ACCURACY COMPARISON BETWEEN FRAMELESS BIOPSY AND FRAME-BASED BIOPSY: A RETROSPECTIVE STUDY OF SERIES CASES

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ABSTRACT

Objective: To compare the efficacy and safety of frameless and frame-based techniques for biopsies of intracranial lesions in an exclusive assistance service at a public health centre in Brazil (SUS). Method: A review of 65 medical records of patients with brain lesions who underwent a frame-based or frameless biopsy from September 2017 to July 2019 was performed. Results: Among the 65 patients who underwent a biopsy, 42 were male, and 23 were female. The mean age was 53,1.years. Most patients (49; 75.4%)presented hemispheric lesions, and of these, 27 were in the frontal lobe(41,5%). The diagnostic rate was 78,5% (51 in 65 patients), and glial neoplasia was the most common diagnosis. In addition to glial neoplasia, a wide range of pathologies were diagnosed, such as toxoplasmosis, metastasis, lymphoma, inflammatory lesions, and abscesses. In the inconclusive results from 14 patients(21,5%), 8 had gliosis without neoplasia (12,3%), 4 had necrosis (6,1%), and 2 had insufficient samples(3%). The morbidity rate was 9,2%, with 4 cases of haemorrhage, 1 case of infection and 1 case of worsening of neurological deficits. The mortality rate was 6,1% and occurred in all cases with haemorrhage. There were no significant differences in the diagnosis or complication (morbidity and mortality) rates between the frame-based and frameless groups. Conclusion: The frame-based and frameless techniques for stereotactic biopsy present similar efficacy and safety.

INTRODUCTION

For patients with intracranial lesions without indication of surgical removal, stereotactic guided biopsy remains the gold standard for diagnosis, since treatment based only on the clinical and radiological aspects is insufficient in up to one-third of the cases, even when modern diagnosis techniques are used [1,2]. Thus, histopathological diagnosis is fundamental in handling these patients [3].

When using stereotaxis in these procedures, the concept of minimally invasive surgery is adopted [4], and the advantages of this approach are countless, including less surgery time, less damage in eloquent areas, and consequently, less morbidity [5].

Stereotactic biopsy is usually performed using the lesion spatial coordinates in an adjustable rigid instrument holder (stereotaxis halo) on the patient's skull (frame-based biopsy). This technique is widely used, and its efficacy and safety have been proven by many studies [6-9].

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More recently, with the development of image-guided surgery, new biopsy techniques are evolving, such as frameless biopsy, which uses fiducial markers in the patient's anatomy as coordinates for the lesion spatial localization, with no need to use a stereotaxis halo [6-9-10].

The objective of this study is to compare frame-based and frameless techniques for intracranial lesion biopsies regarding efficacy and safety in an exclusive assistance service at a public health centre in Brazil (SUS).

MATERIALS AND METHODS

An observational and retrospective study with 65 patients was performed using medical records of patients who underwent intracranial lesion biopsy at Santa Casa de Misericórdia de Belo Horizonte between September 2017 and July 2019. The study was approved by the ethics committees of the Santa Casa de Belo Horizonte (CAAE: 8146331720005138).

The patients were divided into two groups: frame-based and frameless biopsy.

FRAME-BASED BIOPSY

Frame-based biopsies were performed supported by the device for stereotactic biopsy CRW® (Integra ®).

With the patient under local anaesthesia, the stereotaxis halo was placed, and then, the patient underwent a brain tomography scan out of the operating room. The tomography slice thickness was 1 mm with an interval of 1 mm, and 9 fiducial markers were identified for surgical planning.

After imaging, the test was transferred to the StealthStation7® neuronavigation station (Medtronic®). Then, planning was carried out with the definition of coordinates x,y,z arc, and ring for the proposed target.

The surgical procedure was performed with sedation and local anaesthesia. After the coordinates are placed in the halo, a linear incision is made on the skin based on the target centre, followed by trepanation. The needle used for the biopsy of fragments on the proposed target was Micromar®.

FRAMELESS BIOPSY

The frameless procedures were performed with a neuronavigation system based on infrared light StealthStation7® (Medtronic®). The system is composed of portable hands recognized by a set of cameras connected to a mobile workstation that, in turn, displays the hands' position on the monitor screen [12].

Surgical planning was performed from brain tomography or MRI before the surgical procedure and transferred to the neuronavigation system with the patient's record. This procedure was usually preoperative, aiming to obtain a biopsy trajectory with minimal tissue trauma and avoid critical structures. The arteries and veins could be observed in images reconstructed in multiple plans to minimize the risk of intracerebral haemorrhage. The trajectory can be modified interactively with no need for another stereotactic calculation [13,14}.

The patients are submitted to general anaesthesia and then have the brain secured with holders of the type Mayfield® or Sugita®. After the holder was placed, the cranial markers were registered, guided by the portable hands for the neuronavigation procedure.

Once the neuronavigation was set, a skin marking was made with an incision, usually using the direction of the proposed target as a centre, as well as the trepanation. A stereotactic guide using a flexible surgical arm (Vertec - Medtronic®) was projected to allow the fine adjustment trajectory. The arm was locked into place, and the needle was inserted according to the planned target. The necessary depth of needle insertion was calculated by the system. The biopsies were obtained with Micromar® needles.

STATISTICAL ANALYSIS

The frameless biopsy was compared with the frame-based biopsy.

The diagnosis, morbidity and mortality rates were evaluated. These data were compared between the two techniques through the Statistical Package for Social Sciences® software using Fisher's exact test or the X^2 test.

LOCATION

The diagnosis rates of the two techniques were also compared according to the tumour locations. They were divided into two groups: superficial and deep. Superficial lesions were

located in the frontal, parietal, temporal, occipital regions, and cerebellum. Deep lesions were located in the basal ganglia, insula, and brainstem.

RESULTS

Population

A total of 65 patients underwent biopsy by stereotaxis, and their data were analysed. Of these,

42 were male, and 23 were female. The mean age was 53,1. Most patients (49; 75.4%) presented hemispheric lesions, and of these, 27 were in the frontal region (41,5%). In 16 patients with deep lesions (24, 6%), 12 had lesions located in the basal ganglia (18, 5%) (Table 1).

By analysing the data from each group, it can be observed that the frame-based group comprised 26 patients, 20 of whom were male and 6 of whom were female, with an average age of 57,7 years. The frameless group comprised 39 patients, including 22 males and 17 females, with a mean age of 50,3 years.

The main tumor location in both groups was hemispheric, and the frontal region was the most common, as it was observed in 13 patients in the frame-based group (50%) and fourteen patients in the frameless group (35,9%). The frame-based group had a higher incidenceof deep location biopsies, with 9 patients(34,6%) compared with 7 patients in the frameless group (17,9%) (Table 2).

Table 1 - Locations of lesions and characteristics of patients who underwent biopsy by stereotaxis

Characteristics	
Number of procedures, n	65
Gender n (%)	
Female	23 (35,4)
Male	42 (64,6)
Age n (%)	
< 60	36 (55,4)
≥ 60	29 (44,6)
Mean (DP/Min-Max)	53,1(17,8/5-89)
Location, n %	
Hemispheric	49 (75,4)
Frontal	27 (41,5)
Parietal	15 (23,1)
Occipital	1 (1,5)
Temporal	5 (7,6)
Deep	16 (24,6)
Basal ganglia	12 (18,5)
Insula	2 (3)
Brainstem	2 (3)

n: absolute number DP: standard deviation Min: minimal Max: maximal

Table 2 - Location of lesions in the frameless and frame-based groups

Characteristics:	**Stereotactic biopsy method**	
	frame-based	***frameless***
Number of procedures, n	26	39
Location, n (%)		
Hemispheric	17 (65,4)	32 (82,1)
Frontal	13 (50)	14 (35,9)
Parietal	4(15,4)	11 (28,2)
Occipital	-	1 (26,1)
Temporal	-	5 (12,8)
Deep	9 (34,6)	7 (17,9)
Basal ganglia	7 (26,9)	5 (12,8)
Insula	2 (7,7)	-
Brainstem	-	2 (5,1)

n: absolute number DP: standard deviation Min: minimal Max: maximal

Mortality, morbidity, and diagnosis rates

The diagnosis rate was 51 out of 65 patients(78%); glial neoplasia was the most common diagnosis, given that diffuse gliomas of low and high grade account for55,3% of the results.

In addition to glial neoplasia, a large number of pathologies were diagnosed, such as toxoplasmosis, metastasis, lymphoma, inflammatory lesions, and abscesses. In the 14 inconclusive samples (21,5%), the results were 8 patients with gliosis without neoplasia (12,3%), 4 patients with necrosis (6,1%), and 2 patients with insufficient sample (3%).

The morbidity rate was 9,2%, including 4 cases of haemorrhage, 1 case of infection and 1 case of worsening of neurological deficit. The mortality rate was 6,1% and occurred in all the cases that presented haemorrhage (Table 3).

Table 3 - Morbimortality and diagnosis rates of patients who underwent biopsy by stereotaxis

Morbimortality and diagnosis rates	
Number of procedures, n	65
Morbidity, n (%)	
Procedures with complications	6 (9,2)
Haemorrhage	4 (6,1)
Worsening of deficits	1 (3)
Infection	1 (1,5)
Mortality, n (%)	
Deaths	4 (6,1)
Biopsies with histological diagnosis, n (%)	
Conclusive	51 (78,5)
High-grade diffuse glioma	27 (41,5)
Low-grade glioma	9 (13,8)
Unspecified inflammatory lesions	5 (7,6)
Abscess	3 (4,6)
Lymphoma	3 (4,6)
Metastasis	2 (3)
Toxoplasmosis	2 (3)
Inconclusive	14 (21,5)
Gliosis without neoplasia	8 (12,3)
Necrosis	4 (6,1)
Insufficient sample	2 (3)

n: absolute number

In the histological diagnosis analysis separated by group, we observed the largest prevalence for both high-grade gliomas, with 9 patients in the frame-based group (34,6%) and 18 patients in the frameless group (46,2%). (Table 4)

Table 4 - Characteristic and histological diagnosis of lesions in the frame-based and frameless groups

Characteristics	**Stereotactic biopsy method**	
	Frame-based	***Frameless***
Number of procedures, n	26 (100)	39(100)
Biopsies with histological diagnosis, n(%)		
Conclusive	21 (80,8)	30 (76,9)
High-grade diffuse glioma	9 (34,6)	18 (46,2)
Abscess	3 (11,5)	-
Unspecific inflammatory lesions	3 (11,5)	2 (5,1)
Low-grade diffuse glioma	2 (7,7)	7 (17,9)
Lymphoma	2 (7,7)	1 (2,6)
Metastasis	1 (3,8)	1 (2,6)
Toxoplasmosis	1 (3,8)	1 (2,6)
Inconclusive	**5 (19,2)**	**9 (23,1)**
Gliosis without neoplasia	3 (11,5)	5 (12,8)
Necrosis	2 (7,7)	2 (5,1)
Insufficient sample	-	2 (5,1)

n: absolute number

Morbimortality and diagnosis rates: Frame-based versus Frameless

Regarding the diagnosis rate, 21 out of 26 patients in the frame-based group were diagnosed (80,8%), whereas in the frameless group, 30 out of 39 patients showed no significant difference (p= 0,71).

Two patients in the frame-based group had complications (7,7%); one patients had worsening deficits, and the other had bleeding in the surgical site and posterior evolution to death (3,8%). Four patients in the frameless group had complications: one patient had an infection in the surgical site, and the other 3 patients presented bleeding, all of which evolved to death (7,7%). When comparing the complication rates, there was no significant difference between the techniques (p=0,64) (Table 5).

Table 5 - Comparative analysis of the morbimortality and diagnosis rates between the frame-based and frameless groups

Characteristics	Stereotactic biopsy method		
	Frame-based	*Frameless*	Value-p
Morbidity			
Procedures without complications	24 (92,3)	35 (89,7)	
Procedures with complications	2 (7,7)	4 (19,3)	1,00*
Mortality			
No death	25 (96,2)	36 (92,3)	
Deaths	1 (3,8)	3 (7,7)	0,64*
Biopsies with diagnosis			
Conclusive	21 (80,8)	30 (76,9)	
Inconclusive	5 (19,2)	9 (23,1)	0,71**

n: absolute number * Fisher Exact Test ** X^2 Test

Diagnosis rate in superficial and deep lesions: Frame-based versus Frameless

For superficial lesions in the frame-based group, the diagnostic rate was 14 out of 17 lesions (82,4%). In turn, in the frameless group, the diagnosis rate was 24 out of 32 cases (75%). There was no significant difference in diagnostic rates between the two groups. (Table 6)

For deep lesions in the frame-based group, the diagnostic rate was 7 out of 9 cases (77,8%). In the frameless group, the diagnosis was made in 6 out of 7 cases (85,7%). As in the superficial lesions, there was no significant difference in diagnostic rate between the groups. (Table 7)

Table 6 - Comparison of superficial lesions (frontal, parietal, temporal, occipital, and cerebellum) in the frame-based and frameless groups concerning diagnosis

Characteristics **Superficial site lesions**	**Biopsy methods stereotaxis, n (%)** ***Frame-based***	 ***Frameless***	**Valor-p**
Biopsies with Diagnosis			
Conclusive	14 (82,4)	24 (75,0)	0,73*
Inconclusive	3 (17,6)	8 (25,0)	

n: absolute number *Fisher Exact Test

Table 7 - Lesion comparison in deep sites (insula, basal ganglia, and brainstem) in the frame-based and frameless groups, related to diagnosis.

Characteristics **Lesions in deep sites**	**Biopsy methods stereotaxis, n (%)** ***Frame-based***	 ***Frameless***	**Valor-p**
Biopsies with Diagnosis			
Conclusive	7 (77,8)	6 (85,7)	1,00*
Inconclusive	2 (22,2)	1 (14,3)	

n: absolute number *Fisher Exact Test

DISCUSSION

In the present study, we revised our retrospective experience with frameless and frame-based stereotactic intracranial biopsies for 2 years. There are considerable differences regarding the two surgical techniques.

First, frame-based stereotactic biopsy is performed with local anaesthesia and sedation, and general anaesthesia is hardly used, whereas the frameless approach is performed under general anaesthesia due to the holder (Mayfield® or Sugita®) placed on the head. Therefore, in frameless stereotactic biopsy, the patient is unable to cooperate to identify possible complications: the start of a headache, some change in the neurological test, or other signs that could point to some haemorrhage. (Owen et Al, J Neurooncol) [15].

Second, in frame-based biopsy, after securing the stereotactic halo, the patient needed to undergo a brain CT scan out of the operating room. This requires more surgical time. In the frameless group, since the imaging test guiding the biopsy was performed before the procedure, the surgical time was shorter. Dorwardet et al.reported that the procedure in the frameless group

lasted 20-180 minutes, and the frame-based group procedure lasted 80-235 minutes. The surgery time in the frame-based group was longer (p<0,0001 l) [16].

Another point worth mentioning with respect to the frameless technique is that the trajectory can be interactively modified during the surgery, in contrast to the frame-based technique, where a new stereotactic calculation needs to be made in the trajectory change [13,14].

Some authors have suggested that the frame-based technique has greater accuracy in intracranial lesion biopsies. [10,14]. However, when data from the literature on both techniques are analysed, the diagnosis rates do not show significant differences[17,18]. In the meta-analysis performed by Dhawan S. et al (2,400 patients), which comprised 15 studies on both techniques, the diagnostic rate for frame-based biopsy ranged from 84% to 100%, and in the studies on the frameless technique, the results ranged from 86,6% to 100%, with no significant difference between the two techniques [11]. The current study also presented similar results.

With respect to morbimortality, the literature shows that morbidity rates range from 3,8% to 27,8% and that mortality rates range from 1,2% to 3,9% in the frame-based group.Morbidity and mortality rates ranged from 3% to 24,5% and 1,3% to 3,6%, respectively, in the frameless group; there were no significant differences in morbimortality rates between groups [11].

Some authors suggest that the frame-based technique should be indicated in the case of tumours located in the brainstem, basal ganglia, pineal,lesions located less than 10 mm from vascular structures and lesions located less than 5 mm from vascular structures due to its greater accuracy [19,20]. Considering these indications, Owen et al believed that lesions that did not present these criteria should have frameless biopsies; in 100 cases of brainstem biopsies, 82% should undergo a frameless biopsy as an alternative to frame-based biopsies. [15]

In this study, lesions located in the brainstem, basal ganglia, and vascular structures (located in the insula) were classified as deep lesions. Even in these cases, we found similar efficacy resultswhen the two techniques are compared.

One limitation of this study is that it was a single-centre retrospective analysis of a relatively small number of cases. In addition, although the groups were similar, it was a nonrandomized study, and the indication of which technique to usewas in line with the experience of the surgeons in the centre using frame-based or frameless techniques.

CONCLUSION

We have concluded that both frameless and frame-based techniques have similar efficacy and safety to perform stereotactic biopsies, even in the case of deep lesions.

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