## **Original Article**

# Accuracy of Stereotactic Brain Biopsy compared to Histopathological Results after Resection

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**BACKGROUND:** The cornerstone of definitive therapy of cerebral mass lesions is accurate diagnosis. Stereotactic brain biopsy is a commonly used tool for diagnosis of cerebral intra-axial mass lesions with reported high diagnostic yield.

**OBJECTIVE:** The aim of the study was to assess the diagnostic yield and accuracy of stereotactic brain biopsy (SBB) in individuals with intra-axial mass lesions.

**METHODS:** This study comprised 200 individuals (128 males and 72 females) with intra-axial mass lesions (170 single lesions and 30 multiple lesions) with an average age of 52.8 years. Between 2005 and 2014, stereotactic image-guided (126 magnetic resonance imaging (MRI) and 74 computerized tomography (CT)) biopsies for histological verification were done at Department of Neurosurgery, Tanta University Hospital. In 180 patients, the surgery was performed with local anesthetic. In 30 patients, the histopathological results of SBB were compared to resected tissues obtained via craniotomy after SBB.

**RESULTS:** In 197 cases, samples were diagnostic, with a diagnostic yield of 98.5%. The overall rate of biopsy-related morbidity was 1%, with no deaths. The histopathological diagnosis of the two procedures were identical in 25 patients. In three cases, the histopathological findings were somewhat different without affecting patient care. After craniotomy, the diagnosis of stereotactic biopsy was completely revised in two patients. The accuracy was 93.3%.

**CONCLUSION:** Despite the small number of patients who underwent resection, the results of this study showed that SBB of brain masses is a safe and accurate procedure for obtaining sufficient samples for histopathological diagnosis and thus planning the best therapeutic options for patients. The outcome of stereotactic biopsy is largely determined by good communication between the pathologist and the neurosurgeon, to get the best tissue sample possible. It can replace a significant number of open craniotomies for biopsy purposes.

**KEYWORDS:** Intra-axial brain lesion, Resection, Stereotactic biopsy.

## INTRODUCTION

The cornerstone of definitive therapy of cerebral mass lesions is accurate diagnosis, which can only be validated by histopathological study of tissue samples acquired by biopsy or open surgery. Inflammatory and infectious lesions must be differentiated from neoplastic lesions, and histopathological typing of tumors is critical in determining treatment strategy. Although highly sophisticated, the new imaging techniques cannot provide tissue diagnosis. So, the practice of taking a biopsy from intracerebral lesions has become commonplace in neurosurgery. Biopsy techniques have gradually improved with the great advancement in imaging modalities. Therefore, image-guided stereotactic brain biopsy (SBB) is used increasingly to diagnose intracranial lesions. Its diagnostic yield is reported to be between 80 and 99%. Thus it can replace a large number of open craniotomies for the purpose of biopsy.<sup>1-8</sup>

The aim of the study was to compare the findings of

**Correspondence:** Esam Mokbel Department of Neurosurgery, Faculty of Medicine, Tanta University, Egypt Email: esam mokbel@yahoo.com histopathological diagnosis acquired following SBB from intra-axial mass lesions with the results of histopathological diagnosis obtained after excision by standard craniotomy that was done after SBB in 30 patients in this study.

## PATIENTS AND METHODS

#### **Patient population**

Between September 2005 and December 2014, 200 patients (128 men and 72 women) with a mean age of 53.9 years (range 5-87 years) underwent stereotactic frame-based, image-guided biopsy at Department of Neurosurgery, Tanta University Hospital. This research was performed at the Department of General Surgery, Ain Shams University Hospitals. Ethical Committee approval and written, informed consent were obtained from all participants. We excluded any patients subjected to stereotactic procedures other than biopsy.

The indications of stereotactic brain biopsies included deeply seated lesions, small intra-axial lesions, multiple lesions, patients too old and/or medically ill to tolerate craniotomy, lesions located in eloquent areas and biopsy and aspiration of cystic lesions. Exclusion criteria included increased intracranial pressure with midline shift and mass effect in preoperative CT and/or MRI and any blood coagulation problems.

All data about the clinical symptoms, radiology, histopathological diagnosis and management was collected and reviewed retrospectively. In 30 patients, surgical resection of the lesion was done after biopsy. The indication of lesions resection in this study were; decompression due to increase in lesions size with increased mass effect, to get sure from the pathology and unexpected response to management plan based on the result of SBB.

## **Preoperative preparation**

Oral anticoagulant medications were stopped one week before biopsy. Heparin administration was discontinued 2 days prior to the procedure and blood pressure was controlled. Platelet count should be at least 80,000/mm3 while prothrombin activity should be over 70%.

#### **Biopsy procedures**

All SBB were done by neurosurgeons who had experience in stereotactic practices. For stereotactic localization, we used either Cosman-Roberts-Wells (CRW) or Riechert-Mundinger (RM) frames guided by MRI or CT images. In all patients, the Praezis plus 3 (Inomed Company, Germany) multiplanar reconstruction programmer was used to determine the best trajectory to avoid a sulcus and cortical blood vessels.

The trajectories were plotted using multiplanar reformatted imaging before the real probe was positioned. On phantom basis, the stereotactic coordinates were then set and validated. The stereotactic frame was attached to the head after the scalp was disinfected with betadine and alcohol. An 8-mm burr-hole was performed after local anesthetic (lidocaine or marcaine) was provided (general anesthesia was used in children and certain adults). After dural puncture, the biopsy needle was advanced to the target along the pre-planned trajectory (Sedan-type side cutting 2mm with 10-mm opening and 2.5mm-diameter cannula). Until the neuropathologist was satisfied, samples were taken<sup>9</sup>

Intraoperative cytological evaluation (imprint and/ or squash preparations) was performed using a tiny portion from biopsy cylinders. The remainder of the material was sent to a pathologist for a regular histopathological evaluation. Tumors were evaluated and classified using World Health Organization (WHO)-2000 categorization guidelines.<sup>10</sup> All biopsies and resection samples were analyzed by pathologists with expertise in neuropathology.

#### **Post-biopsy CT scans**

After 4 hours, all patients had postoperative CT scans. A neurosurgeon and a neuroradiologist compared postoperative CT scans to pre-operative pictures to see if there were any post-biopsy complications. The patients were neurologically examined immediately after SBB and on the next morning. Any complication related to the biopsy was reported as morbidity. If the postoperative CT scan shows no hemorrhage without any neurological deterioration, the patient was safely discharged.

#### RESULTS

The age and gender of all patients were evaluated, as well as the lesion location, image-guided modality, anesthesia, permanent pathologic diagnosis, morbidity, mortality, and SBB diagnostic yield. (Tables 1,2).

In this study, 200 procedures were done; 184 cases (92%) were subjected to stereotactic brain biopsy (SBB) and 16 cases (8%) were subjected to stereotactic biopsy and aspiration. Entry points were supratentorial in 180 cases (90%), and infratentorial in 20 cases only (10%). Three biopsies were taken in 69 patients (34.5%), 2 biopsies in 58 cases (29%), and 4 biopsies in 48 cases (24%). Eight biopsies were obtained in two cases and was the maximum number of biopsies taken. One biopsy was obtained in 10 cases. The average number of biopsies was 3.07 (Table 3). A definite histological diagnosis was made in 197 individuals, with a diagnostic yield of 98.5 percent (Table 4).

The postoperative CT scan revealed no hemorrhage in 193 subjects (96.5%). Seven patients had intracerebral hemorrhage (3.5%). In five cases, the bleeding was asymptomatic and only found during a post-biopsy CT scan (2.5%). In two cases, the bleeding was symptomatic (1%). One patient experienced left side hemiparesis that improved after a week of medical treatment, and the patient recovered quickly after physiotherapy. The other patient had a disturbed level of consciousness, and CT scan revealed a massive intracerebral hematoma following biopsy. The patient was confined to an intensive care unit and treated with conservative treatments for 13 days till he regained consciousness but still had persistent motor weakness. The overall biopsy related morbidity rate was 1% with no mortality. All patients, who were neurologically intact, and the post-biopsy CT scan showed no hemorrhage, remained intact with no delayed deteriorations.

Thirty patients underwent craniotomy for lesion resection after stereotactic biopsy. The time between the biopsy and craniotomy ranged from 2 to 244 days (average 92.66 days). The histopathological results of the two procedures were similar in 25 cases. The histopathological results of SBB and open surgery were slightly different in three cases, but this had no effect on the therapeutic strategy (minor disagreement). The histopathological result of SBB was anaplastic astrocytoma grade III in two cases, and resection was performed after 140 and 239 days (due to the tumors' increased mass effect), with the histopathology result of glioblastoma multiforme (GBM) in both patients. Both of them received radiotherapy after SBB. Regarding the third case, the histopathological examination of SBB was infiltrating edge of glioma (malignant glioma), resection was done two days for clarification of pathology that proved to be GBM.

In two cases there was a major disagreement, as the pathology revealed by stereotactic biopsy was reactive brain tissue and that of resection that was done 11 and 14

days after biopsy was an abscess. These patients received antibiotics before SBB as they were admitted in internal

medicine department before the biopsy. The results of the stereotactic biopsy were accurate enough to represent the pathology of the intracranial lesions and to start the optimal treatment plan (overall accuracy 93.3%).

Lesion	Single	Multiple
	170 (85%)	30 (15%)
Anesthesia	Local	General
	180 (90%)	20 (10%)
Image modality	MRI	СТ
	126 (63%)	74 (37%)

MRI: Magnetic resonance imaging, CT: Computerized tomography.

#### Table 2: Sites of lesions

Supratentorial targets		Number of patients
Lobar	Frontal	40
	Parietal	32
	Temporal	21
	Occipital	4
Deep seated	Thalamo-ganglionic	47
	Periventricular	13
	Corpus callosum	10
	Sellar/suprasellar	6
	Hypothalamus	5
	Pineal	2
Total		180 (90%)
Infratentorial targets		Number of patients
Cerebellum		4
Pons		5
Midbrain		4
4 <sup>th</sup> ventricle		2
Pons & midbrain		5
Total		20 (10%)

#### **Table 3: Number of stereotactic biopsies**

Number of biopsies	Number of patient	Percentage %
1	10	5%
2	58	29%
3	69	34.5%
4	48	24%
5	7	3.5%
6	4	2%
7	2	1%
8	2	1%
Total	200	100%

Histopathology of SBB	Number of patients
Glioblastoma multiforme (GBM)	54
Anaplastic astrocytoma grade III	37
Astrocytoma grade II	34
Metastatic tumors	18
Oligodendroglioma	14
Lymphoma	13
Juvenile pilocytic astrocytoma	7
Gliosis & radiation effect	6
Pineal tumor	4
Medulloblastoma	3
Ganglioglioma	3
Reactive brain tissue	2
Infiltrating edge of glioma	1
MPL leukoencephalopathy	1
Non diagnostic	3
Total	200

#### Table 4: Final histopathological diagnosis of stereotactic biopsy

## DISCUSSION

Treatment planning for intra-axial mass lesions are more accurate when they depend on histopathologic diagnosis besides the clinical examination and the radiological imaging. A preoperative diagnosis based on the clinical and the radiology alone may miss diagnosis in about 33% of patients. A lot of non-neoplastic lesions may be diagnosed as tumors. Although, MRI and positron emission tomography, can reach the histopathological diagnosis of intracranial mass lesions, however it is not always accurate.<sup>11-14</sup> Many authors reported false-diagnosis rate ranged from 10% to 33% in diagnosis based on MRI and CT alone.<sup>15-18</sup>

Also, there are different types of lesions within the central nervous system. Grading and tumor type are very important to fashion treatment protocol. So, accurate pathological diagnosis is essential for choosing optimal management plan.<sup>4,5</sup>

Due to the relative ease, safety, and accuracy of SBB, many authors think that the indications for "open" biopsy are rare.<sup>16,19-22</sup> The biopsy's success is determined by the neurosurgeon's ability to collect an informative tissue biopsy and the neuropathologist's ability to make an appropriate diagnosis. SBB had a high diagnosis rate of 92% to 97% in major academic institutes where stereotactic neurosurgeons and knowledge in neuropathology are already accessible.<sup>2,23-25</sup> The high level of accuracy is maintained even when biopsy results are compared to postoperative resection.<sup>26</sup>

In this series, MRI was used in 126 cases (63%) and CT in 74 cases for target localization (37%). In CT scans the metallic elements of the stereotactic hardware do not create distortion in CT pictures. Also, linear distortion may be estimated and corrected.

According to several publications CT is accurate and safe for stereotactic localization. MRI techniques produce high-resolution multi-planar images of the brain, but it is more technically demanding and the magnetic fields used in MRI can be spatially distorted, and inaccurate targeting may result. MRI targeting is absolutely contraindicated for patients with implanted medical devices, such as pacemakers. Despite these limitations, the high resolution and fine tissue discrimination of MRI have resulted in its rapid acceptance by stereotactic surgeons.<sup>27</sup>

Some surgeons prefer to target their biopsy procedures with CT for a number of reasons; acquisition times for CT-based methods are shorter than those for MRI, geometric distortion is not a problem with most modern CT devices and CT is more compatible with the existing stereotactic systems.

Because of the advantages of MRI over CT in the posterior fossa (i.e., higher resolution and no bone artifact), MRI has been used in a higher proportion of infratentorial targets. In this study, there were 20 cases that had infratentorial targets. MRI was used in 16 cases and represented 80%. Lee et al. concluded that MRI guiding for stereotactic biopsy was more effective than CT for infratentorial and brain stem lesions. It was determined that MRI was more accurate than CT in CT-invisible or ill-defined lesions, lesions located in eloquent or highly vascularized areas, and lesions located in the brain stem.<sup>19</sup>

In certain situations, the surgeon may need the advantage of CT (accuracy) and the advantage of MRI (high resolution and fine tissue discrimination). In these situations, a CT-MRI fusion using multiplanar and 3-dimensional reconstruction programs may be helpful. Heper et al. used this technique in 33 patients with lesions located in an eloquent area like pineal region and brain stem.<sup>12</sup> In our study, using either CT or MRI in planning had no significant impact on accuracy, results or complication rate of the procedure as we used the imagefusion.

Handling of the biopsy taken by stereotactic techniques is different from that taken by open craniotomy. First, SBB sample is small. Second, the ability to get more tissue from the lesion is more limited. The little amount of biopsy material has long been thought to be unrepresentative of the entire lesion. So, serial biopsies were obtained along the maximum length of the lesion to collect more pathological information about the lesion, like area of infiltration, vital neoplasm, and necrotic areas.

In this study, 3 biopsies were taken in 69 cases (34.5%), 2 biopsies in 58 cases (29%), and 4 biopsies in 48 cases (24%). The maximum number of biopsies was eight, in two cases, while the smallest number was one in ten patients. The average was 3.07 (**Table 4**). We had 16 cases subjected to biopsy and aspiration, in 10 patients we took 1 biopsy and in 6 patients we took 2 biopsies. In the remaining 184 patients (92%) we took serial biopsies to increase the accuracy. Many authors concluded that, getting four or more biopsies raised diagnosis accuracy from 67 to 89%.28 Hall and Revesz et al. recommended to take from 2 to14 biopsy samples from one or more locations to improve the accuracy.<sup>43,24</sup>

After stereotactic biopsy, 30 patients had craniotomy for lesion removal in this study. In 25 cases, the histopathological diagnosis of both procedures were identical (complete agreement). The histopathological diagnoses were somewhat different in three patients, however this did not affect the treatment method (minor disagreement). The histopathological result of SBB was anaplastic astrocytoma grade III in two cases, and resection was performed after 140 and 239 days, respectively, with the histopathology result of GBM in both patients. After SBB, they both had radiation. Stereotactic biopsy undergrading is a common occurrence. SBB diagnosis of anaplastic astrocytoma that is upgraded to GBM following resection is the most prevalent case of this. This form of non-perfect correlation can only be shown if the patients had a surgical resection following SBB, making the incidence of this inaccuracy difficult to estimate.<sup>26,30</sup> The anaplastic astrocytoma were transformed to GBM in 60% of patients in Jackson et al. study.<sup>31</sup> According to Chandrasoma et al., anaplastic astrocytoma grade III on SBB should be treated as a GBM.<sup>26, 28</sup>

Regarding the third case, the histopathological examination of SBB was infiltrating edge of glioma, resection was done two days later for clarification of pathology that proved to be GBM. In highly malignant tumors, there are areas mainly consisting of neoplasm, areas of necrosis, and areas of adjacent brain infiltrated by neoplastic cells. Target selection and obtaining an ideal sample from these lesions is very difficult and challenging. From the perspective of a pathologist, a sample made up of viable neoplasm is optimal. Biopsies are frequently obtained from the enhanced periphery of the lesion rather than the central necrotic area in suspected high-grade lesions. Although this is the best method, it may result in undergrading of high-grade lesions and raise diagnostic complexity if the biopsy is taken from the neoplasm's infiltrative edge. There is a tendency to under-grade GBM since the target site in stereotactic biopsies is chosen to avoid necrotic areas. To distinguish anaplastic astrocytoma from GBM, serial biopsies from numerous target locations within the lesion should be taken<sup>23,28,29</sup>

Low-grade astrocytomas are non-enhancing, ill-defined lesions with little perifocal edema or mass effect. Normal brain tissue is replaced by neoplastic cells in the center of these lesions, with widespread infiltration in the periphery. As a result, the ideal target point is frequently in the lesion's center.<sup>32</sup>

As the sample quality deteriorates, the diagnostic accuracy drops. A sample with neoplastic and normal brain parts acquired from a location where a high-grade astrocytoma infiltrates normal brain is deemed less than ideal.<sup>30,31</sup>

In two cases there was a difference between both procedures (major disagreement), as the pathology revealed by stereotactic biopsy was reactive brain tissue and that of resection that was done 11 and 14 days after biopsy was an abscess. These patients received antibiotics before SBB as they were admitted in internal medicine department before the biopsy. SBB from inflammatory brain lesions is extremely challenging.<sup>33</sup> When the cause of the inflammatory process is determined, usually by identifying the infectious agent, a clear diagnosis can be made in these lesions. It is difficult to verify whether the observed changes represent inflammation and reactive gliosis at the edge of a neoplastic lesion that was not included in the sample or whether it represents the whole lesion. To increase the accuracy of inflammatory lesions, serial biopsies from the peripheral and central regions of the lesions are mandatory. In Chandrasoma et al. series, necrosis and inflammation were observed in 45% and 41% of non-diagnostic samples, respectively.26

Tumors make up the bulk of intracranial lesions that undergo stereotactic biopsy. In larger studies, nonneoplastic lesions accounted for up to 20% of diagnoses and had lower diagnostic accuracy than malignancies.<sup>34,35</sup> This could be explained by the diverse pathological entities of non-neoplastic lesions. Despite the increased risk of diagnostic error, stereotactic biopsy is still a safe and effective that can direct a reasonable management plan for non-neoplastic lesions.<sup>34</sup>

In this study, the results of the SBB were comparable to the results after open surgical resection (identical or minor disagreement) in 28 out of 30 patients, with overall accuracy of 93.3%. Similarly, in Chandrasoma et al. series of 30 patients who underwent surgical removal

of a lesion after initial SBB, the histopathological diagnosis acquired with SBB directed clinical therapy efficiently in 28 individuals (93.3%).<sup>26</sup> In Kim et al. series of 300 patients, 30 patients were subjected to surgical excision after SBB; the histopathological results of both procedures were identical in 29 patients with diagnostic accuracy of 96.7%.<sup>17</sup> In Kreth et al. series of 326 patients, 33 patients underwent craniotomy after stereotactic biopsy. The histopathological results of both procedures were identical in 31 patients with diagnostic accuracy of 93.9%.<sup>33</sup> In Aker et al. study that included 130 patients, in 23 cases, after

a biopsy, the tumor was resected using a craniotomy. In 16 cases, the histopathological diagnosis from biopsy and open surgical resection were identical (complete agreement). In three cases, the histology diagnosis was somewhat different but had no bearing on therapy (minor disagreement). The overall accuracy in their series was 82.6% for the 19 patients in the complete agreement and mild disagreement groups.1 Feiden et al. and Voges et al. found concordance rates of 89% and 88%, respectively, between biopsy and subsequent resection or autopsy.<sup>37,38</sup> (Table 5).

Table 5: The published literature about the accuracy	of the stereotactic biopsy series
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Authors (year)	No of resected specimen and / or autopsy	Percentage of diagnostic accuracy
Broggi et al, 1984 (39)	26	89% (23/26)
Kleihues et al, 1984 (40)	87	87% (76/87)
Scerrati and Rossi 1984 (41)	19	95% (18/19)
Chandrasoma et al, 1989 (26)	30	93% (28/30)
Cappabianca et al, 1991 (30)	100	96% (96/100)
Feiden et al, 1991 (37)	47	89% (42/47)
Voges et al, 1993 (38)	32	88% (28/32)
Grunert et al, 1994 (42)	41	90% (37/41)
Jackson et al, 2001 (31)	80	80% (64/80)
Kim et al, 2003 (17)	30	97% (29/30)
Aker et al, 2005 (1)	23	83% (19/23)
This study	30	93.3% (28/30)

Regarding the diagnostic yield and accuracy rate, the quality of the biopsy is more essential than the quantity of tissue. By using functional imaging information, stereotactic targeting can be more accurate, and biopsy can be taken from representative areas of the tumors.

Biopsy may be obtained by different methods. Some institutes obtain samples from one to three pieces of tissue (1–2 mm in length) from a single point target within the lesion. Despite their small size, these samples have a good diagnosis rate as well as minimal morbidity.<sup>23</sup> Larger numbers of specimens may be gathered in other centers. Additionally, some neurosurgeons apply pediatric bronchoscopic forceps, while others use side cutting biopsy needles that provide a 1 cm-long core of tissue.<sup>38</sup>

The pathologist should have full data about the clinical picture, radiological finding, selected target point and differential diagnoses and should attend in the operating room. The surgeons were taking biopsies until the pathologist was confident that he can make a diagnosis from this sample. The most important issue intraoperatively is to confirm that the sample is from abnormal brain tissue and sufficient for diagnosis.

If the initial biopsy is insufficient to determine a diagnosis,

the pathologist has a chance to intervene. This reduces the number of samples that are insufficient. Brainard et al. found that if they only took one biopsy from the lesion, 1/3 of their cases would be misdiagnosed.<sup>42</sup>

Intraoperative pathological examination of the sample should be performed routinely to get sure that a sufficient amount of tissue has been obtained. In the Kim et al. series, there was a statistically significant difference in diagnostic yield between the SBB with and without frozen section inspection.<sup>17</sup>

The challenging part of a SBB for the pathologist occurs when the biopsies are not ideal regarding the amount and/or the quality of tissue that may cause difficult and/ or incorrect diagnosis. From the neurosurgical point of view, the challenge is taking adequate samples with low complication rates. The risk for hemorrhage increase as more biopsies taken. Cooperation between the neurosurgeon and pathologist could decrease the biopsy specimen to one.<sup>44</sup>

## Stereotactic teamwork

Stereotactic procedures requires a team work involving harmony between neurosurgery, neuroanesthesiology, neuroradiology, oncology, and neuropathology to improve results and to avoid complication.<sup>1,12,19</sup>

## CONCLUSION

Despite the small number of patients who had resection, the results of this study demonstrate that SBB of brain tumors is a safe and accurate approach for obtaining appropriate tissue for histological diagnosis and planning the best treatment options for patients. The outcome of stereotactic biopsy is largely determined on good communication between the pathologist and the neurosurgeon, as well as the collection of the best tissue sample possible. It can be used to replace a significant number of open craniotomies for biopsy purposes.

## **List Of Abbreviations**

CRW: Cosman-Roberts-Wells. CT: Computerized tomography. GBM: Glioblastoma multiforme. MRI: Magnetic resonance imaging. RM: Riechert-Mundinger. SBB: Stereotactic brain biopsy. WHO: World Health Organization.

## Disclosure

The authors report no conflict of interest in the materials or methods used in this study or the findings specified in this paper

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