Frameless robot-assisted stereotactic biopsies for lesions of the brainstem—a series of 103 consecutive biopsies

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Abstract
Purpose Targeted treatment for brainstem lesions requires above all a precise histopathological and molecular diagnosis. In the current technological era, robot-assisted stereotactic biopsies represent an accurate and safe procedure for tissue diagnosis. We present our center’s experience in frameless robot-assisted biopsies for brainstem lesions.
Method We performed a retrospective analysis of all patients benefitting from a frameless robot-guided stereotactic biopsy at our University Hospital, from 2001 to 2017. Patients consented to the use of data and/or images. The NeuroMate® robot (Renishaw™, UK) was used. We report on lesion location, trajectory strategy, histopathological diagnosis and procedure safety.
Result Our series encompasses 96 patients (103 biopsies) treated during a 17 years period. Mean age at biopsy: 34.0 years (range 1–78). Most common location: pons (62.1%). Transcerebellar approach: 61 procedures (59.2%). Most common diagnoses: diffuse glioma (67.0%), metastases (7.8%) and lymphoma (6.8%). Non conclusive diagnosis: 10 cases (9.7%). After second biopsy this decreased to 4 cases (4.1%). Overall biopsy diagnostic yield: 95.8%. Permanent disability was recorded in 3 patients (2.9%, all adults), while transient complications in 17 patients (17.7%). Four cases of intra-tumoral hematoma were recorded (one case with rapid decline and fatal issue). Adjuvant targeted treatment was performed in 72.9% of patients. Mean follow-up (in the Neurosurgery Department): 2.2 years.
Conclusion Frameless robot-assisted stereotactic biopsies can provide the initial platform towards a safe and accurate management for brainstem lesions, offering a high diagnostic yield with low permanent morbidity.

Keywords Brainstem · Frameless · Robot · Stereotactic · Biopsy · Case series

Introduction
Brainstem lesions are a rare and very heterogeneous group of tumors, comprising 10% of brain tumors in the pediatric population [1] and 1–2% in adults [2]. Specific multimodal treatment for these lesions remains challenging, even in the current era of consistent progress in microsurgery and therapeutic advances. A precise histopathological and molecular diagnosis is thus the first step towards a targeted therapy.

Surgical robotics represent an important technological innovation [3], increasing the possibility of accurate and safe procedures. Used in a variety of surgical specialties robotics have integrated the surgeon’s armamentarium, opening new avenues for diagnostics and treatment.

Since first described in 1988 [4], stereotactic cerebral biopsies using a robotic system have rendered possible the targeting of deep seated lesions. In our center the robotic...
system (Neuromate® robot, Renishaw, Gloucestershire, UK) has been used continuously since 1998, in a variety of procedures, as already described by multiple studies, such as deep brain stimulation [5], stereo-electroencephalography (SEEG) [6], intracranial catheter placement [7] or high accuracy biopsies [8]. Stereotactic brainstem biopsies have been described as an alternative to open biopsies for these deep-located lesions, either using frame-based [9–11] of frameless systems [12, 13]. Robot-assisted stereotactic biopsies allow a supplementary increase in accurate sampling and increase in technical ease and safety [8, 14–17].

We present our center’s experience in performing frameless robot-assisted biopsies for lesions of the brainstem.

Methods

Study design and patient population

We performed a retrospective analysis of all consecutive patients benefitting from a frameless robot-guided stereotactic biopsy at our University Hospital, from January 2001 to December 2017. This allowed the recovery of records for an extended follow-up period.

Included cases presented with a brainstem lesion of unknown entity, requiring a biopsy according to a multidisciplinary neuro-oncology board discussion.

Brainstem lesions were defined on prior diagnostic cerebral MRI as involving the mesencephalon (tectum or tegmentum), crus cerebri, pons or medulla oblongata. Lesions occurring in the middle cerebellar peduncle, extending into the cerebellum or in the diencephalon were excluded. There were no exclusion criteria based on age.

All patients have given written informed consent for the procedure and use of anonymized data and/or images. This research study was conducted retrospectively from data obtained for clinical purposes. Our study met the criteria for ethical approval: n° IRB00011687 (IRB of the French College of Neurosurgery). This case series has been reported in line with the PROCESS Guideline [18].

Frameless robot-assisted biopsy technique

The Neuromate® robot (Renishaw, Gloucestershire, UK) was used in all cases. Complete procedure consisted of four stages: fiducial marker placement, cerebral MRI, trajectory planning and frameless robot-assisted stereotactic biopsy.

Fiducial marker placement was performed under local anesthesia in all adult patients. General anesthesia was used for the entire procedure in pediatric patients. Optimal fiducial marker placement requiring a minimal bone fixation was decided according to lesion location and laterality (Fig. 3A, showing fiducial marker necessary instruments).

A T1-weighted 3D Gadolinium-enhanced thin-sliced (≤ 1 mm) cerebral MRI was acquired, using a mounted microscope satellite on the fiducial marker, associated, if necessary, with other MRI sequences.

Trajectory planning was performed after image transfer towards the Neuromate® robot’s computer, using the VoXim® program. Optimal target depended on tumor borders, neighboring anatomic structures (vascular or functional brainstem areas) and lesion enhancement. Final trajectory was planned in double obliquity (trajectory axis from anterior to posterior and from lateral to medial), either transcerebellar (Fig. 1) in lesions extending from the medulla and in the majority of pontine lesions, while the transfrontal (Fig. 2) intraparenchymal or transventricular was chosen in mesencephalic or pontine lesions extending in the mesencephalon (bi-compartmental lesions).

Biopsy procedure was performed under general anesthesia in all patients, using the Neuromate® head-pin fixation system (Fig. 3). Coregistration of patient position in the robot head holder with the patient’s cerebral MRI was achieved using the ultrasound emitter tool specific to this device and the fiducial cranial marker previously placed (Fig. 3B, C). A laser verification trajectory was then performed to verify accuracy of coregistration, using the robotic system’s dedicated laser holder.

Biopsy was performed in a step-wise fashion, with continuous computer input of the Sedan-Valliccioni side-cut needle advancement to the planned target. Specimens were acquired in a circular (rosette) pattern, at different depth levels to acquire pathologic samples for analysis (fresh and in formalin fixed containers).

A biopsy was considered positive if acquired specimens resulted in a diagnosis based on histology analysis and/or molecular markers.

Data acquisition

A patient database was retrospectively created. Patient files were recovered from the Neurosurgical, Pathology and Neuro-oncology Departments, for complete records concerning demographics, lesion location, trajectory choice, histopathological diagnosis, treatment and follow-up.

All patients biopsied between January 2001 and December 2017 were included in final data analysis. There were no exclusion criteria based on age at the time of biopsy.

Statistical analysis

Statistical analysis was performed in the Biostatistics Department of our University Hospital, using the Statistical Analysis Software® (SAS Institute Inc., version 9.4). Quantitative variables were described using mean ± SD (standard deviation) or the median if non-Gaussian...
distribution was observed. Distribution normalization was verified with the Shapiro–Wilk test. Qualitative variables were described using frequencies and percentages.

Localization, trajectory, complications, diagnosis and biopsy accuracy were compared between the adult and pediatric population using the Chi-square distribution or the Fisher test ($p \leq 0.5$).

Results

Our series encompasses 96 patients treated in a 17 years period (January 2001–December 2017), for a total of 103 biopsies.

Demographics

Table 1 describes main demographic data. Mean age at biopsy was 34 years (range 1–78). Biopsies were performed in 31 pediatric patients (<16 years old, 32.3%) and in 65 adults (67.7%).

Most common location was the pontine region, in 64 patients (62.1%), more frequently seen in the pediatric group (23 patients, 74.2%) than in the adult group (41 patients, 56.9%), $p=0.021$. The mesencephalon or/and crus cerebri were involved in 24 patients (23.3%). The medulla oblongata was biopsied in only 1 patient (1%).

Main symptoms and clinical signs at diagnosis (Table 1) were balance impairment, diplopia, motor deficit and facial paresis. Less frequently dysphagia, dysarthria, sensory

Fig. 1 Case example of a transcerebellar trajectory for a pontine diffuse midline glioma: A cerebral MRI with T1 gadolinium sequence in axial, coronal and sagittal views, B trajectory axis view showing direct passage through the middle cerebellar peduncle.
disturbance or signs of intracranial hypertension were described. 68% of patients presented with a combination of three or more symptoms and clinical signs.

**Trajectory**

A transcerebellar—trans middle cerebellar peduncle approach was used in 61 patients (59.2%), with 54 of those patients presenting with a main pontine lesion location. No significant difference was observed between the optimal chosen trajectory in the pediatric versus adult group (p = 0.78).

**Histopathology and diagnostic precision**

Histopathologic diagnosis was achieved in 95.8%. Non conclusive diagnosis was recorded in 10 cases (9.7%) after

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**Fig. 2** Case example of a transfrontal trajectory for a mesencephalic glioma: A cerebral MRI with T1 gadolinium sequence in axial, coronal and sagittal views. B trajectory axis view. C axial view showing the transfrontal trajectory at multiple depths; yellow circle representing the trajectory’s progression, from up to bottom and left column to right column: paraventricular (C₁), lateral to the head of the caudate nucleus (C₂), posterior to the anterior limb of the internal capsule through the internal globus pallidus (C₃), passing the inferior and posterior limit of the thalamus to reach to mesencephalic lesion (C₄ and C₅), through the posterior part of the cerebral peduncle (C₆)
the first biopsy. Non-conclusive diagnosis was reported in 8 cases before the publication of the 2016 WHO classification, suggesting also a certain technical limitation in histopathology. In more detail, of the 10 cases two patients declined a second biopsy (these were followed for 5 and 7 years respectively, suggesting a low-grade component). Two other patients received a diagnosis of inconclusive diagnosis, with no tumoral component; these were followed and had a good outcome at last follow-up. Second biopsy was needed in 6 patients (6.2%), with a cerebral MRI showing the initial biopsy target outside the lesion in only two patients.

Various diagnoses are described (Table 2), most commonly being diffuse glioma (68 patients, 70.8%), metastases (8 patients, 8.3%) and lymphoma (7 patients, 7.3%). Gliomas grade III and IV were the most frequent in their group, with 22 and 26 cases, respectively (23% and 27%, respectively). Overall, gliomas were statistically more frequently diagnosed in the pediatric group (26 patients, 83.9%, p = 0.017). Nine patients (9.4%) presented with a rare histopathologic

### Table 1: Main demographic and clinical presentation data

| Age          | 0–16 years | 17–39 years | 40–69 years | ≥ 70 years |
|--------------|------------|-------------|-------------|------------|
| 31 (32.3%)   | 21 (18.6%) | 40 (41.6%)  | 4 (4.2%)    |            |
| Sex          | F/M        |             |             |            |
| Location     | Mesencephalon |        | Pons         | Medulla Oblongata |
| Main symptoms| (number, %) |             |             | Brainstem (global infiltration) |
| Ataxia       | 24 (46.8%) | 64          | 1           | 7          |
| Motor deficit| 12 (12.5%) |             |             |            |
| Oculomotor disturbance | 13 (13.5%) | | | |
| Sensory deficit | 6 (6.2%)   | | | |
| Dysphagia    | 5 (5.2%)   |             |             |            |
| Intracranial hypertension | 9 (9.4%)  | | | |
| Asymptomatic | 1 (1%)     |             |             |            |
| Other        | 5 (5.2%)   |             |             |            |
| Hydrocephalus| Y/N        | 19 (19.8%)  | 77          |            |
diagnosis for lesions situated in the brainstem: abscess (3 patients, 3.1%), primitive neuroectodermal tumor (PNET, 2 pediatric patients, 2%), cavernoma (1 patient, 1%), hemorrhagic cyst (1 patient, 1%), histiocytosis (1 patient, 1%) and inflammatory lesion (progressive multifocal leukoencephalopathy, 1 patient, 1%).

Since the publication of the 2016 WHO Classification of Tumors of the Central Nervous System [19], histopathology was extended to include systematic genetic analysis, especially for histone mutations. This analysis could be performed in 10 cases, revealing 7 cases of diffuse midline glioma, presenting with a H3.3 (K27M or K28M) mutation, all in the pediatric group.

No statistical difference was found between final histopathology and lesion localization (p = 0.7) or the chosen trajectory (transcerebellar versus transfrontal, p = 0.73).

### Biopsies-related morbidity

Permanent morbidity rate was 2.9% of all performed biopsies (3 patients). Overall morbidity was recorded in 19.4% of cases (Table 3), concerning worsening of existing symptoms (9 patients, 8.7%) or new onset symptoms (11 patients, 10.7%). The most common was oculomotor transitory disorder (10 patients). Of note, a transient deficit was defined by complete resolution of a postoperative symptom during the hospital stay or until first follow-up (usually at 3 months).

All patients presenting with a postoperative complication benefitted from a cerebral scan or MRI, revealing 4 cases of intra-tumoral hematoma (transient symptom worsening in 3 patients).

### Table 2

**Biopsy related details and histopathology**

| Trajectory       | Transcerebellar | Transfrontal |
|------------------|----------------|--------------|
| Patients         | 61             | 42           |
| Postoperative clinical worsening (Yes/No patients, %) | 20 (19.4%)/83 |               |
| Second biopsy (Yes/No patients, %) | 6 (6.2%)/90 |               |
| Anatomopathology (number of patients) | Glioma grade I 3 |                |
|                  | Glioma grade II 17 |               |
|                  | Glioma grade III 22 |              |
|                  | Glioma grade IV 26 |               |
| Midline diffuse glioma (H3K27M) – 7 patients of total glioma diagnosis | Metastases 8 |                |
|                  | Lymphoma 7 |               |
|                  | Abscess 3 |                |
|                  | PNET 2 |               |
|                  | Cavernoma 1 |            |
|                  | Hemorrhagic cyst 1 |            |
|                  | Histiocytosis 1 |           |
|                  | Inflammatory (LEMP) 1 |           |
|                  | Inconclusive result after 2nd biopsy 4 |          |

### Table 3

**Biopsy related morbidity**

| Transient | Definitive |
|-----------|------------|
| Worsening of existing symptoms (n=9) | Oculomotor palsy 2 0 |
|          | Worsening of motor status (hemiparesis, hemiplegia or facial paresis) 3 1 |
| Ataxia 2 0 | |
| Dysphagia 0 1 | |
| New onset symptoms (n=11) | Oculomotor palsy 8 0 |
| Segmental sensory disturbance 1 0 | |
| Hemiplegia 0 1 | |
| Anarthria 1 0 | |

Noteworthy, one death was recorded at day 10 postoperative in a 47 years-old male, due to an intra-tumoral pontine hematoma with important mass effect (transcerebellar approach, ipsilateral to the bleeding, trajectory in the periphery of the hematoma; histopathology had revealed a glioblastoma).

Statistical analysis revealed no difference between complications arising after a transcerebellar or a transfrontal trajectory (p = 0.45).

### Treatment

Postoperative treatment is detailed in Table 4.

Adjuvant targeted treatment was performed in 75 patients (78.1% of patients). Surgery for partial or subtotal resection
was possible in 6 patients (one adult, five pediatric patients, after adjuvant therapy in five cases), all low-grade gliomas (grade I or II WHO), deemed operable due to the presence of an exophytic component. Final operative decision was opted for by a multidisciplinary team, based on the patients’ clinical presentation, young age and biopsies’ results, taking into account a high possibility for clinical and survival benefit.

All surgical approaches were performed in our Neurosurgical Department using either a subtemporal transtentorial approach for mesencephalic lesions (4 patients) or a suboccipital telovelar approach for pontine lesions (2 patients).

Mean follow-up in the Neurosurgery Department was 2.2 years, with a median of 325 days (range 2–4653).

The main endpoint of this study is centered on the impact of frameless robot-assisted biopsies in precision diagnosis and global patient management. Overall survival did not thus represent a secondary endpoint in this study.

Robot-assisted surgery allows accurate and safe interventions, often reducing postoperative risks and shortening burdensome recovery periods. In neurosurgery, robotics expanded the depth of stereotactic and functional neurosurgery, integrating the team as a tool of utmost importance.

Biopsy procedures have been a constant part of the neurosurgical armamentarium, constantly evolving in the last decades. Even more so in the subtle field of brainstem lesions that historically were considered mostly inoperable and related to significant morbidity [20]. In the era of microsurgical techniques, these lesions remain challenging, requiring a precise approach through safe entry zones, in meticulously selected cases [21].

Robot-assisted biopsies can increase the potential of targeting eloquent deep-seated locations with lowered risk of complications and high diagnostic yield. Optimal trajectory planning takes into consideration lesion location, traversing grey and white matter, vessels but also vascular structures (pia layer, ependymal cells, choroid plexus) and ventricle avoidance [22–24].

Table 4  Treatment strategies

| Total (96 patients, %) | Adult / Pediatric |
|------------------------|------------------|
| Surveillance           | 4 (4.2%)         | 3/1                          |
| Surgery                |                  |                              |
| Surgery alone          | 1 (1.0%)         | 1/0                          |
| Surgery followed by    |                  |                              |
| chemotherapy and/or    |                  |                              |
| radiotherapy           | 5 (5.2%)         | 0/5                          |
| Chemotherapy only      | 10 (10.4%)       | 9/1                          |
| Radiotherapy only      | 30 (31.2%)       | 23/7                         |
| Combined radio-chemo-  | 30 (31.2%)       | 19/11                        |
| therapy                |                  |                              |
| Palliative care        | 7 (7.3%)         | 5/2                          |
| Targeted antibiotics   | 2 (2.1%)         | 2/0                          |
| Corticotherapy only    | 4 (4.2%)         | 3/1                          |
| NA                     | 3 (3.1%)         | 0/3                          |

Follow-up

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Discussion

Brainstem lesions have always generated debates from operability to adequate management. In a quest to minimize morbidity safe passageways have been methodically described from the microsurgical point of view, encompassing multiple supra and infratentorial approaches [21, 25–27]. Two stereotactic safe routes to the brainstem have proven their versatility to reach intrinsic brainstem lesions and deserve special consideration: the transcerebellar and the transfrontal routes.

The most frequently used is the transcerebellar approach, automatically linked in our opinion to the more frequent localization of lesions in or extending towards the pontine region. This approach implies an entry point on the surface of the cerebellar hemispheres, navigating the height and width of the middle cerebellar peduncle to reach mainly pontine lesions but also low-hanging mesencephalic or higher bulbar lesions. In our study, this approach was used in 59.2% of cases.

The transcerebellar approach has been described using a stereotactic frame [9, 11, 28, 29] or frameless [14, 16], with favorable results concerning complications, varying from 0% (in small cohorts) to 19.2% for transitory morbidity. Main advantages are related to shorter trajectories, passing through the middle cerebellar peduncle, thus lowering the theoretical risk of hemorrhage. In our study 16.4% of patients (10/66 cases) benefitting from a transcerebellar approach presented a biopsy-related complication, most often transitory balance impairment or motor status worsening. One noteworthy technical advantage of using a stereotactic robot regards the easiness of patient positioning, independent to frame adaptations described for brainstem lesions [29].

This versatile approach is complemented by the transfrontal approach, especially for mesencephalic or rostral pontine lesions. The transfrontal route is planned frequently from a precoronal entry point, navigating between the lateral ventricle, head of the caudate, basal ganglia, and internal capsule (Fig. 2B, C). Despite longer trajectories, the transfrontal approach remains a viable option, with a low rate of complications (in our study, most often diplopia or motor status worsening) [22, 30].
Our study shows no statistical difference in biopsy-related morbidity between the transfrontal and transcerebellar trajectories ($p = 0.45$). Concerning diagnostic yield and biopsy-related morbidity we have compared the present series with previously published studies for robot-assisted biopsies of lesions of the brainstem (Table 5), showing similar rates for diagnosis and morbidity albeit in smaller sample series [12, 14–17, 31].

In their meta-analysis, Kickingereder et al. [32] report that the weighted average proportion calculated by random-effects was 7.8% (95% CI: 5.6%-10.2%) for overall morbidity, 1.7% (95% CI: 0.9%-2.7%) for permanent morbidity, and 0.9% (95% CI: 0.5%-1.4%) for mortality. In an updated meta-analysis for pediatric brainstem tumors, Hamisch et al. [33] report similar results: 6.7% (95% CI 4.2%-9.6%) for overall morbidity, 0.6% (95% CI 0.2%-1.4%) for permanent morbidity, and 0.6% (95% CI 0.2%-1.3%) for mortality. Both studies showed no significant differences between the transcerebellar and transfrontal routes to the brainstem.

**Impact in molecular diagnosis evolution**

In our retrospective study, histopathological diagnosis was achieved in 95.8% of cases, similar to available data. A second biopsy was necessary in 6 patients. Kickingereder et al. [32] reported on 1480 cases of frame-based or frameless stereotactic brainstem biopsies, comprising 38 studies, with a final diagnosis achieved in 96.2%. Interestingly, the authors underlined the need for highly specialized centers to increase diagnostic success, with a significant correlation between diagnostic rates and the number of biopsies performed annually in each center ($p = 0.011$). Additionally, Hamisch et al. [33] reported in their meta-analysis on 18 studies a diagnostic rate of 96.1% in a total of 735 pediatric brainstem biopsies.

Our center’s philosophy is to biopsy all brainstem tumors before discussing appropriate adjuvant treatment. In the era of integrated molecular analysis stereotactic brainstem biopsies could assist in early initiation of targeted therapies, especially in the diffuse intrinsic pontine glioma (DIPG) subgroup with the analysis of histone mutations (e.g., H3.3 K27M) [34]. This has marked an important change in the treatment paradigm of brainstem lesions, from the initial concept of MRI exclusive diagnosis [35] towards precise molecular diagnosis [36–38] and current targeted treatment [39, 40].

Noteworthy, our study did not allow statistical analysis based on molecular diagnosis, covering a long period prior to the integration of molecular biology data.

**Differential diagnosis for brainstem tumors**

In our study we report 68 cases of diffuse glioma, representing 70.8% of the total number of successful biopsies. Brainstem metastasis was confirmed in 8 patients (8.3%) while lymphoma was reported in 7 patients (7.3%). Noteworthy, 9 patients presented with a rare histopathologic diagnosis (Table 2), illustrating the difficulty of radiologic diagnosis solely on cerebral MRI, thus warranting a stereotactic biopsy even in non-tumoral pathologies.

As reported by several studies, a step-wise MRI-based approach could help differentiate between several etiologies, especially tumor-like mimics: infectious and inflammatory lesions, vascular lesions or even uncommon cysts [41–43]. While morphology details can be quickly helpful in some pathologies, differential diagnosis of immune-mediated and inflammatory lesions of the brainstem can remain as elusive as ever. Law et al. proposed integrating essential clinical, biological and radiological data into the differential diagnosis, reviewing a remarkable large spectrum of these disorders based on cerebral MRI findings [41]. Routine cranio-spinal morphology MRI sequences could be coupled with more advanced modalities: PET-CT, MRI spectroscopy and MRI/CT perfusion scans [41, 42, 44].

| Author and publication date | Number of patients (pediatric/adult) | Number of biopsies | Robotic system | Diagnostic yield | Permanent morbidity | Transient morbidity |
|----------------------------|-------------------------------------|--------------------|----------------|------------------|---------------------|-------------------|
| Haegelen et al.* (2010)    | 15 (5/10)                           | 17                 | Neuromate, Renishaw® | 88.2%            | 5.8% (1 patient)    | 11.7% (2 patients) |
| Coca et al. (2016)         | 5 (5/0)                             | 5                  | ROSA, Medtech®      | 100%             | None reported       | None reported     |
| Carai et al. (2017)        | 7 (7/0)                             | 7                  | ROSA, Medtech®      | 100%             | 14.2% (1 patient)   | 14.2% (1 patient) |
| Dawes et al. (2019)        | 11 (11/0)                           | 12                 | Neuromate, Renishaw® | 90.9%            | None reported       | None reported     |
| Gupta et al. (2020)        | 22 (22/0)                           | 23                 | ROSA, Medtech®      | 91.3%            | None reported       | 4.3% (1 patient)  |
| Machetanz et al. (2022)    | 25 (7/18)                           | 26                 | Renaissance, Mazor Robotics® or ROSA, Medtech® | 96.2%            | None reported       | 3.8% (1 patient)  |
| Present series             | 96 (31/65)                          | 103                | Neuromate, Renishaw® | 95.8%            | 2.9% (3 patients)   | 16.5% (17 patients) |

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Accuracy of frameless robot-assisted biopsies

In our series covering a total of 103 biopsies for brainstem lesions a definitive histopathologic diagnosis was reached in 95.8%. Even though a second biopsy was needed in 6 patients, the cerebral MRI performed postoperatively showed a final target outside the lesion in only 2 cases (1.9%). Of these, one pediatric patient benefitted from surgery, revealing a pilocytic astrocytoma while the second patient benefited from repeat biopsy (final diagnosis of grade II glioma).

While multiple studies analyze the feasibility of biopsies for brainstem lesions in a frame-based system or frameless, technical studies recording strict accuracy measures are scarce. In a comparative study, comparable accuracy results between frameless, frame-based or infrared tracked systems, with an average error of 1.95 mm (SD ± 0.44 mm, maximum error 2.69 mm) for frameless robot-assisted biopsies was reported [45]. Interestingly, a statistical difference was noted between frameless and frame-based robotic procedures (p < 0.001), possibly due to the accuracy of the ultrasound tracking technique. Similar results using a frameless robotic system with bone fiducial markers (2.9 mm, range 0.7–3.2) were reported [46].

More specifically, a mean accuracy of 0.81 mm for frame-based robotic surgery versus 0.7 mm for frameless robotic procedures using fiducial markers or 1.22 mm for frameless robotic procedures with surface recognition was reported [47]. Concerning the robotic system used in our series (Neuramate®, Renishaw, UK) an accuracy in a frame-based setting, resulting in an in vivo accuracy of 0.86 ± 0.32 mm and a maximum error of 1.55 mm was measured [48]. Other studies have analyzed biopsy accuracy in a true frameless, navigation-only setting, rendering an accuracy in a range of 4.4–5.4 mm [49] or of 2.3 mm (SD ± 1.9 mm, linear error) and of 4.8 mm (SD ± 2 mm, Euclidean error) [50]. We can thus appreciate the improvement in accuracy brought by the use of robotic systems in neurosurgery, should it be in frame-based or frameless procedures.

Limitations

We acknowledge several limitations in our study. Firstly, it is a retrospective series with data acquisition limited by the 17 years period encompassed in our analysis. Secondly, while it is a monocentric study, patients were referred from other neurosurgical centers and thus were sometimes lost early at follow-up. This was nonetheless not the main focus in our analysis, permitting the inclusion of all consecutive patients for final analysis. Thirdly, improving diagnostic precision should be discussed for deep situated lesions of the brainstem. This could be addressed in a prospective study, using adjuvant intraoperative radiologic techniques (for example, intraoperative O-arm™ needle placement confirmation). Fourthly, histopathology results were limited by the absence of systematic molecular testing prior to the 2016 WHO Classification, limiting our insight into a developing and promising avenue for clinical research.

Conclusion

Frameless robot-assisted stereotactic biopsies can provide the initial platform towards a safe and accurate management for brainstem lesions. This single center series focuses on high diagnostic yield for frameless robot-assisted stereotactic biopsies, complemented by low permanent morbidity.

Author Contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Iulia Peciu-Florianu and Victor Legrand. The first draft of the manuscript was written by Iulia Peciu-Florianu and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data Availability The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical Approval This research study was conducted retrospectively from data obtained for clinical purposes. We consulted extensively with the IRB of College de Neurochirurgie who determined that our study meet the criteria for ethical approval: n° IRB00011687.

Consent to participate Informed consent was obtained from all individual participants included in the study.

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