



Original Article

# Indicators of correct targeting in stereotactic biopsy of intracranial lesions

Oswaldo Vilela-Filho, Jairo Porfírio Jr, Lissa C. Goulart

Division of Neurosurgery, Department of Surgery, Medical School, Federal University of Goiás, Goiânia, Brazil.

E-mail: \*Oswaldo Vilela-Filho - ovilelafilho@clanfer.com; Jairo Porfírio - jairopoj@gmail.com; Lissa C. Goulart - lissa.carrilho@gmail.com



**\*Corresponding author:**

Oswaldo Vilela-Filho,  
Division of Neurosurgery,  
Department of Surgery, Medical  
School, Federal University of  
Goiás, Goiânia, Brazil.

ovilelafilho@clanfer.com

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## ABSTRACT

**Background:** Confirmation of whether a stereotactic biopsy was performed in the correct site is usually dependent on the frozen section or on novel tumor-specific markers that are not widely available. Immediate postoperative computed tomography (CT) or magnetic resonance (MR) is routinely performed in our service after biopsy. In this retrospective study, we have carefully analyzed these images in an attempt to determine the presence of markers that indicate appropriate targeting.

**Methods:** Medical records and neuroimages of patients who underwent stereotactic biopsy of intracranial lesions were reviewed. The following variables were assessed: age, sex, anatomopathology, lesion site, complications, diagnostic accuracy, and the presence of image markers.

**Results:** Twenty-nine patients were included in this case series. About 96.6% of the biopsies were accurate according to the permanent section. Of the 86.2% of patients with intralesional pneumocephalus on the postoperative images, 51.7% additionally presented petechial hemorrhage. In 13.8% of the cases, no image markers were identified.

**Conclusion:** This is the first report of intralesional pneumocephalus and petechial hemorrhage as indicators of appropriate targeting in stereotactic biopsy. In the majority of the cases, an immediate postoperative head CT, which is widely available, can estimate how adequate the targeting is. To use intralesional pneumocephalus/petechial hemorrhages as not only postoperative but also as intraoperative markers of appropriate targeting, it is advised that the surgical wound should be temporarily closed and dressed after the biopsy so that the patient can undergo a CT/MR scan and be checked for the presence of these markers before removing the stereotactic frame.

**Keywords:** Brain tumor, Computed tomography, Magnetic resonance, Petechial hemorrhage, Pneumocephalus, Stereotactic biopsy

## INTRODUCTION

Stereotactic brain biopsy has been used for many years to collect fragments of intracranial lesions that are usually deep seated or located in eloquent brain areas. It presents a high diagnostic accuracy, despite minimal invasion. The safety and reliability of this procedure are often paramount to the indication and optimization of therapies.<sup>[22,34,37,51,52]</sup>

The gold standard for intraoperative diagnosis of the acquired tissue samples is frozen section.<sup>[52]</sup> However, on reviewing the literature over a period of 5 years (pubmed.com: June 2015/June 2020), only 13 out of the 59 original publications on stereotactic biopsy in humans<sup>[11-59]</sup> reported

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the use of frozen section.<sup>[2,6,12,28,32,34-36,51,52,54,55,57]</sup> In cases of cystic lesions, such as brain abscesses, the mere aspiration of pus is enough to confirm appropriate targeting, making pathology consultation unnecessary.

Recently, new techniques that include pathologic tissue-specific markers, such as 5-aminolevulinic acid (5-ALA) and fluorescein, have been introduced, allowing intraoperative detection of fluorescence in the obtained sample, and thus providing prompt verification of targeting adequacy.<sup>[35,36,51,52]</sup> These techniques, however, are only useful for tumors and are not widely available.

Therefore, there seems to be a need to search for new markers that confirm whether the biopsied site was correct. Such markers should be, preferably, easily accessible and available at any neurosurgical center.

The main goal of this study was to verify the existence of these indicators on early postoperative computed tomography (CT) or magnetic resonance (MR) images of patients submitted to stereotactic biopsy of intracranial lesions.

## MATERIALS AND METHODS

This is a retrospective study based on the review of medical records and neuroimaging studies of patients who underwent stereotactic biopsy of intracranial lesions performed by a single neurosurgeon (OV-F) at our institution, from May 2016 to October 2021. This study was approved by the Local Research Ethics Committee (technical report # 5.055.873) that waived the need for patient consent.

Early postoperative nonenhanced CT and/or MR images (first 24 h) were carefully analyzed for the presence of signs indicating appropriate lesion targeting and correlated with the preoperative images. The anatomopathology and immunohistochemistry reports were reviewed to determine the diagnostic yield. Procedure-related complications were recorded. Finally, the findings on the postoperative images were compared with the anatomopathology/immunohistochemistry results.

### Surgical technique

The stereotactic frame (AimSystem, Micromar, Diadema, Brazil) was placed with local anesthesia using a mixture of lidocaine 2% with vasoconstrictor and bupivacaine 0.5% (blockade of the greater and lesser occipital nerves and of the supraorbital nerves). A stereotactic post contrast CT scan was obtained and merged or not with frameless MR images (MNPS, Mevis, São Paulo, Brazil) acquired on the previous day, depending on the adequate identification of the lesion on CT images. The stereotactic coordinates, entry point, and trajectory of the biopsy needle were calculated using the aforementioned software. Sometimes, the coordinates were

determined directly on the CT scanner using the available tools. The entry point varied according to the location of the lesion, but was placed at the precoronal parasagittal region with greater frequency.

The point elected for targeting depended on the following lesion characteristics: the margin and center of ring enhancing lesions; the center of homogeneous lesions; hotspots on MR perfusion; and areas with low apparent diffusion coefficient map on diffusion-weighted MR.

For tissue sampling, we used the Sedan needle with a lateral window of 5.0 or 10.0 mm, depending on the size of the lesion. The center of the lateral window was placed at the target. Specimens were usually collected at the four quadrants of the target, 5.0 mm above, and 5.0 mm below, totaling 12 samples.

The fragments were placed in a 10% formalin solution and sent to the pathology laboratory. Frozen section was not performed in these cases.

To rule out complications, a nonenhanced head CT or MR was performed up to 24 h after the procedure, more commonly within the first 6 h.

### Inclusion criteria

Patients who underwent stereotactic biopsy at our institution, from May 2016 to October 2021, performed by a single neurosurgeon (OV-F), according to the technique described above.

### Exclusion criteria

Unavailability of the pre- and/or postoperative CT or MR performed up to 24 h after the procedure, as well as of the pathology report.

### Data availability

All the data reported in this manuscript are available on reasonable request from the corresponding author (OV-F). These data are not publicly available due to the risk of compromising patient privacy.

## RESULTS

Thirty-eight patients fulfilled the inclusion criteria. Of those, nine were excluded based on missing postoperative neuroimaging studies for analysis. The remaining 29 patients were included in this study, being that 13 were male and 16 were female, with ages ranging from 20 to 79 ( $50.8 \pm 17.9$  years).

The planning of the stereotactic biopsy was based on CT alone in 23 patients and on CT/MR imaging fusion in six. Postoperatively, CT was performed in all patients and MR

in six. Anatomopathology was performed in all patients and immunohistochemistry in 20.

A diagnosis could be established in 28 out of the 29 patients (96.6%), distributed as follows: low-grade gliomas, 20.7%; high-grade gliomas, 31.0%; metastases, 13.8%; primary lymphoma, 3.4%; autoimmune diseases, 17.2%; and infectious diseases, 10.3% [Table 1]. A single patient (3.4%) had an inconclusive pathology report (gliosis) and underwent a new biopsy, which showed a high-grade glioma.

The morbidity rate was 6.9%, presenting as a superficial wound infection in one patient and asymptomatic intracerebral hemorrhage (1.0 cm in diameter) at the biopsy site in another [Figure 1].

There was no mortality in this case series.

Three patients underwent microsurgical resection of intracranial lesions, being the anatomopathology reports congruent with those of the stereotactic biopsy in all cases.

The evaluation of the postoperative neuroimaging studies revealed two distinct findings at the lesion (biopsy) site:

pneumocephalus and petechial hemorrhage (defined as a hemorrhage with a diameter  $\leq 5.0$  mm, without mass effect). Pneumocephalus was observed in 25/29 patients (86.2%), being the only finding in 10 (10/29 = 34.5%) [Figures 1-5] and associated with petechial hemorrhage in 15 patients (15/29 = 51.7%) [Figures 1 and 2]. Petechial hemorrhage in isolation did not occur in any instance. Anatomopathological diagnosis could be established in all the 25 patients with pneumocephalus. On the other hand, none of these findings was observed in the other 4 patients (13.8%), including the one with inconclusive anatomopathological diagnosis [Table 1].

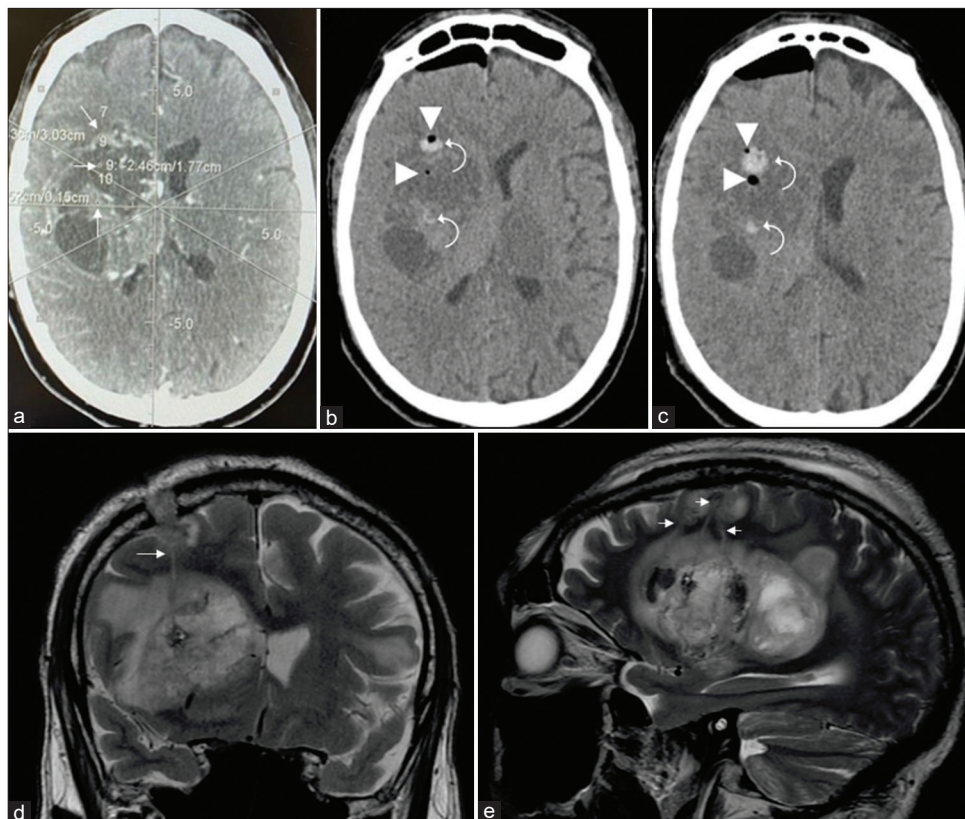
## DISCUSSION

Stereotactic biopsy allows the neurosurgeon to diagnose lesions in any location, by the safe acquirement of small samples. It is a tool of utmost importance for the diagnosis of intracranial lesions, particularly those with a difficult approach or located in eloquent areas, ensuring great accuracy and, therefore, adequate treatment.<sup>[22,34,37,51,52]</sup>

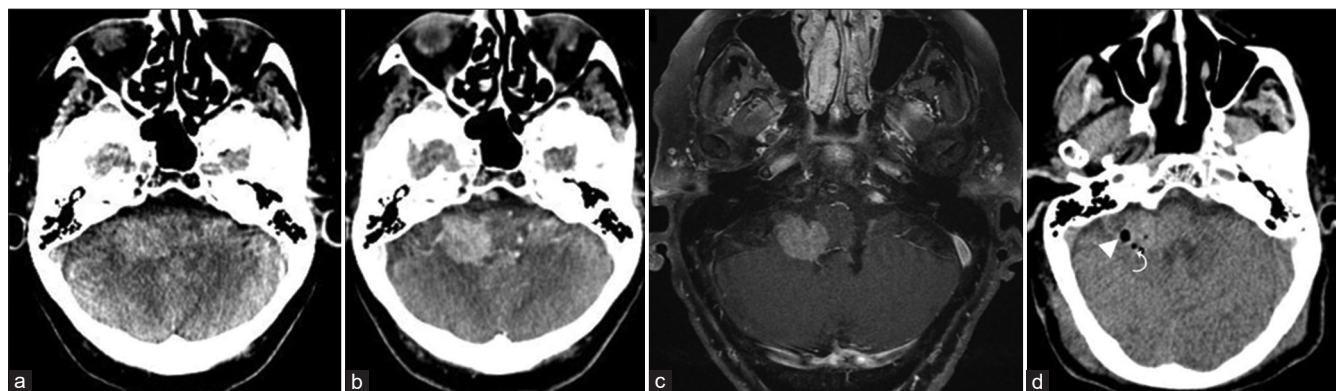
**Table 1:** Summary of the patients submitted to stereotactic biopsy considering the diagnosis, site of the lesion, and the presence or absence of pneumocephalus and/or petechial hemorrhage.

Patients	Diagnosis	Site	PC	PH
1	Lung adenocarcinoma metastasis	Rt frontal lobe	No	No
2	Low-grade glioma	Lt temporal lobe	Yes	Yes
3	Low-grade glioma	Midbrain	Yes	Yes
4	High-grade glioma	Lt parieto-occipital lobe	Yes	No
5	Metastatic lymphoma	Rt frontal lobe	No	No
6	High-grade glioma	Lt thalamus	Yes	Yes
7	Brain abscess	Lt parieto-occipital lobe	Yes	Yes
8	High-grade glioma	Rt thalamocapsular region	Yes	Yes
9	High-grade glioma	Lt nucleocapsular region	Yes	Yes
10	High-grade glioma	Lt temporal lobe	Yes	No
11	High-grade glioma	Rt frontal lobe	Yes	Yes
12	High-grade glioma	Rt thalamus	Yes	No
13	Low-grade glioma	Rt frontal lobe	Yes	No
14	Low-grade glioma	Bilateral frontal lobe	Yes	Yes
15	Diffuse large B-cell lymphoma	Rt middle cerebellar peduncle	Yes	Yes
16	High-grade glioma	Lt thalamus	Yes	No
17	Oat cell carcinoma metastasis	Lt parieto-occipital lobe	Yes	Yes
18	Autoimmune encephalitis	Rt thalamus / brainstem	No	No
19	Gliosis	Lt thalamus	No	No
20	Low-grade glioma	Rt temporal lobe	Yes	Yes
21	Brain abscess	Lt parietal lobe	Yes	Yes
22	High-grade glioma	Rt nucleocapsular/thalamus	Yes	Yes
23	Low-grade glioma	Lt temporal lobe	Yes	Yes
24	Lymphoproliferative disorder	Lt frontal lobe	Yes	Yes
25	Demyelinating disease	Lt frontal lobe	Yes	No
26	Erdheim-Chester disease	Rt frontal lobe	Yes	No
27	Toxoplasmosis	Lt parietal lobe	Yes	No
28	Rasmussen's encephalitis	Lt hemisphere	Yes	No
29	Lung adenocarcinoma metastasis	Rt frontal lobe	Yes	No

PC: Pneumocephalus, PH: Petechial hemorrhages, Rt: Right, Lt: Left



**Figure 1:** (a) Preoperative stereotactic-enhanced CT showing an expansive lesion in the right nucleocapsular region and thalamus, presenting heterogeneous density, and contrast enhancement. The lesion was biopsied in three points (straight arrows): anterior part of the enhancing peripheral ring, anterior hypodense area, and enhanced solid region. (b and c) Postoperative unenhanced CT showing pneumocephalus (arrowheads), petechiae, and a small hemorrhage (curved arrows) at the biopsied sites. (d and e) Postoperative T2-weighted coronal (d) and sagittal (e) MR images showing the needle tracks (arrows) and the presence of hemosiderin (petechiae)/air (pneumocephalus) inside the lesion at the three biopsy sites. Diagnosis: high-grade glioma (patient #22).



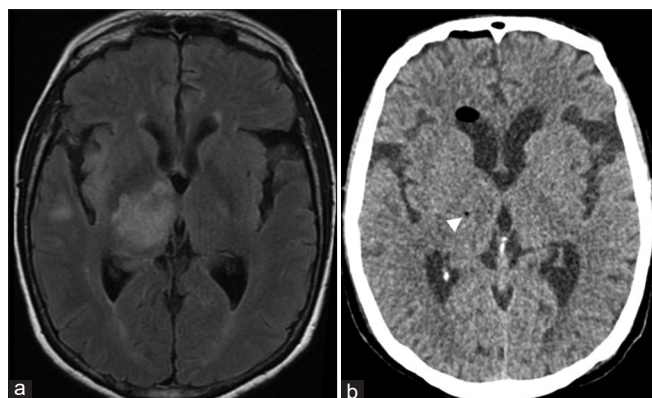
**Figure 2:** (a) Preoperative unenhanced CT showing a hyperdense lesion in the right middle cerebellar peduncle and cerebellum. (b and c) Preoperative enhanced CT and MR showing that the lesion presents intense and homogeneous contrast enhancement. (d) Postoperative unenhanced CT demonstrating pneumocephalus (arrowhead) and petechial hemorrhage (curved arrow) at the biopsy site. Diagnosis: diffuse large B-cell lymphoma (patient #15).

The accuracy rate in the present study was 96.6%, which is within the range reported by other authors (87.6–100%).<sup>[2,12,16,21,22,23,27,34,52,51,53]</sup> This result may be related to the relatively great number of samples ( $n = 12$ ) collected

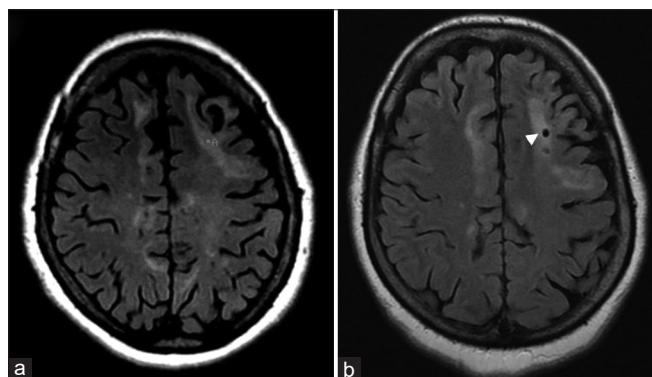
during the procedure, contrarily to others who usually harvest four samples or less.<sup>[3,4,7,10-13,18,20-24,27]</sup> On the other hand, the collection of a greater number of samples may theoretically increase the chance of bleeding complications. However,



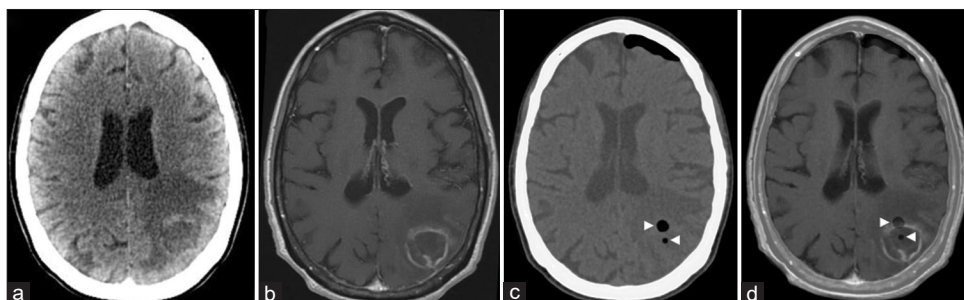
intralesional hemorrhage occurred in a single occasion in this series (3.4%), which fortunately was asymptomatic and



**Figure 3:** (a) Preoperative FLAIR MR image showing a hyperintense lesion in the right thalamus, extending to the ipsilateral nucleocapsular region. (b) Postoperative unenhanced CT showing a pneumocephalus at the biopsy site (arrowhead). Diagnosis: high-grade glioma (patient #12).



**Figure 4:** (a) Preoperative FLAIR MR image showing various areas of high signal in the subcortical/juxtacortical white matter of the left frontal lobe. "A" indicates the target chosen for stereotactic biopsy. (b) Postoperative FLAIR MR showing pneumocephalus at the biopsy site (arrowhead). Diagnosis: demyelinating disease (patient #25).



**Figure 5:** (a and b) Preoperative enhanced CT and T1-weighted MR axial images showing a ring enhancing lesion in the left parietal lobe, with a hypodense/hypointense central region, and marked vasogenic edema in the adjacent parenchyma. Both the central and anterior parts of the enhanced ring were targeted. (c) Postoperative unenhanced CT with two foci of pneumocephalus (arrowheads) at the biopsy sites. (d) Postoperative unenhanced CT merged with the preoperative enhanced T1-weighted MR image showing two foci of pneumocephalus (arrowheads) at the two biopsy sites: central and peripheral enhancing ring regions of the lesion. Diagnosis: toxoplasmosis (patient #27).

did not produce any mass effect (diameter = 10 mm). Other authors have reported a bleeding rate of 0–19%.<sup>[2,37,49,51,52,53]</sup>

The gold standard to determine the accuracy of the stereotactic biopsy is frozen section, as it allows prompt diagnosis and verification if the biopsy was performed at the intended site.<sup>[22,34,37,51,52]</sup> However, as aforementioned, its use has been reported only in 13 out of 57 studies on stereotactic biopsy in humans.<sup>[2,6,12,28,32,34-36,51,52,54,55,57]</sup> Furthermore, it increases the operative time and, consequently, the risk of complications.<sup>[35]</sup> Maybe even more importantly, the accuracy rate of this technique in the central nervous system lesions is only 77.9%, when compared to permanent section.<sup>[5]</sup>

In cases of brain abscess or cystic lesions, aspiration of pus or fluid is sufficient to confirm targeting.

Newer techniques, such as fluorescein<sup>[12,14,30,55]</sup> or 5-ALA for intraoperative identification of tumor cells,<sup>[35,36,51,52]</sup> have been used in some centers as an alternative to frozen section. These techniques not only cut down operative time but also the costs (medical personnel and frozen section preparation).<sup>[52]</sup> However, the frozen section may be waived only if fluorescence is strong; if moderate or light, intraoperative pathology consultation is still required.<sup>[41]</sup> Furthermore, these techniques are not widely available<sup>[41]</sup> and are useless in cases of nonneoplastic lesions.

Intraoperative MR or CT may also be used to confirm appropriate targeting.<sup>[9]</sup> These techniques, though, are very expensive and available only in a few centers.

Therefore, in institutions where frozen section is not part of the routine in stereotactic biopsy and intraoperative MR/CT or the fluorescein/5-ALA techniques are unavailable, there is a need to determine some widely accessible indicators of proper targeting. In our series, pneumocephalus, accompanied or not by petechial hemorrhage, at the biopsy site, presents on neuroimaging studies performed within 24 h of surgery, proved to be reliable indicators, being found in 86.2% of the cases (25/29). The permanent section was

conclusive in all of the cases with pneumocephalus (25/25), but only in 75% of the procedures where these indicators were not present (3/4). It is possible that the high frequency of these findings is related with the number of specimens ( $n = 12$ ) collected during the procedure, but as previously mentioned, it did not increase the morbidity rate. Therefore, it is our belief that the petechial hemorrhages, along with the pneumocephalus at the lesion (biopsy) site, always asymptomatic, should be regarded as indicators of proper targeting, and not as procedure-related complications.

In cases of lesions identified only on MR images, a postoperative MR, instead of CT, is mandatory to confirm the presence of these markers. Alternatively, one could merge postoperative CT with preoperative MR images to achieve the same goal.

The presence of these findings exclusively outside, but near the lesion site, is probably indicative of inadequate targeting, which should raise a red flag and indicate the need for another biopsy even before the result of the permanent section. The same may not be said when these indicators are not present, though, since it happened in four of our patients and the permanent section was conclusive in three of them.

One may argue that it is necessary to know whether the targeting is adequate during surgery and not afterward, once the stereotactic frame has already been removed. Considering that, if one has no accessibility to frozen section, 5-ALA/fluorescein or intraoperative CT/MR, we suggest, after tissue sampling and before the frame is removed, to temporarily close and dress the surgical wound, take the patient to the CT/MR suite, and check for the presence of intralesional pneumocephalus/petechial hemorrhage.

It should be highlighted that this study does not allow us to conclude for how long the markers may be observed since all postoperative imaging studies were performed within 24 h from surgery. In addition, we cannot say if they are present when fewer specimens are collected for permanent section. In this regard, it is relevant to mention that, in a single patient, biopsy was performed at two distinct sites and only four samples were collected from one of them. Nevertheless, intralesional pneumocephalus occurred at the two sites and a head CT, repeated 5 days after the procedure, due to a complaint of headache, demonstrated that the pneumocephalus was still present.

## CONCLUSION

This study describes, for the 1<sup>st</sup> time, two markers, intralesional pneumocephalus and petechial hemorrhage that are easily identifiable on immediate postoperative CT and/or MR, indicating appropriate targeting in stereotactic biopsy of brain lesions. These markers were present in 86.2% of our patients and permanent section was diagnostic in

all of them. The use of this technique has some significant advantages: it cuts down the surgical time, is widely available, is highly accurate, and apparently dispenses the use of other more expensive and not universally available techniques such as frozen section, 5-ALA, fluorescein, and intraoperative CT or MR. To use intralesional pneumocephalus/petechial hemorrhages not only as postoperative but also rather as intraoperative markers of appropriate targeting, it would be advisable, after the biopsy and before the frame is removed, to temporarily close and dress the surgical wound, take the patient to the CT/MR suite, and check for the presence of these markers.

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## Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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