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ORIGINAL ARTICLE - BRAIN TUMORS

Stereotactic brain biopsy: evaluation of robot-assisted procedure in 60 patients

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Abstract

Background Frameless stereotactic biopsies, particularly robot-assisted procedures are increasing in neurosurgery centers. Results of these procedures should be at least equal to or greater than frame-based reference procedure. Evaluate robot-assisted technology is necessary in particular, when a team has chosen to switch from one to another method.

Objective The objective of our prospective work was (i) to evaluate the success rate of contributive robotic-assisted biopsy in 60 patients, to report the morbidity and mortality associated with the procedure and (ii) to compare it with literature data.

Methods We performed a prospective and descriptive study including 60 consecutive patients having had robotic-assisted stereotactic biopsy at the Rouen University Hospital, France. All patients had presurgical imaging before the procedure included Magnetic Resonance Imaging merged with Computed Tomography scan acquisition. Registration was mostly performed with a touch-free laser (57/60). A control Computed Tomography scan was always realized at day 0 or day 1 after surgery. Data collected were success rate, bleeding, clinical worsening, infection, and mortality.

Results All the biopsies were considered as contributive and lead to the final diagnosis. In 41/60 patients (68%), the lesion was glial. Six in 60 patients (10%) had visible bleeding without clinical worsening related, 5/60 patients (8.5%) showed clinical impairment following surgery, which was permanent in 2 patients, and 1/60 patient presented generalized seizures. We did not report any infection and mortality.

Conclusion Robot-assisted frameless surgery is efficient and provides a reasonable alternative to frame-based procedure. The operating time can be reduced, without increasing morbidity and mortality rates.

Keywords Robot assisted · Stereotactic · Biopsy · Oncology · Brain

Introduction

Stereotactic biopsies require strict and rigorous methodology to provide accurate histological diagnosis, especially in small lesions, located in a functional area or in the brainstem. The objective of both frame-based and frameless techniques is the same, to reach an intracerebral target in a precise and safely manner. The first robotic procedures date back in 1993 and since then frameless procedures have been used increasingly and represent a high proportion of all stereotactic procedures performed today [6–8, 18, 38].

However, few data are currently available on robot-assisted technology and evaluation is necessary to guide surgical practices. Robotic surgery has the potential to improve surgical precision and accuracy through motion scaling and tremor filters, by reducing human interference (i.e., manual parameter settings, calibrations, and adjustments) with a diagnostic yield comparable, even more accurate than frame-based stereotaxy [27, 28, 35, 47]. Robot-assisted frameless stereotactic biopsy appears to be a safe and effective alternative to frame-based stereotactic procedures for supratentorial lesions [4, 36]. Robotic biopsy optimizes the needle trajectory to avoid sulcal

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vessels, bridging veins, and ventricular penetration, without the drawbacks of application or the limitations of a stereotactic frame [5, 26]. The merging of Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) acquisitions is all the more pertinent as combined MRI and CT achieved higher application accuracy values than CT alone [42]. For the brainstem, the use of robot-assisted frameless stereotactic techniques should improve the diagnostic yield and accuracy of the technique [32]. A transfrontal approach is associated with a higher rate of diagnosis than a suboccipital transcerebellar approach [15]. In a pediatric study, authors reported improved safety and feasibility of minimally invasive robotic approaches, thus optimizing surgical results, while minimizing postoperative morbidity [14]. In another pediatric study, authors found frameless robot-assisted biopsy of Diffuse Intrinsic Pontine Gliomas to be an easier, more effective, and safer technique to achieve diagnosis [12].

Until 2016, most of the stereotactic procedures performed in our tertiary care center were done using a frame-based technique. In April 2016, our center acquired a surgical robot and we started using frameless robot-assisted technology. To date, more than 60 stereotactic brain biopsies have been done using the ROSA® platform (Medtech, Zimmer-Biomet, Warsaw, USA). In this prospective work, we report the results of this change in brain biopsy management in our center.

The objective of our work was to evaluate the success rate of robot-assisted frameless brain biopsy, to report the morbidity and mortality associated with the procedure and to compare our results with data in the literature.

Material and methods

Patients

This prospective and descriptive study included all consecutive patients who had robot-assisted stereotactic biopsy (ROSA®; Medtech Zimmer-Biomet, Warsaw, USA) at Rouen University Hospital, France between April 2016 and May 2017. There were no age exclusion criteria.

Procedure

Presurgical imaging

Pre-surgical imaging was performed the day before the procedure, with a specific radiological protocol, which included a CT scan (General Electric CT, thickness of cuttings 0.625 mm, join cuttings, matrix = 512 × 512 pixels, Field Of View FOV = 270 mm), and an MRI (MRI Siemens 1.5 T, sequence 3Dimension(3D)-T1 gadolinium, 1 mm thick, (FOV) = 256 mm, matrix = 512 × 384 pixels, axial acquisition). Depending on the lesions, other MRI sequences could be necessary, specifically a 3D-Flair. All the acquisitions were merged automatically, using Rosa v3.0 software. Merging was checked and corrected manually by an expert neurosurgeon before the surgery.

Planning of stereotactic trajectory

Planning of the stereotactic trajectory was performed the day before the procedure. The reference investigation regarding 3D reconstruction was the CT scan. The target (contrast enhancement, hyperinfused areas, hypersignal flair in the absence of contrast) was defined on MRI (Fig.1). The entry point was chosen from 3D T1-Gadolinium sequence, in order to obtain a trajectory avoiding vessels, sulci, and if possible the ventricles and functional areas.

Surgical procedure

All procedures were performed under general anesthesia. The head of the patient was fixed in a Mayfield head holder (Integra LifeSciences Corporation, Saint-Priest, France) which was connected to the robot. Patients were placed in supine position. Two registration were performed with the aid of a touch-free laser (surface registration recording between 5000 and 8000 regions on the face) for 57 patients and with bone fiducials for 3 patients. For the latter, a supplementary acquisition performed in the operating room using a 3D imaging system (O'arm, Medtronic) was merged with the pre-surgical planning acquisitions. Whatever the calibration mode used, a checking procedure enabled the operator to control the accuracy before continuing. After cutaneous asepsis and placement of surgical drapes, the robotic arm was positioned in line with the trajectory (Fig.2). On the instrument holder, were consecutively installed a 3.2 mm drill, a coagulation probe (Dixi, 2.1 mm) to coagulate the dura, and a biopsy needle (Cormedica, 190 mm, sample pane of 8 mm, lateral opening) which was lowered onto the target. "Rosette-like" biopsies were performed on the target and repeated if necessary a few millimeters below or above the target. No 3D-intraoperative imaging was done to check the placement of the needle, except in 2 patients. Biopsy samples were analyzed in our center's on-site pathology laboratory. Blood samples were evaluated for molecular biology. A control CT scan was systematically performed at day 0 or day 1 after surgery to check absence of bleeding complications along the route or at biopsy sites and postsurgical swelling.

Except in cases of lymphoma, patients had presurgery corticotherapy which was continued postsurgery, with intravenous high dose at day one, 2 mg/kg/day, and then decreasing oral treatment until a complete stop after 5 to

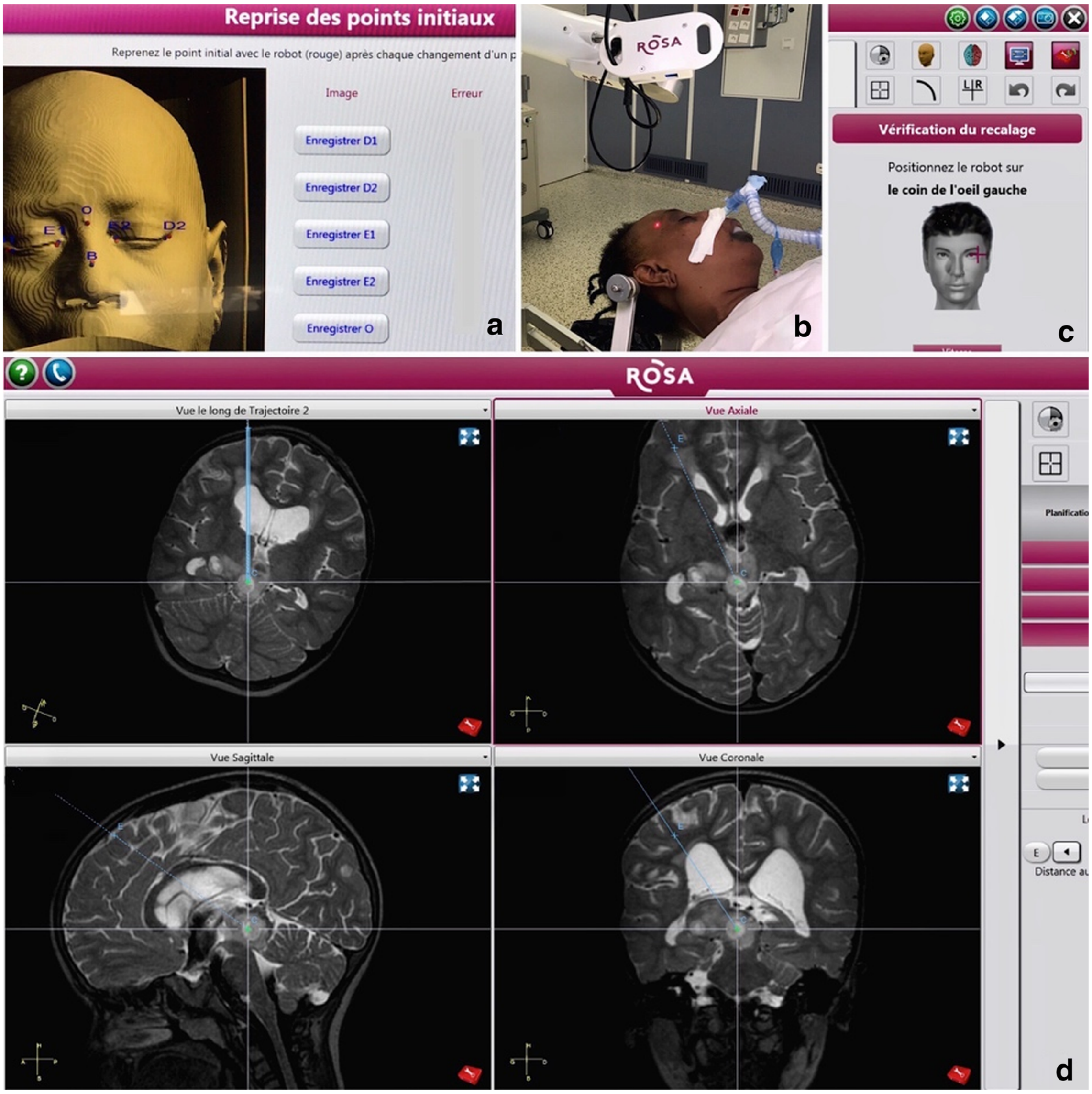

Fig. 1 Planning software of stereotactic trajectory, **a** waypoints recording, **b** laser marking, **c** calibration control, **d** trajectory/targets in different views

7 days. In the absence of any complication, the patient was discharged 1 or 2 days later.

Histological diagnosis

For the histological identification, we used a classification from the world health organization, amended in 2016 [37], which includes molecular biology-based data.

Complications

Complications were bleeding, clinical worsening, infection, and mortality.

Analysis

This is a descriptive study. Results are presented as mean (± standard deviation) or extreme values for quantitative variables and as absolute number and/or percentage for qualitative variables.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Fig. 2 Intraoperative **a** patient and robot installation, **b** robotic arm with needle for biopsy, **c** "Rosette" samples

Results

Patients

Sixty patients (44 men and 16 women, sex-ratio 2.75) had a robot-assisted stereotactic biopsy between April 2016 and May 2017. The mean age of patients was 59.6 years (4–79). A supratentorial approach was used in 58/60 (96.6%) patients and an infratentorial transcerebellar approach in 2/60.

Procedure

Registration was made by laser for 57/60 patients and by bone fiducials for 3/60 (5%). Two of these 3 patients had an intraaxial lesion located in the low protuberantial area. For these 2 patients, intraoperative 3D-control was performed, to confirm the accurate placement of the needle before biopsy. The average operating time was 46.5 min. The operating time included patient setup, head positioning, "imaging/patient" adjustment, and surgical procedure. This operating time did not include trajectory planning, performed the day before the procedure. The operating time was longer for procedures performed with bone fiducials (90 min) and intraoperative 3D-control (110 min).

Histological diagnosis

All the biopsies were considered as contributive and led to the final diagnosis. The lesion was glial in 41/60 patients (68%) including 34 grade IV glioblastomas (83%) and 7 grade II or III astrocytomas or oligodendrogliomas (17%). Histological and immunohistochemical aspects were compatible with a diffuse large B cell lymphoma in 11/60 cases (18.3%) classified as follows: nongerminal center B cell-like ($n = 8$), germinal-center B cell-like ($n = 2$) and B lymphoproliferative syndrome ($n = 1$) linked to Epstein–Barr virus occurring in an immunosuppression context with multiple brain lesions. In 3/60 patients (5%), there were secondary lesions of carcinoma with no primary tumor found, colorectal adenocarcinoma, and small cell neuro-endocrine lung carcinoma, respectively. Biopsy found germinoma in 2/60 patients (3.3%) who had a pineal lesion. In 3/60 patients, a diagnosis of brain toxoplasmosis was found in one immunosuppressed patient (1.7%), of an histiocytic sarcoma in one patient (1.7%) and of multiple sclerosis in one patient (1.7%), respectively (Fig.3).

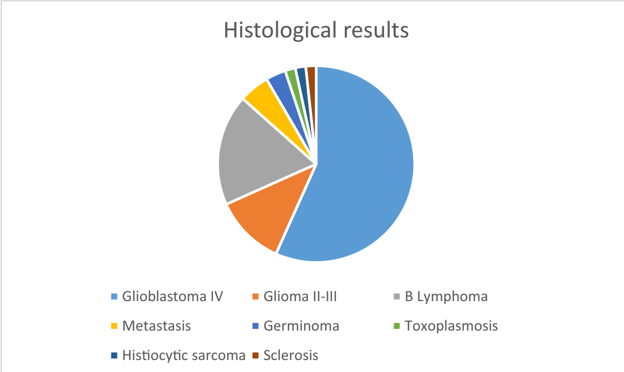

Fig. 3 Histological results

Complications

Bleeding

Six of the 60 patients (10%) had visible bleeding on the postoperative CT scan. The maximum mean diameter of these hematomas was 17.1 mm. In 3/60 patients (5%) the hematoma measured less than 15 mm. For all patients, bleeding was located within the lesion. No patient had clinical worsening related to bleeding complications.

Clinical worsening

Five of the 60 patients showed clinical impairment following surgery. Three of these 5 patients (5%) had a temporary worsening of a preexisting hemiparesis. These 3 patients had a frontal glioblastoma, a left thalamic metastasis and a B-type diffuse large cell lymphoma, located on the right lenticular area, respectively. The other 2 patients (3.3%) had a permanent deficit: a monoparesis (4/5) following the biopsy of a thalamic lesion for one and a language disability worsening with a right hemiparesis following the biopsy of a left ventricular junction lesion for the other. None of these 5 patients had hematoma on the postoperative CT scan. One of the 60 patients (1.7%) presented generalized seizures following biopsy of a pineal lesion. No recurrence was observed after the introduction of an antiepileptic agent.

Other complications

In our series, there was no infection or mortality following the biopsy.

The mean duration of hospitalization was 5 days with more than 55% of patients discharged on day 2.

Discussion

In this study, we report a 100% success rate in our first series of 60 robot-assisted stereotactic brain biopsies (contributive biopsies for diagnosis), with a permanent and transitory complication rate of respectively 3.3% and 5% and no mortality.

Procedure

The central nervous system requires the highest surgical precision. Indeed, even a minor deviation of surgical instruments can lead to severe complications [50]. Like other teams, we believe that robotic technology represents an interesting tool for stereotaxy, notably, to target small lesions located in the brainstem or in eloquent area [2, 16, 17, 20, 49]. In the first instance, we used this technique to conduct stereotactic biopsy ("learning curve" stage) before expanding its use to the implantation of depth electrodes.

Histological diagnosis

The advances of imaging and presurgery planning tools have modified the practices of stereotactic procedures lowering their morbidity and increasing their accuracy [4, 5, 12, 14, 28, 32, 34, 35, 41, 47, 48, 50]. The main aim of performing stereotactic biopsy is to collect informative samples of tissue to obtain histological diagnosis. In the literature, the success rate of robot-assisted biopsy is between 87% and 99% [5, 14, 32, 35, 36]. In our series, the rate was 100%. Nevertheless, histological analysis showed tumoral necrosis in one of our patients. The combination of histological and radiological data established the final diagnosis of glioblastoma. It is interesting to note that biopsy is more commonly performed for supratentorial lesions than for brainstem lesions [1, 11, 17, 30, 31, 40, 44, 46]. Authors reported a biopsy success rate of 95.1% for lesions approached by a frontal trajectory and of 84.2% for a transcerebellar approach [15]. In interpreting these results, we opted for registration by bone fiducials (more accurate than laser registration) for all biopsies done by transcerebellar approach. As other authors, biopsies of the midbrain and top half of protuberancial lesions are driven by a frontal, transgyral, and/or transventricular approach [23, 33]. Below this anatomical limit, biopsies are performed by a transcerebellar approach via homolateral middle cerebellar peduncle. For this latter approach, the particularly ergonomic robot improves procedure against frame-based techniques. All our brainstem biopsies were contributive but the small number in our series makes it difficult to compare our results with those from larger series.

Complications

The main complication of stereotactic procedure is the risk of bleeding. In the literature, this risk is estimated between 0% and 14.5% [13, 15–17, 19, 23, 24, 27, 29, 33, 34, 43]. In our study, there were 10% of hematomas (6/60 patients) but all were asymptomatic. No bleeding was found in the route of biopsy and we report only intralesional bleeding. Six of our 60 patients (10%) had permanent or temporary neurological complications. This rate varies from 0% to 9.3% in the literature, but usually only permanent worsenings have been reported [10, 21, 45]. In the brainstem, this rate is slightly higher and varies from 2.5 to 11% [3, 9, 24, 39]. For this location, authors found a morbidity rate of 9.8% and of 5.3% for transfrontal and transcerebellar biopsies, respectively. The mortality rate in this series was 5.3% but only concerned one patient [15].

Accuracy of the stereotactic tool

The accuracy of the stereotactic tool is another key point. According to the literature, robotic technology offers a very high degree of accuracy. The surgical accuracy of a robot-assisted procedure in combination with an intraoperative 3D imaging system was measured at 0.3 mm. In clinical situations, surgical accuracy using either surface registration (laser) or bone fiducial registration was measured at 1.22 mm or 0.7 mm, respectively [20]. Interestingly, the accuracy of frame-based biopsies was measured at 0.86 mm [44]. This is rather close to a robot-assisted procedure using laser registration. It is of note that the accuracy of the robots is much higher than onboard biopsy systems on our neuronavigators. Thus, with VarioGuide system (Brainlab), the mean trajectory deviation was 2.2 mm ± 1.1 mm for intracerebral targets located in the brain stem with a transfrontal approach [22, 25]. The deviation from the planned trajectory is correlated with the distance from the parenchyma [50]. In our series, we did not measure the accuracy of the procedure. Indeed, to do so, we would have needed to systematically add an intraoperative 3D imaging control. This control can be performed without difficulty but its interest is rather limited in the vast majority of stereotactic biopsies. We only did this once for a young child with a lesion located in the brainstem. These first results pave the way for further analysis in a future study on the implantation of deep brain electrodes.

Strengths and limits

Our study has several strengths. Nevertheless, as for all new techniques, the learning curve and the cost may be seen as limits of this technology. Indeed, the learning curve is relatively short and all neurosurgeons should be trained in robot-assisted technology as soon as the fundamentals of stereotaxy have been acquired. The cost must be balanced against the advantages as accuracy, safety, and gain of operative time notably for biopsy and other stereotactic procedures.

Conclusion

We report in this study 60 robot-assisted stereotactic brain biopsies with low morbidity and no mortality.

In this study, we report our first experience in a series of 60 stereotactic frameless brain biopsies using a robot-assisted technique. Our results are similar to those of other teams, and allow us to confirm that robot-assisted frameless stereotactic biopsy is a safe, accurate, and efficient technique. Extended to other fields of stereotactic applications, robotics could provide a higher degree of accuracy than other frame-based or neuronavigated applications.

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Author contributions LT wrote the manuscript. VG was a major contributor in writing the manuscript. SD performed the surgeries and described and revised the manuscript. FM and MF supervised and revised the manuscript. All authors have read and approved the submitted manuscript.

Compliance with ethical standards

Conflict of interest Authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Statement of informed consent Informed consent was obtained from all individual participants included in the study.

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