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ORIGINAL ARTICLE - BRAIN TUMORS

Safety and accuracy of frameless electromagnetic-navigated (AXIEM™)-guided brain lesion biopsies: a large single-unit study

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Abstract

Background Brain biopsies are required to establish a definitive histological diagnosis for brain lesions that have been identified on imaging in order to guide further treatment for patients.

Objective Various navigation systems are in use but little up to date evidence is available regarding the safety and accuracy of a frameless, electromagnetic technique to target brain lesions.

Methods Data was collected retrospectively on all patients that had brain biopsies at our institution from 01/01/2010 to 31/12/2017. Operation notes, neuropathology reports, and clinical notes on electronic patient record were used to determine whether biopsy of adequate identifiable abnormal tissue was achieved, whether a definitive diagnosis was established, any adverse events occurred, and if a repeat biopsy was carried out.

Results Three hundred seventy-one AxiEM (Medtronic, Minneapolis, USA)-guided brain tumor biopsies were performed in this 8-year period. Three hundred forty-nine (94.07%) procedures provided definitive tissue diagnosis, 22 (5.93%) were non diagnostic; in 6 cases (1.62%), repeat biopsy was performed and adverse events which caused clinical compromise were observed in 4 patients (1.08%).

Conclusions The AxiEM is a fast, effective, and safe frameless and pinless neuronavigational system. It offers a high degree of accuracy required for the establishment of a definitive diagnosis, permitting optimal further treatment, and thus improving patient outcomes.

Keywords AxiEM · Brain · Tumor · Biopsy

Introduction

With the advent of ever more specialized technology, advanced neurosurgical techniques abound in this current era. Such technology has been designed to improve patient safety and surgical outcomes, and there is little that requires better safety and outcomes than brain tumor surgery. Making a diagnosis via a successful biopsy is the first step in many patients.

Brain biopsies are required to establish a definitive diagnosis for brain lesions that have been identified on imaging, to guide further treatment for patients. In 2006, the National Institute of Clinical Excellence in the UK recommended that, following a multidisciplinary meeting, a histopathological diagnosis should be achieved if a central nervous system neoplasm is suspected [12]. To that end for those tumors not amenable to open surgery and thus excision biopsy, three key methods of stereotactic neuronavigation are used in this current era: frame based, frameless, and intraoperative MRI (IoMRI) based. The key focus of this article will be that of frameless technology by the Medtronic © StealthStation AxiEM navigation system (Minneapolis, USA) developed in 2003, which has been in use at our hospital for more than a decade.

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Frameless technology works on the principle of tracking the movement of instruments in space by virtue of electromagnetic field generation, optics, and ultrasound. Pioneered in Japan in 1986, it has since gone through multiple iterations to reach its current state [17]. The technique now has multiple uses, both in brain tumor surgery and biopsy and outside of that—such as in paediatric complex hydrocephalus [3]. Unfortunately, with regard to tumor surgery and biopsy, most of the data collected for frameless technology has several disadvantages. Whilst still valid, the bulk of the best data was taken in the early-to-mid 2000s [18] with little up-to-date information having been produced since, particularly on the newer biopsy systems. Regarding AxiEM-guided brain biopsies, to the best of our knowledge, there is only one previous study [4, 8]. Thus, this large, single-unit study seeks to provide updated information on the safety, accuracy, and efficacy of the frameless AxiEM system over a clearly outlined 8-year period.

Methods

Data was collected retrospectively on all patients who had brain biopsies using AxiEM navigation system at our hospital over the date range 01/01/2010 to 31/12/2017. Operation notes, neuropathology reports, and clinical notes on electronic patient records were used to determine whether biopsy of adequate identifiable abnormal tissue was achieved, whether this was consistent with the final definitive diagnosis, any adverse events directly related to the procedure, and if a repeat biopsy was carried out.

Pre-operative planning MR or CT imaging was performed for each patient on the day of the procedure or the day before, and the Medtronic AxiEM workstation was used to plan the target site, entry point, and the needle trajectory. There was no intraoperative imaging used. Biopsies were performed under general anesthesia with the head of the patient positioned on a horse shoe. Registration to the system involved attachment of a small reference electromagnet on the surface of the patient's head using stickers followed by a combination of point-merged anatomic and surface-merged registration.

Data on complications directly occurring as a result of the intervention was also collected.

All data are unidentifiable and the collection retrospective; therefore, no IRB/ethics committee approval and patient consent were required.

Results

Three hundred seventy-one AxiEM-guided brain tumor biopsies were conducted in our Unit from January 2010 to December 2017. The patients ranged in age from 1 to 82 years, with a median of 59 years. There were 223 males and 148 females (Table 1).

A positive final definitive diagnosis was obtained in 349 of 371 biopsies (94.07%). Twenty-two biopsies were non diagnostic (normal brain tissue) (5.93%). Six patients (1.62%) received repeat biopsies, 100% of which were successful in returning abnormal tissue from which a definitive pathological diagnosis could be achieved (Table 2).

The vast majority of the tumors were gliomata (grades I–IV) at 73.04% (271) followed by lymphoma 9.97% (37) and metastasis 3.23% (12) (Fig. 1).

In 70% of the cases, MRI guidance was used and in 30%, CT imaging.

In 80% (298) of the cases, an intraoperative frozen sample was sent and out of these, in 97% (288), abnormal tissue was identified, and in 86% (257), the frozen sample was consistent with the final histology (Fig. 2).

Almost in half cases 49.86% (185), the location sampled was in frontal or temporal lobes (Fig. 3). The study was not powered for localization prediction of definitive tissue diagnosis.

In terms of complications, 4 patients (1.08%) suffered biopsy-related significant clinical compromise and died within 30 days (Table 3). Three patients died from postoperative hematoma and cerebral edema in the region of the biopsy tract within 24 h. One died from new onset postoperative status epilepticus. Three had a diagnosis of Glioblastoma Multiforme IV and the fourth had diffuse B cell lymphoma. One patient was previously on prophylactic anti-platelet therapy with aspirin which was stopped 7 days prior to the procedure. In 2 cases, contrast MRI was used for navigation and in the other 2, contrast CT was used. The biopsy needle trajectory was appropriate avoiding vessels as confirmed from the navigation station planning and the operation records. Furthermore, the performing surgeons did not report multiple attempts or other technical challenges. There were otherwise no complications directly caused from the procedure such as infection, seizures, or new neurological deficits in our series.

Discussion

The AxiEM navigation system was developed to use an electromagnetic field to guide biopsy sampling without the use of a frame or pins. The field generator produces a three-dimensional magnetic field encompassing the cranium, with each point in the field having a unique magnetic strength. A dynamic reference frame is then non-invasively attached to the patient's head via adhesive. The location of the real tip of the probe is then calculated by its relative position from the dynamic reference frame within the magnetic field.

Although traditionally frame-based technology is considered gold standard for accuracy, the accuracy of the various

Table 1 Patient demographics and diagnostic yield

Median age (years)	Total patients	Number of male	Number of female	Non diagnostic (number)	Diagnostic yield (%)	Deaths from biopsy
59 (1–82)	371	223	148	22	94.07008086	4
				% non diagnostic	5.929919137	
				% deaths	1.081081081	

forms of frameless technology in tracking the real tip of the probe is measured within 1–2 mm of its actual position, a range essentially equivalent to that of frame-based technology[11]. Dammers et al. comparing 227 frame based versus 164 frameless biopsies performed in the 1996 to 2006 period found that in addition to having no differences in terms of accuracy between procedures; there was also no difference in safety ($p = 0.81$), with a statistically significant increase in time of operation with frame-based operations [4]. Indeed, time of operation is around 20 to 30 min shorter with frameless technology [7].

Others have found advantages in frameless technology compared with frame based in terms of operation theatre occupancy, anesthetic time, safety, ITU bed occupancy, hospital stay, and overall cost incurred by the hospital [5]. Though not statistically significant, the study by Dammers et al. also noted a tendency towards quicker discharge, whilst the UK's AxiEM study also concluded that day-case biopsies were considered plausible with frameless technology. The lack of pins further improves patient comfort with clear advantage in the pediatric age group where concerns about damaging the skull with the pin fixation are a real consideration [13].

The data from our large series regarding diagnostic yield and postoperative mortality and morbidity is consistent with the literature from the smaller series (Table 4) [1, 2, 6, 8–10, 14, 16, 19] and supports a move from frame-based technology towards applications such as the AxiEM. The primary advantage of using a frameless setup during brain biopsy is its speed and flexibility. Our experience revealed that the whole procedure takes under an hour including general anesthesia and the approximately 20 min

Table 2 Features of non-diagnostic cases

Targeting imaging modality	Size of the lesion	Location of lesion	Neuropathology consistent with smear
MRI	Diffuse white matter process	Right peritrigonal and splenial area	Yes
MRI	33 × 42 × 31 mm	Right subcentral gyrus	Yes
MRI	5 × 6 × 5 mm	Right hippocampus	No
MRI	20x18x20 mm	Right cuneus	n/a
MRI	Diffuse white matter process	Left lingual gyrus	No
MRI	9 × 10 × 9 mm	Right uncus	n/a
MRI	Diffuse signal change	Left corpus striatum	Yes
CT	20 × 16 × 19 mm	Rright peritrigonal area	Yes
MRI	12 × 7 × 9 mm	Right middle frontal gyrus	Yes
CT	Diffuse white matter process	Left peritrigonal area	No
CT	26 × 19 × 21 mm	Right supplementary motor area	n/a
MRI	Diffuse white matter process	Right peritrigonal area	Yes
MRI	Diffuse white matter process	Right peritrigonal area	Yes
CT	34 × 50 × 48 mm	Right insula	No
MRI	Diffuse white matter process	Left mesial temporal lobe	Yes
MRI	27 × 17 × 23 mm	Right cerebellum	No
MRI	14 × 10 × 12 mm	Pineal region	Yes
MRI	15 × 18 × 12 mm	Right middle frontal gyrus	Yes
MRI	19 × 10 × 14 mm	Pineal region	n/a
MRI	40 × 55 × 50 mm	Right posterior thalamus	n/a
MRI	21 × 16 × 18 mm	Right thalamus	n/a
MRI	Diffuse white matter process	Right middle frontal gyrus	n/a

n/a: frozen sample was not sent

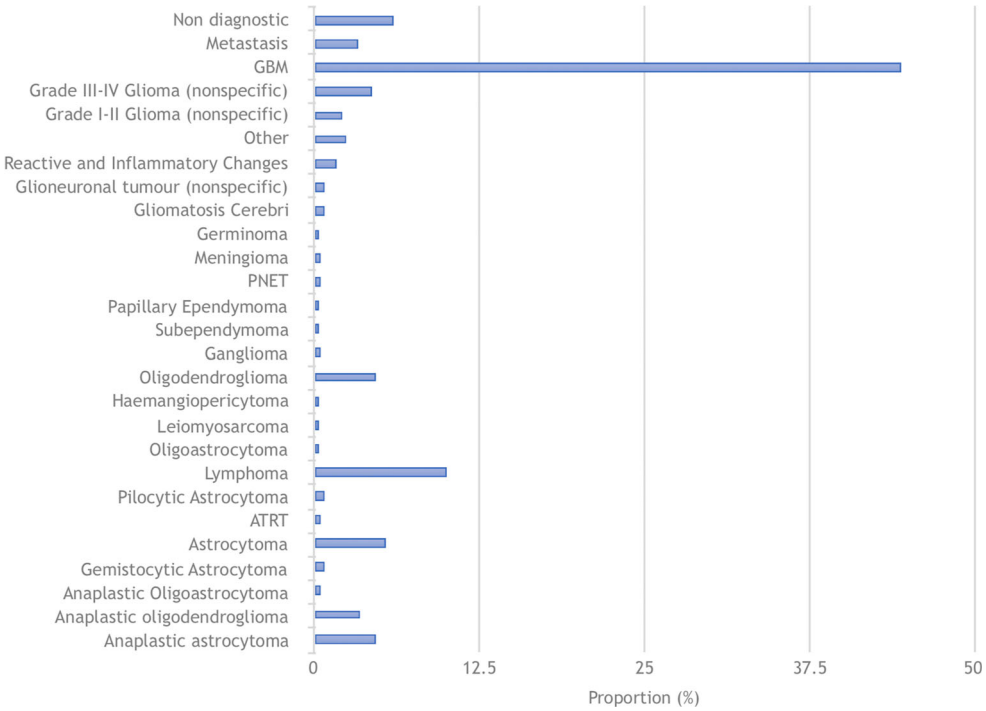

Fig. 1 Histopathological diagnoses

waiting time for the analysis of the frozen sample. The main advantage over other frameless pinless systems is the free-hand technique and the lack of adjunct intraoperative equipment.

One disadvantage of neuronavigation systems is that whilst the surgical instrument is tracked in real time, it does not track the brain in real time, so changes causing a shift in the neuroanatomy can lead to inaccuracies. Such changes include mainly brain shift from cerebrospinal fluid loss changing the geometry of the target lesion [15]. Furthermore, accuracy of frameless systems can be compromised by accuracy of probe tracking, quality of pre-operative imaging, and method of image-to-patient registration, though the latter is less likely with electromagnetic tracking. Clearly such issues are most likely to lead to miss targeting when the lesions are small. The vast majority of the non-diagnostic cases in our study were tumors of size < 20 mm or diffuse white matter processes, deep seated in eloquent areas and periventricular regions. Particular care therefore is required when targeting such lesions.

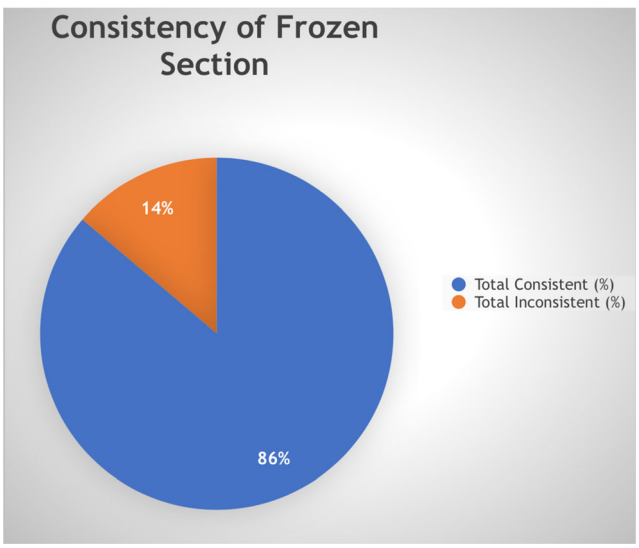

Fig. 2 Consistency of frozen section with the final histology

Patients undergoing a biopsy in whom the histology returns as non diagnostic or normal brain tissue present difficult challenges. In our series of 22 non-diagnostic samples, the neuro oncology multidisciplinary team (MDT) requested a repeat biopsy in 6 patients. In the remaining, the decision was made against a repeat biopsy either because of patients' significant co morbidities or because the non-diagnostic sample put into the context of the radiology was judged sufficient to guide management decisions. For example, in some cases, presence of no specific necrosis on the histology together with the typical appearance of a high-grade glioma on the MRI was deemed sufficient to start adjuvant therapy, whilst in others, nonspecific inflammation on histology in the presence of MRI features of intracranial inflammation was convincing enough for our MDT neurologist to commence appropriate therapy. This further underpins the importance of an experienced MDT in the management of patients with brain tumors, working together to integrate the clinical, radiological, and neuropathological data for optimal management decision-making. Another point to highlight is that in one-third of the non-diagnostic cases, a frozen sample was not sent, primarily due to the availability of the neuropathologist. We strongly

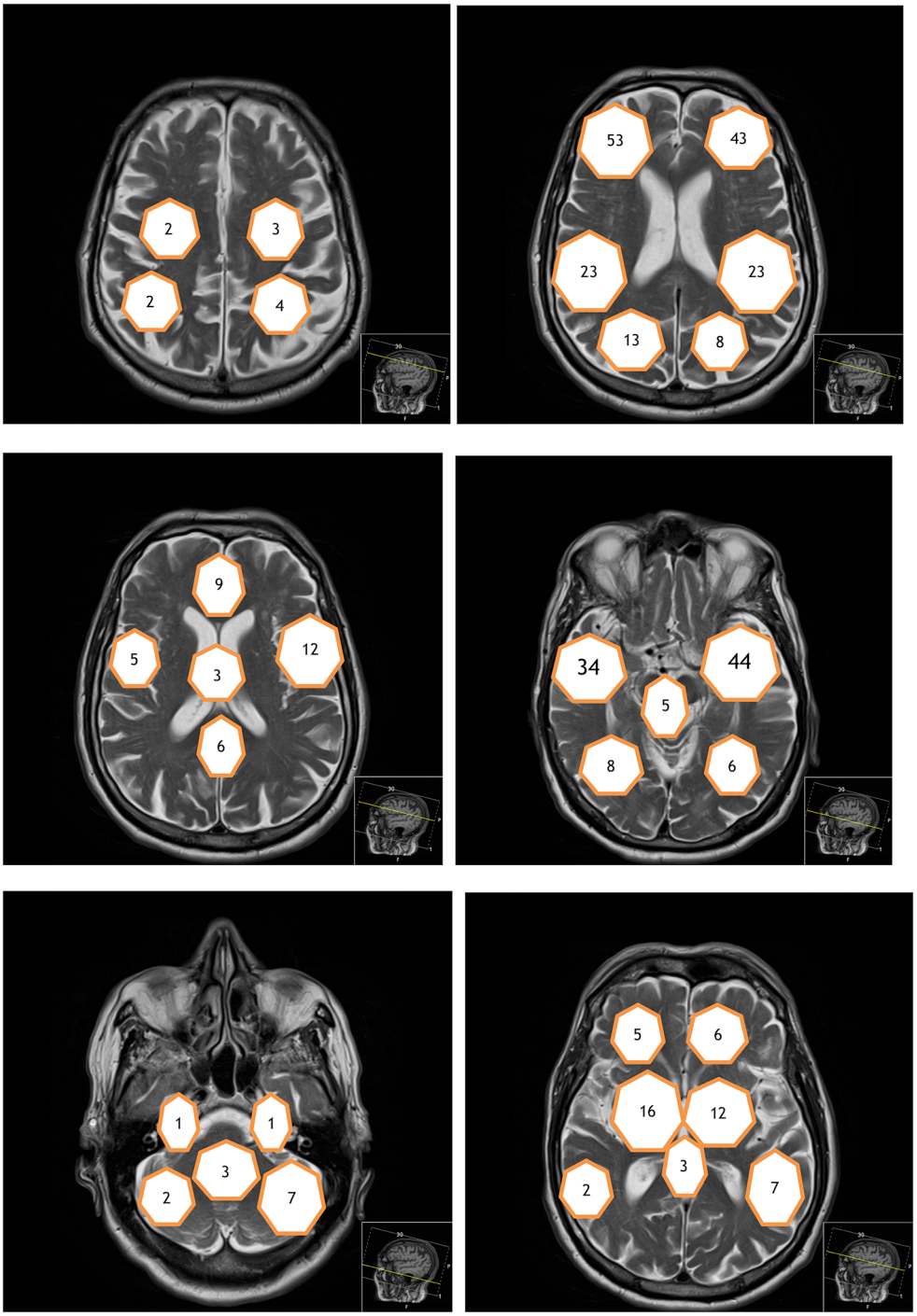

Fig. 3 Anatomical locations of tumors sampled

Table 3 Feature of patients who died

Targeting imaging	Diagnosis	Location	Neuropathology consistent with smear
MRI	GBM IV	Posterior corpus callosum	Yes
MRI	diffuse large B cell lymphoma	Left temporal lobe	n/a
CT	GBM IV	Left temporal lobe	Yes
CT	GBM IV	Right frontal lobe	Yes

Table 4 Comparison with other frameless series

Series	Number of cases	Non-diagnosis (%)	Mortality rate (%)	Morbidity rate (%)	Type of frameless system
Yi et al., 2015** [10]	113	10.6	5.3	NA	General Electrics
Shooman, Belli and Grundy, 2010 [14]	134	0.7	1.49	4.5	Stryker
Harrisson, Shooman and Grundy, 2011 [8]	150	0.7	0	0	Medtronic Stealth AxiEM
Lefranc et al., 2015 [9]	100	3	0	0	Medtech ROSA
Amin et al., 2011 [1]	50	2	0	2	iNtellect
Frati et al., 2010 [6]	296	0.3	0	1	Navigus
Verploegh et al., 2015* [16]	247	5.4	0.8	12.9	Medtronic Stealth Treon™ Vertek® and BrainLAB® Varioguide
Dammers et al., 2008 [4]	164	10.6	1.5	10.6	Stealth neuronavigation stationTM and the Stealth TreonTM
Bekelis et al., 2012 [2]	41	2.2	0	4	SurgiScope
Woodworth et al., 2006 [18]	110	11	1	6	Olivier Free Guide
Zhang et al., 2013 [19]	62	6.5	0	21	Brainlab
Georgiopoulos et al., 2018 [7]	28	10.7	0	3.6	Navigus
Our series	371	5.93	1.08	0	AXIEM™

*Testing two frameless systems against each other

**Lists serious complications only (death, neurological deficit, and/or return to theatre for emergent clot evacuation)

recommend doing so to minimize the risk of the final samples being non diagnostic. Interestingly, from this non-diagnostic group of 22 cases, in 5 occasions, the frozen sample raised the possibility of abnormal tissue, mainly due to increased cellularity or presence of atypical cells, but the final histopathology revealed normal brain tissue. Thus, even when arrangements for intraoperative frozen section are in place, there is still a risk of non-diagnosis and patients should be told of this small risk when obtaining informed consent. In keeping with other series, we found 1% risk of significant morbidity/mortality, primarily due to hemorrhage, which should also be highlighted at consent.

Notwithstanding the small burr hole and durotomy when performing a biopsy, given the concerns over brain shift, IoMRI-guided biopsy is recommended by some. Lu Y et al. compared the three methods of IoMRI, frameless, and frame-based biopsy technologies. Overall, the diagnostic yield of the IoMRI-guided technique was the lowest at 82.1%, compared with the frame-based (95.2%) and frameless (89.4%) techniques, although there was a significant selection bias in that a large proportion of IoMRI patients had already received radiation or prior resection which could have made the targeting difficult. The complication rate with the IoMRI technique was however slightly less than the other two techniques, warranting further research in defining its role in patients requiring biopsies.

Nevertheless, the up to date and large volume data of our study support currently the clear efficacy of the AxiEM system but we would also consider other techniques, such as open biopsy, in case the target lesion appears highly vascular or lies in a superficial area.

Conclusions

The AxiEM is a fast, effective, and safe frameless and pinless neuronavigational system. It offers a high degree of accuracy required for the establishment of a definitive diagnosis, permitting optimal further treatment, and thus improving patient outcomes.

Compliance with ethical standards

Conflict of interest The 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 (name of institute/committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

References

1. Amin DV, Lozanne K, Parry PV, Engh JA, Seelman K, Mintz A (2011) Image-guided frameless stereotactic needle biopsy in awake patients without the use of rigid head fixation. J Neurosurg 114: 1414–1420
2. Bekelis K, Radwan TA, Desai A, Roberts DW (2012) Frameless robotically targeted stereotactic brain biopsy: feasibility, diagnostic yield, and safety. J Neurosurg 116:1002–1006
3. Clark S, Sangra M, Hayhurst C (2008) The use of noninvasive electromagnetic neuronavigation for slit ventricle syndrome and complex hydrocephalus in a pediatric population. J Neurosurg Pediatr 2:430–434

4. Dammers R, Haitsma IK, Schouten JW, Kros JM, Avezaat CJJ, Vincent AJPE (2008) Safety and efficacy of frameless and frame-based intracranial biopsy techniques. Acta Neurochir 150:23
5. Dorward NL, Paleologos TS, Alberti O, Thomas DG (2002) The advantages of frameless stereotactic biopsy over frame-based biopsy. Br J Neurosurg 16:110–118
6. Frati A, Pichierri A, Bastianello S, Raco A, Santoro A, Esposito V et al (2011) Frameless stereotactic cerebral biopsy: our experience in 296 cases. Stereotact Funct Neurosurg 89:234–245
7. Georgiopoulos M, Ellul J, Chroni E, Constantoyannis C (2018) Efficacy, safety, and duration of a frameless fiducial-less brain biopsy versus frame-based stereotactic biopsy: a prospective randomized study. J Neurol Surg 79:31–38
8. Harrison SE, Shooman D, Grundy PL (2012) A prospective study into the safety and efficacy of frameless, pinless electromagnetic image-guided biopsy of cerebral lesions: electromagnetic image-guided biopsy of cerebral lesions. Neurosurgery 70:29–33
9. Lefranc M, Capel C, Pruvot-Occean A-S, Fichten A, Desenclos C, Toussaint P et al (2015) Frameless robotic stereotactic biopsies: a consecutive series of 100 cases. J Neurosurg 122:342–352
10. Lu Y, Yeung C, Radmanesh A, Wiemann R, Black PM, Golby AJ (2015) Comparative effectiveness of frame-based, frameless, and intraoperative magnetic resonance imaging-guided brain biopsy techniques. World Neurosurg 83:261–268
11. Mascott CR (2006) In vivo accuracy of image guidance performed using optical tracking and optimized registration. J Neurosurg 105:4
12. National Institute for Health and Clinical Excellence (2006) Guidance on cancer services: improving outcomes for people with brain and other CNS tumors https://www.nice.org.uk/guidance/csg10/resources/improving-outcomes-for-people-with-brain-and-other-central-nervous-system-tumours-update-27841361437. Accessed 8 Jan 2019
13. Reavey-Cantwell JF, Bova FJ, Pincus DW (2006) Frameless, pinless stereotactic neurosurgery in children. J Neurosurg Pediatr 104(6):392–395
14. Shooman D, Belli A, Grundy PL (2010) Image-guided frameless stereotactic biopsy without intraoperative neuropathological examination. J Neurosurg 113:170–178
15. Spetzger U, Laborde G, Gilsbach JM (1995) Frameless neuronavigation in modern neurosurgery. Minim Invasive Neurosurg 38:163–166
16. Verploegh ISC, Volovici V, Haitsma IK, Schouten JW, Dirven CM, Kros JM et al (2015) Contemporary frameless intracranial biopsy techniques: might variation in safety and efficacy be expected. Acta Neurochir 157:2011–2016
17. Watanabe E, Watanabe T, Manaka S, Mayanagi Y, Takakura K (1987) Three-dimensional digitizer (neuronavigator): new equipment for computed tomography-guided stereotaxic surgery. Surg Neurol 27:543–547
18. Woodworth GF, McGirt MJ, Samdani A, Garonzik I, Olivi A, Weingart JD (2006) Frameless image-guided stereotactic brain biopsy procedure: diagnostic yield, surgical morbidity, and comparison with the frame-based technique. J Neurosurg 104:233–237
19. Zhang QJ, Wang WH, Wei XP, Yu YG (2013) Safety and efficacy of frameless stereotactic brain biopsy techniques. Chin Med Sci J 28:113–116