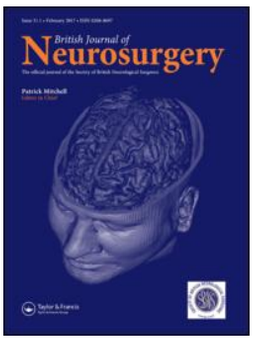

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# A comparison of the efficacy, safety, and duration of frame-based and Remebot robot-assisted frameless stereotactic biopsy

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ORIGINAL ARTICLE



# A comparison of the efficacy, safety, and duration of frame-based and Remebot robot-assisted frameless stereotactic biopsy

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**ABSTRACT**

**Objective:** The aim of this study was to compare the efficacy, safety, and duration of Remebot robot-assisted frameless brain biopsy with those of standard frame-based stereotactic biopsy.

**Patients and methods:** A retrospective analysis of 66 patients undergoing stereotactic brain biopsy in our department from January 2015 to January 2019 was performed. We divided the patients into two groups: the frame-based group ($n = 35$) and the Remebot robot group ($n = 31$). Data on clinical characteristics, total procedure length, overall discomfort, diagnostic yield, complications, and postoperative length of hospital stay were retrospectively reviewed and compared between these two groups.

**Results:** No significant difference in diagnostic yield was detected in the two groups, with frame-based biopsy having a diagnostic yield of 91.4% and Remebot robot-assisted frameless brain biopsy having a diagnostic yield of 93.5%. The duration of the total procedure was 116.5 min for the frame-based biopsy and 80.1 min for the Remebot robot-assisted frameless brain biopsy ($p < 0.001$). There were no statistically significant differences in complication rate or postoperative duration of hospitalization between the two groups. The overall patient discomfort in the frame-based group was significantly greater than that in the Remebot robot group (visual analog scale score $2.7 \pm 1.2$ versus $1.5 \pm 0.7$, $p = 0.001$).

**Conclusions:** Remebot robot-assisted frameless brain biopsy was as efficacious and safe as standard stereotactic frame-based biopsy. However, frameless biopsy can alleviate the suffering of the patient and reduce the total duration of the procedure. Remebot robot-assisted frameless brain biopsy is easy to use and better accepted by patients than frame-based biopsy.

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Brain biopsy; frame-based stereotaxy; frameless stereotaxy; Remebot robot

## Introduction

With the rapid development of neuroimaging techniques, the diagnostic rate of intracranial lesions has significantly improved. Nevertheless, many diseases cannot be definitively diagnosed because of their atypical clinical and imaging features. Thus, frame-based stereotactic biopsy has come to be the 'gold standard' for the diagnosis of brain lesions because it is a minimally invasive and effective procedure.[1]

The preparation for and tissue sampling in frame-based stereotactic biopsy can be performed under local anaesthesia. It is time consuming and an uncomfortable experience for the patient. Therefore, many frameless stereotactic systems have been developed and used, such as the Robotized Stereotactic Assistant (ROSA, Germany) and NeuroArm robot (Canada).[2–4] In our country, we have created another frameless stereotactic system, the Remebot robot system (developed by Beijing Baihuiweikang Technology Company, and approved by the National Medical Products Administrations, China), which consists of one arm with 6 degrees of freedom of movement, one master computer, and one binocular camera. Wang *et al.*[5] showed that robot-assisted surgery using a Remebot is a safe and effective treatment method for haematoma removal and tube drainage in patients with hypertensive intracerebral haemorrhage, and the target error is less than 1 mm. The purpose of this study was to compare the efficacy, safety, and duration of Remebot robot-assisted frameless intracranial biopsy with those of standard frame-based stereotactic biopsy.

## Material and methods

### Patient population

This retrospective study was permitted and sponsored by Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. Between January 2015 and January 2019, we reviewed 66 patients who underwent frame-based or frameless intracranial biopsy at the Department of Neurosurgery, Tongji Hospital. The patients were divided into two groups according to the surgical strategy: the frame-based group and the Remebot robot-assisted frameless group. The clinical data regarding patient age, sex, symptoms, neuroimaging features, outcomes, postoperative complications, and the duration of the operation procedure and hospitalization were retrospectively analysed.

### Surgical techniques

All surgeries were performed by the same neurosurgeon, Professor Kai SHU, Department of Neurosurgery, Tongji Hospital. Thirty-five patients underwent standard frame-based stereotactic biopsy, and 31 patients underwent Remebot robot-assisted frameless brain biopsy.

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For the frame-based stereotactic biopsy procedures, we placed the Leksell-Frame-G stereotactic frame on the patient's head preoperatively under local anaesthesia. Then, a preoperative magnetic resonance imaging (MRI) scan was performed with the frame, and the target was selected. In addition, we determined the target coordinates before the operation. The surgeon used a drill to make a burr hole with a diameter of 1 cm at the predescribed site and inserted a biopsy needle (Sedan side-cutting needle with a diameter of 2.5 mm) into the brain lesion. Finally, after the biopsy specimens were attained using the standard suction-aspiration technique, we sutured and disinfected the wound. All of the above procedures were performed under local anaesthesia.

For the Remebot robot-assisted frameless biopsy, the patients underwent head MRI and some special examinations (diffusion tensor MRI, magnetic resonance venography, magnetic resonance angiography, etc.), if necessary, one or two days before the operation. On the operation day, the surgeon attached three markers to the temple and forehead of the patient, and then computed tomography (CT) scans were performed. All images were copied to the Remebot robot system, and then the entry point, biopsy target and optimal needle trajectory were carefully planned by the surgeon. The patients' heads were immobilized in a Mayfield clamp after general or local anaesthesia. After accurate registration, a burr hole was drilled, and biopsy specimens (Sedan side-cutting needle with a diameter of 2.5 mm) were taken using the standard suction-aspiration technique. Finally, the wound was disinfected and sutured (Figure 1).

### *Statistical analysis*

Statistical analysis was performed using SPSS Statistics 22.0 (IBM Corporation, USA). Data are described as $\bar{x}\pm s$. The intergroup comparison was performed using Student's $t$ test and the $\chi^2$ test. $p < 0.05$ was considered to be statistically significant.

## Results

Baseline characteristics are all shown in Table 1. There were no significant differences in patient age, sex, symptoms and signs, duration of symptoms, localization of the lesion, size of the lesion or the preoperative KPS between the frame-based group and the Remebot robot group.

Table 2 summarizes the histological results from the biopsies of the two groups. The three most common tumour entities encountered were astrocytoma grade II (28.8%), astrocytoma grade III (10.6%), and diffuse large B cell lymphoma (33.3%). Moreover, the diagnosis was incorrect or missed in 3 cases in the frame-based group and in 2 cases in the Remebot robot group. The overall diagnostic yield of this study was 92.4%. There was no statistically significant difference in diagnostic yield between

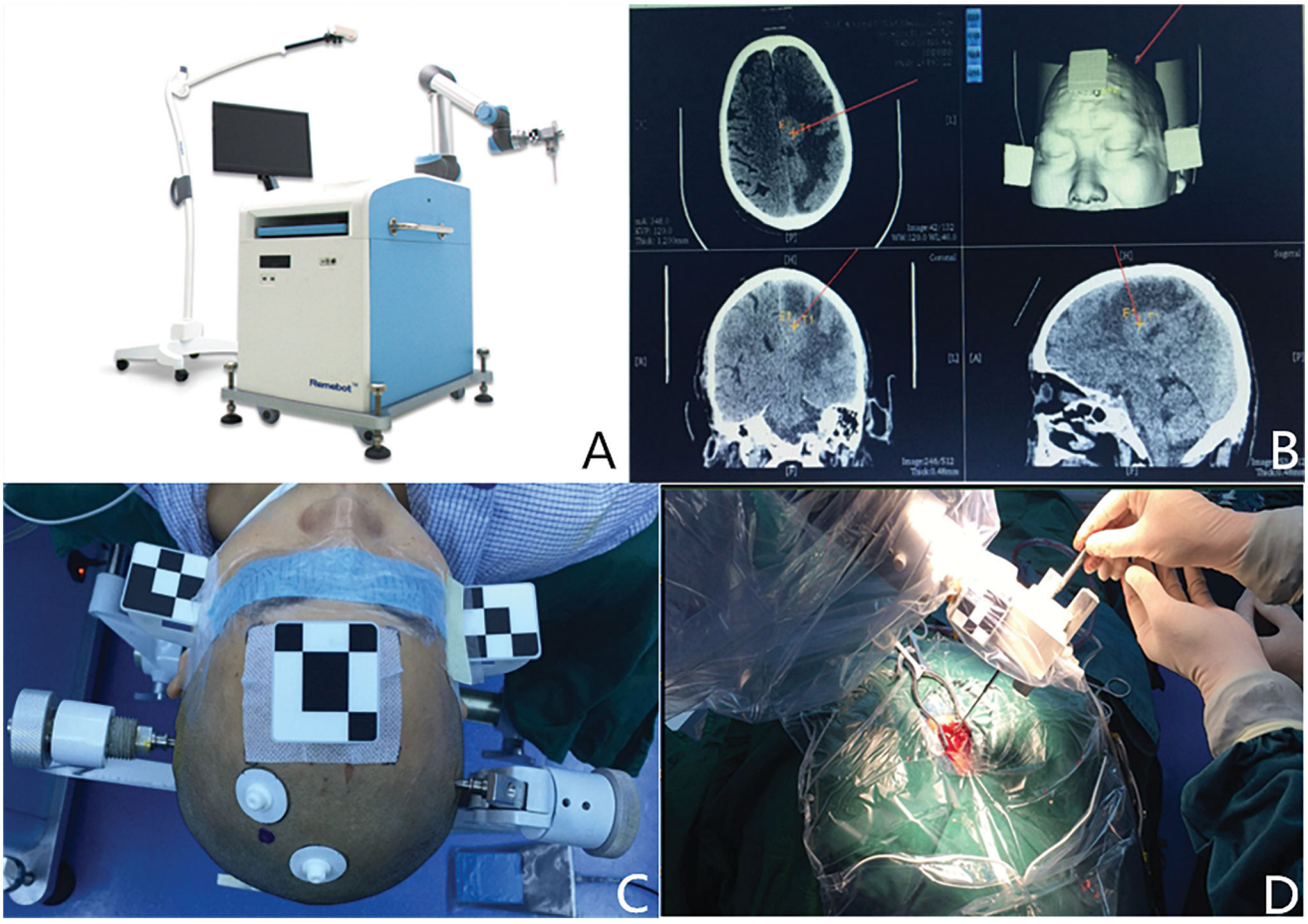


**Figure 1.** Representative images of the Remebot robot and surgical workflow. (A) Robot and planning station. (B) Surgical plan: preoperative magnetic resonance imaging including the trajectory is combined with the computed tomography (CT) reference. (C) Patients' heads were immobilized in a Mayfield clamp after general anaesthesia. We determined the entry point after accurate registration. (D) A burr hole was drilled, and biopsy specimens were taken through the instrument holder along the trajectory.

**Table 1.** Summary of the patients' baseline characteristics.

| | Frame-based group ($n = 35$) | Remebot robot group ($n = 31$) | $p$ |
|---|---|---|---|
| Age (mean ± SD), years | 45 ± 16 | 46 ± 13 | 0.78 |
| Sex ratio (male/female) | 21:14 | 18:13 | 0.87 |
| Symptoms and signs | | | |
| Headache/dizziness | 19 | 13 | 0.32 |
| Seizure | 6 | 4 | 0.63 |
| Motor deficit | 15 | 12 | 0.73 |
| Aphasia | 3 | 2 | 0.75 |
| Conscious disturbance | 2 | 2 | 0.90 |
| Regions of biopsy | | | 0.96 |
| Frontal lobe | 7 | 5 | |
| Temporal lobe | 4 | 4 | |
| Parietal lobe | 6 | 3 | |
| Occipital lobe | 3 | 3 | |
| Ventricles | 1 | 1 | |
| Basal ganglia region | 11 | 13 | |
| Cerebellum | 3 | 2 | |
| The maximum diameter of the target, mm | 25.4 ± 5.9 | 24.1 ± 6.2 | 0.53 |
| Preoperative KPS (mean ± SD) | 82 ± 11 | 80 ± 9 | 0.43 |
| Duration of symptoms, months, median (IQR) | 25 ± 8 | 28 ± 9 | 0.16 |

**Table 2.** Histopathological findings of the two groups.

| Histopathological findings | Frame-based group ($n = 35$) | Remebot robot group ($n = 31$) | $p$ |
|---|---|---|---|
| Diagnostic yield | 32/35 | 29/31 | 0.75 |
| Astrocytoma grade II | 10 | 9 | |
| Astrocytoma grade III | 4 | 3 | |
| Astrocytoma grade IV | 2 | 2 | |
| Neuroblastoma | 0 | 1 | |
| Diffuse large B cell lymphoma | 13 | 9 | |
| Inflammatory disease | 2 | 3 | |
| Metastatic neoplasm | 1 | 2 | |
| No diagnosis | 3 | 2 | |

the frame-based group and the Remebot robot group (91.4% versus 93.5%, $p = 0.75$).

The total duration of the procedure of the frame-based group was significantly longer than that of the Remebot robot group (mean time 116.5 ± 14.1 vs. 80.1 ± 12.3 min, $p < 0.001$). However, there was no significant difference in the operation time (49.4 ± 12.1 vs. 52.1 ± 9.0 min, $p = 0.31$). In our study, there were 5 complications in 66 stereotactic biopsy procedures (7.6%), 3 in the frame-based group and 2 in the Remebot robot group. There was no statistically significant difference in the complication rate between the two groups. We also used the visual analog scale (VAS) score to evaluate the discomfort of the patients during the entire treatment process. We found that there was a significant difference in overall discomfort, with less discomfort experienced by patients undergoing the Remebot robot-assisted frameless brain biopsy procedure than by patients undergoing the frame-based procedure (2.7 ± 1.2 versus 1.5 ± 0.7, for the frame-based and Remebot robot groups, respectively, $p = 0.001$). However, the length of hospital stay (7.3 ± 2.1 VS. 7.0 ± 1.2 days, $p = 0.49$) and KPS on discharge (82 ± 11 vs. 80 ± 9, $p = 0.47$) of the two groups were not significantly different. These results are all summarized in Table 3. There is a typical example of the Remebot robot group in Figure 2.

## Discussion

Stereotactic brain biopsy has been considered to be a safe and effective method for the diagnosis of cerebral lesions that can help us establish a diagnosis.[6] Thus, many patients can receive proper adjuvant treatments. With advances in modern artificial intelligence and neuronavigation systems, many frameless stereotactic techniques have been used by neurosurgeons with promising results and expanding possibilities. The Remebot robot is a robot-assisted stereotactic system that was designed and produced in China and has been successfully used in a variety of situations. We have examined the accuracy of the Remebot robot in several applications and have shown it to be accurate. Our hospital introduced the robot in 2016 and used it in stereotactic brain biopsy. Until then, we mainly used frame-based stereotactic biopsy. The present study describes our experience of a series of brain lesion biopsies using framed-based and frameless techniques under the same circumstances, that is, at a single centre, with a single surgeon and the same surgical team.

**Table 3.** Comparison of the total procedure length, complications, overall discomfort and clinical outcome.

| | Frame-based group ($n = 35$) | Remebot robot group ($n = 31$) | $p$ |
|---|---|---|---|
| Total procedure length, mean, min | 116.5 ± 14.1 | 80.1 ± 12.3 | 0.00 |
| Operation time, mean, min | 49.4 ± 12.1 | 52.1 ± 9.0 | 0.31 |
| Complications | 3 | 2 | 0.75 |
| Overall discomfort | 2.7 ± 1.2 | 1.5 ± 0.7 | 0.001 |
| Postoperative duration of hospitalization, days, (mean ± SD) | 7.3 ± 2.1 | 7.0 ± 1.2 | 0.49 |
| KPS on discharge (mean ± SD) | 82 ± 11 | 80 ± 9 | 0.47 |

As is well known, the fundamental goal of brain biopsy is to maximize biopsy accuracy and reduce complications. The current frameless systems have been able to reach an accuracy of 3 mm and offer a similar degree of spatial accuracy and reliability to that of frame-based systems.[7–10] As previous literature reported, frameless stereotactic biopsy can provide a diagnostic yield of 89% to 99.3%, and a frame-based technique can provide one of 81.3–99.2%.[11–15] To the best of our knowledge, numerous studies have been published that compared frame-based and frameless stereotactic biopsy methods in terms of the diagnostic yield and the complication rate. These reports found no significant difference. For example, Woodworth *et al.*[13] found no difference in frame-based and frameless stereotactic brain biopsy with a combined 90% diagnostic yield and no difference in complication rates between the 2 methods. Yi *et al.*[11] reported a retrospective analysis of 288 consecutive brain biopsies, and no significant difference was found in diagnostic yield, with frame-based biopsies having a diagnostic yield of 96.9% and frameless biopsies having a diagnostic yield of 91.8%.

In our study, we performed 66 biopsies with frame-based and Remebot robot techniques, and the diagnosis was incorrect or missed in 3 cases in the frame-based group and in 2 cases in the Remebot robot group. The overall diagnostic yield of this study was 92.4%, and no statistically significant difference was found between the two groups. Khatab *et al.*[10] performed a meta-analysis that included 1628 frameless biopsy procedures, and the diagnostic yield was 93.8%, ranging from 87–100%, in their review of 16 papers. Our results obtained in both groups are in accordance with those reported in the literature. It has been reported that younger age, smaller lesion size and deep-seated location contribute to decreased biopsy diagnostic yield.[16] Therefore, all these factors were taken into consideration in our study, and there was no significant difference in the age, localization of the lesions or size of the lesion. It has been reported that the complications of stereotactic biopsy mainly include intracranial haemorrhage, neurologic deficits, infection, epilepsy and so on, and intracranial haemorrhage is the most common complication among them.[17–19] Malone *et al.*[19] analysed

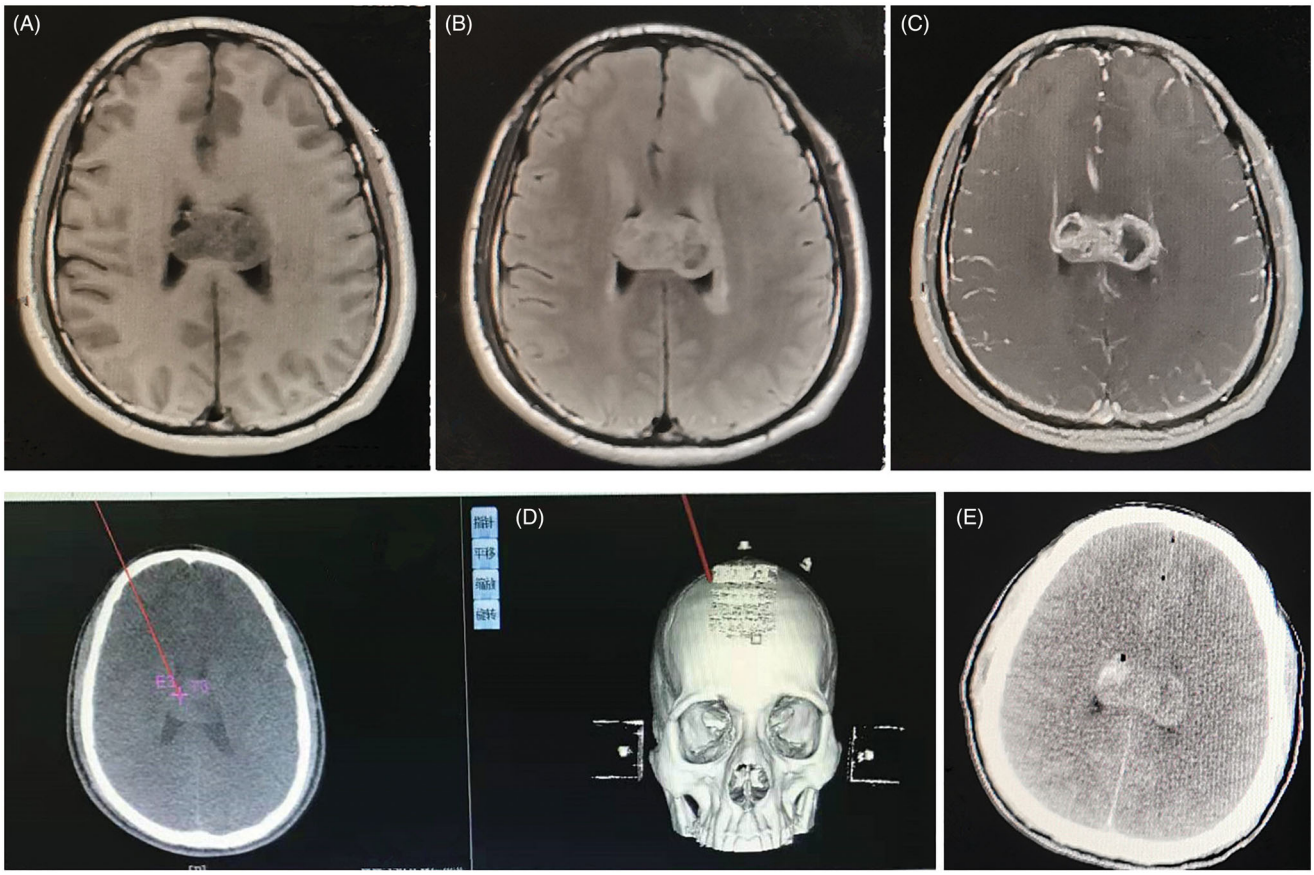


**Figure 2.** An example of the Remebot robot group. A 29-year-old male visited our hospital for headache, which had started 3 days previously. No other neurologic deficit was found. (A), (B) and (C) The preoperative MRI revealed a bilateral ventricular tumour. (D) The surgical plan of the patient. (E) Postoperative CT scans obtained in the patient. There was a small haemorrhage <10 mm and an air bubble (arrow) at the biopsy site, but the patient had no symptoms after the operation. The histologic diagnosis was astrocytoma grade IV.

7514 cases of stereotactic brain biopsy, and the incidence of complications was 6.1%, of which the rate of intracranial haemorrhage was 5.8%. Hall *et al.*[1] reviewed several large series with 7471 stereotactic brain biopsies and obtained a mortality rate of 0.7% and a morbidity rate of 3.5%. In our present study, there were 5 complications in 66 stereotactic biopsy procedures (7.6%), 3 (8.6%) in the frame-based group and 2 (6.5%) in the Remebot robot group. All five cases suffered from intracranial haemorrhage, and emergency surgical decompression was performed in 1 case; the rest of patients received conservative treatment, no deaths occurred, and all patients were discharged uneventfully. The results are in accordance with those of previous literature.[12,17,20,21] Although the diagnostic yield and complication rate did not differ significantly between the two groups, we think that Remebot-robot assisted stereotactic biopsy is better for the patients. Because we can take full advantage of MRI, diffusion tensor MRI, magnetic resonance angiography, CT and other imaging data before surgery, we can determine the best path for the puncture to avoid crossing vessels and cranial nerves, and there is more flexibility to change targets. Wang *et al.*[15] reported that susceptibility-weighed imaging can provide a better visualization of vessels, and they used it to minimize postoperative complications successfully. In addition, if an exception occurs during an operation, we can change the path easily through multiplanar image reconstruction and three-dimensional planning.

We also found that there was a significant difference in overall discomfort, which was felt less by patients undergoing Remebot robot-assisted frameless brain biopsy procedures. There are several disadvantages of frame-based biopsy. Before a brain MRI is performed, the surgeon must fix the frame on the head of the patient with pins. The preparation for frame-based biopsy is time-consuming and a painful experience for the patient. However, for robot-assisted frameless biopsy, we affix the marker to the head of the patient without any discomfort. Therefore, the patients in the frame-based group felt more stressed during the operation. In addition, Remebot robot-assisted frameless stereotactic biopsy is suitable for patients who are comatose or uncooperative (e.g. young children or patients with epilepsy) and cannot undergo frame-based biopsy. For this reason, we think that Remebot robot-assisted frameless biopsy would be a better option for the patients. In terms of the total duration of the procedure, that of the frame-based group was significantly longer than that of the Remebot robot group ($116.5 \pm 14.1$ vs. $80.1 \pm 12.3$ min, $p < 0.05$), which is consistent with previous reports. A recent meta-analysis by Neumann *et al.*[22] also showed that the total procedure had a 14.2 [−36.3, 64.6] min time gain when comparing frame-based stereotactic biopsy to frameless stereotactic biopsy. However, there was no statistically significant difference in the operation time ($49.4 \pm 12.1$ vs. $52.1 \pm 9.0$ min, $p = 0.31$). This could be explained by the time spent on the preoperative procedure (i.e., the surgeon must fix the frame on the head of the patient with pins), whereas we affixed the marker to the head of the patient in the Remebot robot-assisted frameless biopsy, which was easier and less time-consuming.

There are several limitations of our study. The primary limitations are its retrospective design and the limited number of

patients, which limits the power of statistical tests. Moreover, the findings are clearly limited by the presence of selection bias, as described previously, and the lack of multicentre participation. Another limitation is the fact that several pathologists were involved with the pathologic diagnosis of the brain lesions, which might have affected the diagnostic yield.

## Conclusion

The Remebot robot-assisted frameless biopsy procedure was shown to be as safe and effective as frame-based stereotactic biopsy. Furthermore, there would be a shorter total procedure duration and less discomfort for the patients when using the Remebot robot system. Collectively, the Remebot robot-assisted frameless biopsy is better accepted by patients than the frame-based technique, and we recommend its routine use for stereotactic biopsies in brain lesions where available.

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## Disclosure statement

No potential conflict of interest was reported by the author(s).

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