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Frameless stereotactic brain biopsy: technical considerations and clinical results regarding safety and efficacy

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While frame-based stereotactic techniques have been the gold standard for highly precise, reliable, and accurate approaches to intracranial targets for decades, frameless stereotactic systems have evolved, with advantages including greater flexibility and patient comfort, and are widely used. Numerous studies have demonstrated comparable results regarding target accuracy and procedure-related complications in frameless stereotactic methods compared to frame-based systems. However, there are several technical concerns. This review examines frameless stereotactic brain biopsy techniques in the context of diagnostic yield and safety (i.e., procedural mortality or morbidity).

KEY WORDS: Biopsy, Neuronavigation, Stereotaxic techniques

INTRODUCTION

After stereotactic brain surgery was first described by Zernov using the 'encephalometer' in 1889, stereotaxis was introduced into the animal by Horsely and Clarke in 1908 and into humans by Spiegel and Wycis in 1947 [1,2]. Frame-based techniques have been an integral part of many other neurosurgical procedures for a long time and have been regarded as the gold standard method for reliable and accurate sampling of intracranial lesions for decades. However, frame-based techniques are regarded as troublesome due to a few factors, such as frame structure, patient discomfort, imaging after frame application, calculations of the entry point, prolonged surgical time, and complication of frame fixation [3,4].

With the advancement in modern neuroimaging and neuronavigation technologies, frameless stereotactic brain biopsy has been developed and widely utilized in recent years. A number of previous studies reported that frameless stereotactic brain biopsy has accuracy and complication rates comparable to frame-based stereotactic systems [1,2]. Furthermore, frameless techniques do not depend on burdensome stereotactic frames, have fewer limitations in space and handling during preoperative imaging, and allow easier planning, making it a time- and cost-saving procedure [5]. Nevertheless, it may provide less stability and accuracy during drilling and positioning, which ultimately might lead to the occurrence of a targeting error.

Here, we performed a comprehensive review of recently reported data on the accuracy, safety, and technical considerations of frameless stereotactic brain biopsy.

TECHNICAL CONSIDERATIONS

The frameless stereotactic system enables cranial registration in the stereotactic space using skin- or bone-mounted fiducials and markerless registration, instead of a rigid frame mounted on the patient's cranium. A neuronavigation reference star was attached to the head clamp after the patients being positioned. Navigation was then registered by laser pointer surface registration [6]. After registration, the skin surface accuracy was finally checked. The surgical plan (entry point, biopsy target, and needle trajectory) was determined using a navigation software module within the cranial application. The most frequently applied systems to date are the Stealth neuronavigation stationTM or Stealth TreonTM (Medtronic Inc., Minneapolis, MN, USA) [1] and the Brainlab® Varioguide system (Brainlab AG, Munich, Germany) [7].

Comparing frameless with frame-based techniques with regard to registration accuracy in controlled phantom settings presented no significant differences [8,9]. However, a decrease in accuracy primarily occurs at the beginning of the procedure due to reduced patient registration accuracy in routine clinical situations. In particular, patient registration is performed in the operating room using fiducials attached to the skin the day before surgery, which can be a considerably error-prone and user-dependent practice, resulting in registration errors of up to several millimeters [10]. A few clinical studies have addressed the quantitative accuracy of frameless neuronavigation for brain biopsies in patients, with an accuracy varying from 2 to 4.8 mm [11].

Recently, rapid advanced imaging and stereotactic biopsy have been integrated to significantly improve diagnostic accuracy and reduce periprocedural morbidity and mortality. The introduction of modern intraoperative computed tomography (CT), such as the O-arm (Medtronic Inc.) or the AIRO-CT (Brainlab AG), allows user-independent automatic registration with high accuracy and low radiation exposure in cranial procedures [12,13]. A recent study found a slightly higher diagnostic rate of 96.7% with intraoperative CT registration and 95% with standard registration, likely a result of the consequent implementation of intraoperative examination of the specimens in the workflow [14]. In addition, the application of intraoperative magnetic resonance imaging (MRI) technology to stereotactic biopsy could also abolish misdiagnosis secondary to targeting error, provide real-time feedback for needle trajectory, endorse accurate biopsy cannula position, and obtain immediate imaging of complications [15]. In another study, with the help of intraoperative MRI, a 100% diagnostic yield was achieved without any procedure-related complications [16].

Meanwhile, several advanced imaging modalities have been suggested, such as spectroscopy, perfusion, and metabolic studies, aim-

ing to improve the efficacy of biopsy and decrease biopsy-related complications [17-19]. In particular, diffusion tensor imaging tractography represents an innovative method that can examine the individual fiber tract conformation in cases of brain tumors and consequently identify the best biopsy trajectory, preserve the white matter tract, and reduce secondary brain damage [20].

In addition to the incorporation of neuroimaging, robot-assisted stereotactic procedure systems are among the newest technological improvements at the time of writing in contemporary neurosurgery. Robot technologies have been coupled with stereotactic surgery, leading to the introduction of robotized devices that assist the surgeon in guiding instruments along planned trajectories [21,22]. Consequently, robotic surgery has the potential to enhance surgical precision and accuracy through motion scaling and tremor filters by reducing human interference, such as manual parameter settings, calibrations, and adjustments, with a diagnostic yield comparable to or even more accurate than frame-based stereotactic systems [23]. A recent review on robotic stereotactic methods showed that, overall, robotized frameless systems have a nondiagnostic rate ranging from 2.2–4.3%, a hemorrhagic rate ranging from 8–10%, and a mortality rate between 0–0.5%, which is similar to the results of frame-based and frameless manual stereotactic devices [24].

CLINICAL RESULTS OF ACCURACY AND SAFETY

According to the literature, diagnostic yield and procedure-related complications are not significantly different between frame-based and frameless brain biopsies. Table 1 summarizes the results of recent reports investigating the safety and diagnostic yield of frameless stereotactic biopsy [6,25-34]. The frame-based technique provides a diagnostic yield of 81.3–99.2%, while the diagnostic yield of frameless stereotactic brain biopsy has been presented to range between 89% and 99.3% for various techniques [7,33,35,36]. Complications of frameless biopsy are as frequent or even rarer compared with frame-based stereotactic biopsy [1]. Various researchers have determined low rates of permanent neurological deficit (1.4–1.5%), hemorrhage (1.8–9%), and procedure-related mortality (1.0%) due to frameless stereotactic brain biopsy [1].

A prospective randomized study comparing 28 frame-based and 28 frameless biopsies performed in 56 adult patients showed that a diagnosis was not made in four cases (14.3%) of the frame-based biopsy group and in three cases (10.7%) of the frameless biopsy group, despite accurate targeting ($p > 0.99$). There were no statistically significant differences between the two methods regarding new neurological symptoms and findings in the postoperative period

Table 1. Recent studies on diagnostic yield and complications of frameless stereotactic brain biopsy

Study (year)	Total No.	Diagnosis (%)	Mortality (%)	Morbidity (overall, %)	Morbidity (major, %)
Zhang et al. [34] (2013)	62	93.5		21	16.1
Khatab et al. [28] (2014)	235	94.5	0.9	8.5	
Nishihara et al. [31] (2014)	38	97.4		0	
Castle et al. [26] (2014)	75	97.1		10	
Lu et al. [29] (2015)	113	91.8		19.6	5.3
Verploegh et al. [33] (2015)	204	94.6	0.8	12.9	1.2
Georgiopoulos et al. [27] (2018)	28	89.3		3.6	
Taweesomboonyat et al. [6] (2019)	89	87.6		19	
Sciortino et al. [32] (2019)	140	93.6	0	7.8	2.1
Mader et al. [30] (2019)	180	92.4	0.8		1.7
Bishokarma et al. [25] (2019)	46	89.1		4.35	

[27]. One meta-analysis including 15 studies and 2,400 patients suggested that no significant differences exist between frame-based and frameless biopsy regarding the diagnostic yield (odds ratio [OR] = 1.01, 95% confidence interval [CI] = 0.71–1.41), biopsy-related morbidity (OR = 1.13, 95% CI = 0.76–1.66), or biopsy-related mortality (OR = 0.94, 95% CI = 0.40–2.17) [37]. Recent meta-analysis comparing 1,206 frameless and 2,050 frame-based stereotactic brain biopsies did not demonstrate any significant difference between the two stereotactic systems in term of diagnostic yield (risk ratio [RR] = 1.00, 95% CI = 0.99–1.02). In addition, the only significant difference was the increased frequency of asymptomatic hemorrhages in the frameless group (RR = 1.37, 95% CI = 1.06–1.75) [38].

However, several issues should be considered when comparing these results due to various factors that influence the diagnostic yield and complications. The volume or size of the biopsied lesion is a vital component affecting diagnostic yield. One clinical study found that a lesion diameter of > 3 cm is essential in predicting diagnostic yield, while small lesions were associated with postoperative hematoma [6]. On the other hand, the reported meta-analysis results are unlikely to be applicable to lesions < 1 cm in maximal diameter [37]. Other factors associated with postoperative neurological decline in previous research include a high serum glucose level, diabetes, intraoperative bleeding complications, biopsy needle size, multiple needle tracks, pathological diagnosis of lymphoma, and the location of the lesion, such as the basal ganglia, thalamus, frontotemporal locations, or posterior fossa.

Currently, as decisions regarding the treatment strategy for brain tumors are increasingly based on molecular characteristics of the tissue, tissue sampling of small molecular imaging hotspots is vital and thus requires a higher precision of stereotactic biopsy techniques [39]. In several biopsied glioma cohorts applying the frameless system, diagnostic yield ranged from 92.4–93% [30].

In addition to the advantages of greater patient acceptance and tolerance, there is growing evidence that there is no significant difference in the biopsy diagnostic yield and presence of negative clinical outcomes between standard frame-based and frameless stereotactic techniques. Furthermore, the continuing evolving technologies can allow frameless systems to be progressively more user-friendly, allow more accurate targeting, and even yield less neurological deficits. On the contrary, there have been conflicting results concerning hospital stay, operating time, and cost of the two methods. Therefore, further studies on unsolved issues, such as efficiency, cost-effectiveness, end-user satisfaction, intraoperative stress, and patients' overall comfort are warranted to draw definite conclusions regarding the role of frameless stereotactic biopsy.

CONCLUSION

This study, which conducted a recent literature review, has shown no differences exist between frame-based and frameless

biopsy in terms of diagnostic yield, morbidity, and mortality. However, further well-designed cohort studies regarding some issues, including molecular diagnosis, are required to validate and extend these conclusions and to improve patient therapy.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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