.0%)	6 (35.3%)	
19–60 years	49 (52.1%)	9 (52.9%)	
≥61 years	14 (14.9%)	2 (11.8%)	
Gender			.64
Male	50 (53.2%)	8 (47.1%)	
Female	44 (46.8%)	9 (52.9%)	
Approach			.41
Transoccipital	75 (79.8%)	15 (88.2%)	
Transfrontal	19 (20.2%)	2 (11.8%)	

The P-value was determined using the chi-squared test.

with lesions in the brainstem. Furthermore, STB was not associated with any neurological complications in patients with lesions in the sellar or pineal regions. However, neurological complications occurred in around 15% of patients who underwent brainstem biopsy, and the mortality rate was 2.7%. Age, gender, and puncture approach were not associated with neurological complications in patients who underwent biopsy of the brainstem. Taken together, our findings indicate that STB of lesions in the brain midline is associated with a complication rate of 15.3% and a mortality rate of 2.7%, although it is possible that the added challenges of brainstem biopsy may result in higher complication and mortality rates than those seen for biopsy of the sellar or pineal regions.

The sellar region, pineal region, and brainstem are among the most important deep brain structures. STB is an important method for the definitive diagnosis of cases that cannot be diagnosed by imaging examinations. Since only selected cases undergo STB, the frequencies of the various lesion types identified by STB inevitably differ from the overall prevalence data. In particular, uncommon diseases are disproportionately represented in pathological diagnoses made using STB. For example, the most common sellar lesion is pituitary adenoma in adults and craniopharyngioma in children.^[15] In contrast, germ cell tumor was the most common lesion of the sellar region in our cohort of patients (43.8%) followed by glioma (25.0%). Although germ cell tumors account for only about 5% of all primary intracranial tumors, they occur more commonly in the sellar and pineal regions,^[16] likely explaining why germ cell tumors represented about 47% of all lesions in the sellar and pineal regions in our study.

A confirmed pathological diagnosis was obtained in all 16 cases of sellar region lesions and all 18 cases of pineal region lesions, and the diagnosis rate was 96.4% (107/111) in patients with brainstem lesions. There are very few published reports describing the biopsy of lesions in the sellar region, and the present research contains the largest number of cases of sellar region biopsy described in a primary study to date. Our diagnosis rate is in agreement with that reported by Frighetto et al, who successfully achieved biopsy and diagnosis in all four of their patients with parasellar lesions.^[11] With regard to lesions in the pineal region, previous studies were able to obtain a pathological diagnosis in 100%^[12] and 98.9%^[17,18] of patients. Furthermore, two reviews of the literature indicated that successful biopsy was achieved in 94% (86–100%)^[19] and 93.7% (82–100%)^[20] of cases involving pineal region lesions. Therefore, our diagnosis

rate of 100% for STB of the pineal region is consistent with the high rates reported previously. Our biopsy success rate for brainstem lesions (96.39%) also concurs with data in the literature. For example, previous studies have reported diagnosis rates of 93.3%,^[21] 95.8%,^[22] 96.6%,^[23] and 100%.^[2] Furthermore, a meta-analysis of 38 studies including 1480 procedures reported a diagnostic success rate of 96.2%,^[14] while another meta-analysis of 18 research reports with 735 pediatric patients determined a biopsy success rate of 96.1%.^[24] We believe that the high diagnostic rate in our patients was in part due to the adoption of a stereotactic frame whenever possible, which maximizes the accuracy. Lu et al compared the results of 288 biopsies and found that the diagnosis rates with a frame, without a frame and with intraoperative nuclear magnetic positioning were 96.9%, 91.8%, and 89.9%, respectively.^[25] Although other studies concluded that the use of a frame did not significantly affect biopsy success rate or safety,^[26,27] these studies did not investigate deep brain lesions. Because the approach for deep brain lesions is longer than that for cerebral cortex, the error rate would be expected to be higher. Indeed, the probability of successfully obtaining tissue from deep brain lesions was 2.7 times lower than for the cerebral cortex.^[27] However, an important disadvantage of stereotactic frames is that the patient cannot receive endotracheal intubation, precluding general anesthesia. Thus, a stereotactic frame cannot be used in patients unable to cooperate during local anesthesia (e.g., young children). Therefore, we used a stereotactic frame as standard, except in patients who could not cooperate with surgery under local anesthesia.

The most common complication of STB is bleeding, which can be classified into three categories. The first category includes bleeding caused by incision of the skin, cranial drilling, and incision of the dura mater. This category of bleeding is usually visible and controllable, so it generally does not have a notable impact on the safety of the biopsy procedure. The second category includes bleeding caused by damage to micro-vessels in brain tissue as the puncture needle is advanced toward the target. This category of bleeding is not controllable and is difficult to visualize because the path of the needle after its insertion cannot be directly observed and because existing CT and because MRI methods cannot display the relatively small blood vessels that are damaged by a puncture needle. In order to minimize such bleeding, the cerebral gyrus (which has a relatively sparse distribution of blood vessels) is selected as the cranial entry point during the design of the approach, and the needle is inserted slowly. The third category includes bleeding at the target site during aspiration of the specimen. This category of bleeding is closely related to the pathological features of the lesion. Compared with normal brain tissue, malignant tumors tend to have higher rates of bleeding and necrosis due to rapid tumor growth and abnormalities in the structure of the blood vessel walls, which increases the risk of bleeding during biopsy. The risk of this type of bleeding can be reduced by initially using a relatively small negative pressure during specimen collection and then gradually increasing the negative pressure according to the specific texture of the tumor. In our cohort, 1 patient with glioblastoma died during biopsy due to bleeding in the surgical area. Preoperative MRI of this patient indicated that the tumor showed evidence of hemorrhagic necrosis (Fig. 5), which likely increased the risk of bleeding. We suggest that particular attention should be paid to the risk of bleeding during biopsy in patients with evidence of hemorrhagic necrosis of the lesion.

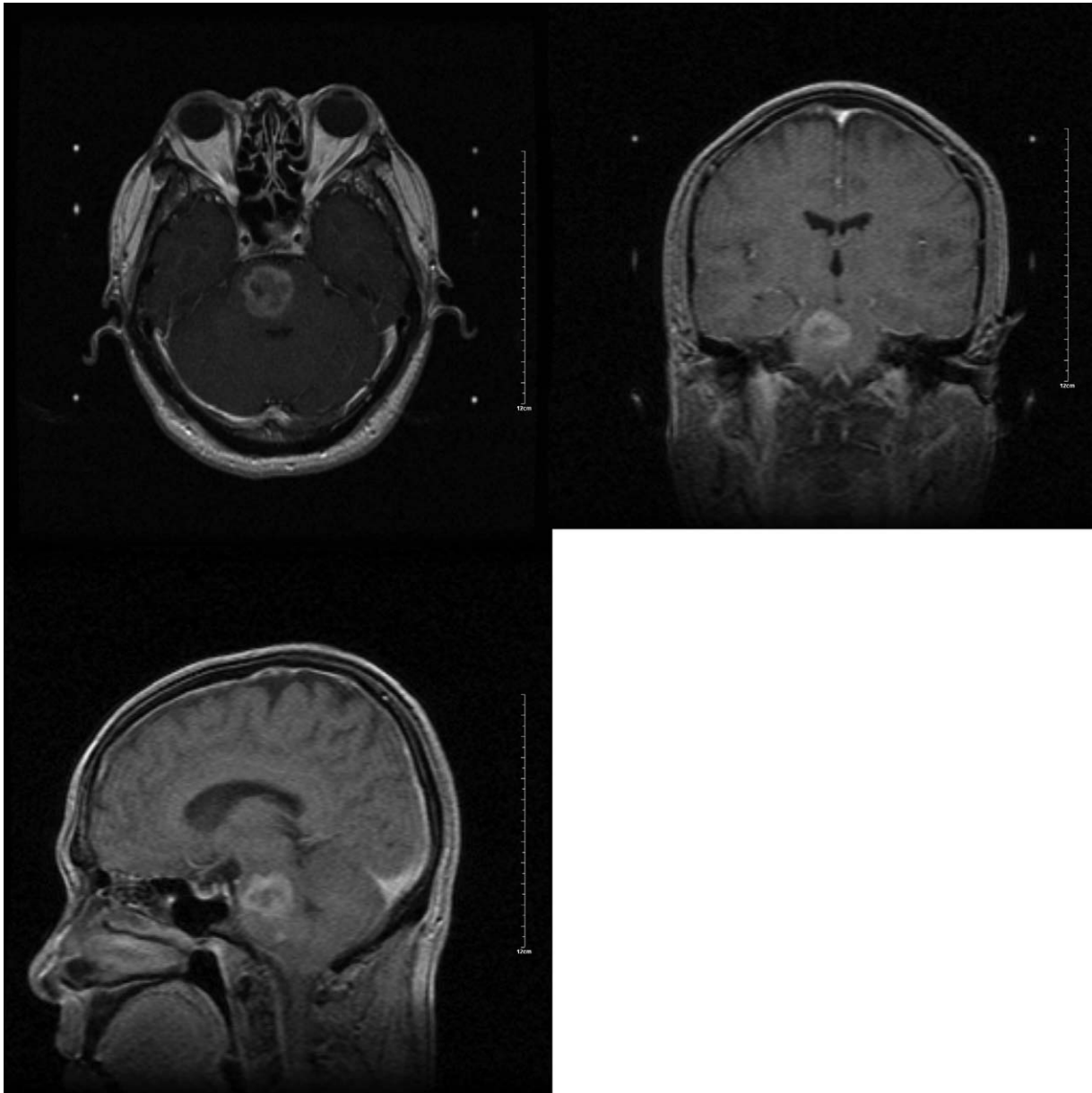


Figure 5. Preoperative MRI of a patient with glioblastoma showing evidence of hemorrhagic necrosis within the lesion. This patient died during biopsy due to bleeding in the surgical area.

Nonetheless, STB is considered a safer procedure than craniotomy. Motiei-Langroudi et al analyzed data from 48 patients with pineal tumors and found that the perioperative mortality and disability rate were 4.3% and 0%, respectively, in patients who underwent biopsy and 32.0% and 4.0%, respectively, in patients who underwent craniotomy.^[28]

The occurrence of complications is related to the anatomical characteristics of the lesion site. In the present study, there were no neurological complications in patients who underwent STB of the sellar region, which would be consistent with previous data.^[11] However, the risk of biopsy of the pineal region is considered higher than that of the sellar region. The complication and mortality rates for STB of the pineal region have been reported to be, respectively, 8% and 1.3%,^[17] 6.8% and 0%,^[18] and 0–14% and 0–1.9% (meta-analysis).^[19] There are two main

features underlying the higher risks for pineal lesions. First, lesions in the pineal region are closely surrounded by numerous blood vessels including the deep brain veins. Since the tentorium cerebelli prevents access via the superior and lateral aspects, the window for safe puncture is limited, which increases the risk of biopsy in the pineal region. Indeed, endoscopic direct biopsy is often used for this region as a way to improve safety.^[29] Second, obstructive hydrocephalus is prone to occur with space-occupying lesions of the pineal region. If drainage and shunting of the lateral ventricle is not performed before STB, there is a risk that bleeding or edema due to biopsy could result in life-threatening hydrocephalus. Indeed, Quick-Weller et al reported that 42.8% of their patients with pineal lesions required a ventriculoperitoneal shunt.^[12] In the present study, 5 patients underwent ventriculoperitoneal shunting before STB due to

hydrocephaly (3 patients with pineal region lesions and 2 patients with brainstem lesions), and STB resulted in no complications.

Glioma is the most common malignant tumor in the brainstem and is difficult to control effectively with surgery. STB of the brainstem is an important way of obtaining pathological specimens and thus guiding subsequent treatment. A meta-analysis of 18 studies including 735 procedures reported an overall morbidity rate of 6.7%, a permanent morbidity rate of 0.6% and a mortality rate of 0.6%.^[24] Another meta-analysis of 293 adults and children with brainstem lesions found that the incidence of short-term and permanent neurological deficits after STB was 4% and 1%, respectively, and the mortality rate was 0.3%.^[30] A third systematic review and meta-analysis obtained rates of 7.8% for overall morbidity, 1.7% for permanent morbidity and 0.9% for mortality.^[14] Comparable results have been reported by others.^[2,21–23,30] In the present study, all complications occurred in patients with brainstem biopsy. Among those with brainstem lesions, there were 17 cases (15.3%) of neurological complications, and 3 of these patients (2.7%) died. The main clinical manifestations (facioplegia, facial pain, changes in blood pressure/heart rate, and difficulty breathing) relate to the dense distribution of functional nuclei and tracts in the brainstem, which are difficult to completely avoid during the design of the ideal puncture path. We further found that age, gender, and puncture path showed no significant association with the incidence of biopsy complications. Of relevance to our findings, previous analyses showed that biopsy approach (transfrontal vs transcerebellar), age and number of biopsies had no effects on outcome^[24] and that approach (frontal vs trans-cerebellar) and anesthesia type (local versus general) did not exhibit differences with regard to complications.^[2]

Of course, STB has its limitations. The most important of these is that the pathological specimens obtained are limited, which may affect the rate and accuracy of diagnosis. For example, relatively few pathological specimens were obtained for some of our patients, and this prevented establishment of the precise pathological grade or type. Importantly, the brainstem biopsies represented the majority of the patients. The groups of patients with saddle or pineal gland biopsies were small, and the conclusions might be limited regarding those patients. Nevertheless, since the brainstem, pineal gland, and saddle are all located in the same brain region, the approaches to biopsy those three structures are basically the same, and this is why the complications were analyzed together.

In conclusion, STB of lesions in the sellar region, pineal region, and brainstem had a high success rate, but mortality was 2.7%. The occurrence of complications (15.3%) was closely related to the anatomical and functional characteristics of the region biopsied. Proficiency in stereotactic techniques and detailed knowledge of the anatomical features of each site are important prerequisites for ensuring the safety of biopsy.

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