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Original Article

Improving Diagnostic Yield and Accuracy of Stereotactic Biopsies through Changes in Practice and Techniques: An 8-Year Single-Center Comparative Study

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Abstract

Background Stereotactic biopsies are used to aid neurosurgeons in clinching the diagnosis of intracranial lesions that are difficult to access surgically. A published study of stereotactic biopsies in our center demonstrated a diagnostic yield of only 76% for biopsies from the year 2014 to 2019. A set of criteria/prerequisites was applied to increase yield.

Objective The aim of the study was to identify the improvement in accuracy and yield after implementation of a set of criteria/prerequisites.

Materials and Methods This was a retrospective and prospective analysis of all patients who underwent stereotactic biopsies from the year 2014 to 2022. This study was conducted at Sarawak General Hospital, Malaysia. A set of stereotactic criteria/prerequisites was introduced since 2020, which include preoperative careful, meticulous trajectory planning and target selection, regular checking and maintenance of equipment, larger burr holes, and good sampling techniques.

Results A total of 83 patients underwent stereotactic biopsies from the year 2014 to 2022. Frameless and frame-based methods were used for 45 (54%) and 38 (46%) patients, respectively. The overall diagnostic yield of all biopsies was 84%. Fifty patients underwent stereotactic biopsies prior to implementation of good practice guidelines in 2020 with a positive histopathological yield and accuracy of 76 and 88%, respectively. Thirty-three biopsies done postimplementation demonstrated a yield and accuracy of 97% ($p < 0.05$). There was also a shift of preference toward frame-based methods after 2019, with 85% of these biopsies being frame based.

Conclusion This comparative study shows that adherence to specific stereotactic biopsy guidelines and techniques introduced in our center has successfully improved our biopsy yield and accuracy.

Keywords
- stereotactic biopsy
- diagnostic yield
- accuracy

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Introduction

Intracranial lesions often present neurosurgeons with diagnostic challenges when they are found in areas with difficult surgical access or when they display features of lesions that would require nonsurgical treatment.[1] Accurate histopathological diagnosis and molecular profiling are vital in determining the course of treatment. This can be obtained through excision of the lesion or a biopsy. Stereotactic brain biopsy, since its advent in the 19th century, has undergone major modifications and innovations to improve its accuracy and clinical use.[2] Frameless and frame-based systems are often subjected to head-to-head comparisons. While the frame-based stereotactic method has traditionally been considered the "gold standard" method of biopsy, a recent large meta-analysis has proven that the frameless system is comparable to its counterpart.[3]

An initial experience with the Cosman–Roberts–Wells (CRW) stereotactic frame was published by Couldwell and Apuzzo in the 1990.[4] They cited comparable accuracy to the preexisting Brown–Roberts–Wells (BRW) system. The CRW frame employs an arc-radius design that many find easy to use and is currently used regularly in the neurosurgical centers in our country. The Albert-Wong (AW) stereotactic frame, created by a Malaysian neurosurgeon in the year 2015, is based on linear algorithm.[5] A recent phantom-based accuracy study demonstrated that its accuracy is noninferior to the traditional and well-established stereotactic frames.[5] The AW frame also boasts a simple and easy algorithm and stereotactic calculation method. This frame is presently being used for intracranial lesion biopsies in hospitals in the state of Sarawak, Malaysia. Methods used for stereotactic biopsies should not be confined to a select few and ought to be modified and developed to suit and adapt to the ever-expanding knowledge of stereotaxy. The frameless stereotactic biopsy method has gained popularity and its widespread use is due to its versatility, efficiency, and low complication rate.

We published a 5-year series of stereotactic biopsies in 2021, looking into factors affecting diagnostic yield. The overall diagnostic yield acquired was only 76%, which was below the average positive yield of other series.[6] Dhawan et al in their systematic review and meta-analysis of frame-based and frameless stereotactic biopsies presented diagnostic yields ranging from 84 to 100%.[3] This prompted a review of methods and practices that we employed during our procedures. Subsequently, we added new guidelines and made modifications, which we incorporated into subsequent biopsies with the objective of improving our diagnostic yield.

Materials and Methods

This is a retrospective and prospective cross-sectional analytical study conducted by the Department of Neurosurgery, Sarawak General Hospital. This study encompasses a period of 8 years from the year 2014 to 2022. Sarawak General Hospital is a tertiary hospital and serves as the largest hospital in the state of Sarawak. It involves all patients undergoing stereotactic biopsies to diagnose intracranial lesions. The decision for stereotactic biopsies was made by the neurosurgeon in charge on a case-to-case basis.

Sample size was calculated using an 80% power and 90% confidence level using values from previous studies.[5,6] The minimum number of patients required in each group was 30, which was achieved in this study.

Biopsy Method

Stereotactic biopsy techniques used in our center consists of both frameless and frame-based systems. These include the Portable Brainlab Vector Vision, Brain-suite Brainlab Curve, CRW stereotactic frame, and the AW stereotactic frame. The choice of system used is decided by the neurosurgeon based on his or her familiarity with the technique. These biopsies were performed electively with a large proportion of frame-based biopsies done under local anesthesia and monitored sedation in suitable patients. Frameless biopsies were performed under general anesthesia. We used the Nashold biopsy needle, Radionics (United States), which has a sampling window of 9.5×1.2 mm, located 2 mm from the needle tip. The needle diameter is 1.8 mm, lumen is 1.5 mm, and the total length is 29.8 cm. The tip of the needle is dome shaped with a window in the inner cannula. This window can be aligned with the outer cannula window through rotation. All biopsy specimens are sent for histopathological examination to the Pathology Department of Sarawak General Hospital. A postoperative brain computed tomography (CT) is performed immediately following the procedure to rule out a postbiopsy hemorrhage and to examine the accuracy of the biopsy.

Changes in Practice

In an effort to improve our diagnostic yield and accuracy, we devised nine criteria/prerequisites that would need to be fulfilled for each stereotactic biopsy procedure. They were created and introduced after careful and meticulous examination of our previous biopsies with negative yield and inaccuracy. A retrospective analysis of previous biopsy data showed that a large proportion of negative yield (67 vs. 33%, >6 vs. <6 weeks) occurred in the cases where prebiopsy scans were greater than 6 weeks. Although this result was not statistically significant ($p < 0.05$), we included this into our criteria as the proportion of negative yield was considered high and the absence of statistical significance may be due to a limited sample size. Preoperative steroids were given in 16 (32%) patients preoperatively, with 6 of those patients having a negative biopsy yield ($p < 0.05$). With a large proportion of central nervous system (CNS) lymphoma in our biopsy results, corticosteroids were seen as a major factor that may influence diagnostic yield.

The new stereotactic biopsy criteria/prerequisites that were introduced in the year 2020 are the following:

- Preoperative contrasted CT/magnetic resonance imaging (MRI) less than 6 weeks.
- Selection of entry point, target, and trajectory planning on stereotactic/3D multiplanar reconstruction (3D MPR) software.

- Regular maintenance of equipment: biopsy needle check for bend or fault, phantom check for frame.
- No preoperative corticosteroids.
- Burr hole made centered at the entry point.
- Careful dura opening without breaching the arachnoid layer or losing cerebrospinal fluid (CSF).
- Sampling is taken from all four quadrants using "negative-pressure and rotation" technique. The biopsy needle is repositioned to take another sample superior and inferior to the initial target. The first sample is taken by the most experienced surgeon performing the operation.
- Inspection of sample after removal for color and buoyancy.
- Intraoperative postbiopsy scan after injecting 0.1 to 0.2 mL of air.

All cases of stereotactic biopsies for intracranial lesions performed to acquire histopathological diagnosis were included in this study. Cases done before the year 2014 and after 2022 were excluded. Our previous published study[6] was used as a comparison to evaluate the effects of the current changes in practice. We compared the diagnostic yield and accuracy of 50 patients from 2014 to 2019 previously reported by us with a new group of patients undergoing biopsy from 2020 to 2022. These patients were grouped into two groups, with group 1 being cases done before the year 2020 prior to the introduction of new stereotactic biopsy criteria/prerequisites and group 2 being cases done after the year 2020. The authors along with the operating surgeon were responsible to ensure the adherence of each procedure to the criteria/prerequisites for patients in group 2.

Data Collection and Analysis

Data were collected retrospectively for cases done before the year 2020 and prospectively for cases after that year. Fifty patients who were included in the study published from our center previously were also included in this present study for analysis.[6] These patients meet the inclusion criteria for our study and their inclusion adds significant value to the present study. Patients' sociodemographic, clinical, and radiological data were acquired from medical records and radiology database. Operative details were collected from the operating theater database. The data were tabulated in Microsoft Excel and analyzed using the SPSS software version 20.0 (SPSS Inc., Chicago, IL, United States). Frequency distribution table, bar charts, means, and percentage were used for descriptive data. Chi-squared, independent sample *t*-test, odds ratio, and 95% confidence interval were calculated. A *p*-value of less than 0.05 was considered statistically significant.

Outcomes

The primary outcome was measured via the yield of the histopathological specimen sent for analysis. Positive yield includes but is not limited to a histopathological report of a neoplasm, infection, inflammation, demyelination, etc. The secondary outcome was measured via postoperative CT showing iatrogenically inserted air within the lesion. Air present outside of the lesion was defined as an inaccurate biopsy radiologically.

Results

Of a total of 83 patients undergoing stereotactic biopsy, the mean age was 50.8 years, with the majority (63%) of patients being of male (►**Table 1**). A large proportion of lesions were located in deep sites (64%), with 53% being less than 10 mL in volume (►**Table 1**). The overall diagnostic yield of all biopsies from 2014 to 2022 was 84% (►**Table 1**). There was a shift of preference toward frame-based methods after 2020, with 85% of the 33 biopsies being frame based (►**Table 2**).

Fifty patients underwent stereotactic biopsies prior to implementation of the new stereotactic biopsy criteria/prerequisites in 2020 with a positive histopathological yield of 76% and a radiological accuracy of 88% (►**Table 2**). Thirty-three biopsies were done postimplementation, with a positive histopathological yield of 97% and a radiological accuracy of 97% (►**Table 2**). This improvement was statistically significant ($p < 0.05$).

Subgroup analyses were performed to determine the effects of confounding factors on the outcome between the two groups. ►**Table 3** demonstrates no significant difference in diagnostic yield between frameless and frame-based biopsies for both groups and even when analyzed separately for groups 1 and 2. ►**Table 3** also demonstrates a significant difference between lesion size (<10 vs. >10 mL) and diagnostic yield. However, when separately analyzed between the two groups, no statistically significant difference was found.

Subgroup Analysis to Determine the Effects of Confounding Factors

Findings of the subgroup analysis to determine the effects of confounding factors are shown in ►**Table 3**.

Discussion

This 8-year analysis of stereotactic biopsies in our center clearly demonstrates a significant improvement in positive diagnostic yield resultant from the introduction of good practice criteria and prerequisites for these procedures. The improvement was statistically significant (76 vs. 97%, $p < 0.05$). Following a review of stereotactic biopsies done in our center before the year 2020, we identified numerous reasons and factors that we believe played a role in the inaccuracy and negative histopathological yield.

Preoperative Scan Timing and Biopsy Planning

Preoperative scans closer to the time of biopsy would aid with the accuracy of the planning of the target. Malignant tumors of the brain, in particular glioblastoma, have a propensity for rapid growth, which would alter the selection of optimal biopsy target; hence, a scan performed at a longer

Table 1 Sociodemographic, lesion, and biopsy characteristics ($n = 83$)

Variables	Frequency (%)
Gender	
Male	52 (63)
Female	31 (37)
Age (mean)	50.8
Lesion location	
Lobar	24 (29)
Cerebellum	4 (5)
Basal ganglia	16 (19)
Brainstem	5 (6)
Thalamus/hypothalamus	14 (17)
Pineal	3 (4)
Corpus callosum	14 (17)
Periventricular	3 (4)
Deep location	53 (64)
Lesion size	
$>$ **10** mL	39 (47)
$<$ **10** mL	44 (53)
Biopsy method	
Frameless	45 (54)
Frame based	38 (46)
Anesthesia	
General anesthesia (**GA**)	59 (71)
Local anesthesia (**LA**)	24 (29)
System used	
Portable Brainlab Vector	15 (18)
Brain-suite Brainlab Curve	30 (36)
Cosman–Roberts–Wells (**CRW**) **frame**	19 (23)
Albert-Wong (**AW**) **frame**	19 (23)
Complications	12 (14)
Hemorrhage	5
Brain edema	1
Seizures	–
Neurological deficit	9
Cerebrospinal fluid (**CSF**) **leak**	–
Death	–
Positive histopathological yield	70 (84)
Glioblastoma	6 (7)
Central nervous system (**CNS**) **lymphoma**	31 (37)
Glioma other than glioblastoma	18 (22)
Infection/abscess	9 (11)
Metastasis	3 (4)
Germinoma	2 (2)
Infarct/necrosis	1 (1)
Radiological accuracy	76 (92)

time interval from the day of biopsy might not be representative of the actual tumor at that time.[7] Although being rather rudimentary in the planning of biopsies, the importance of meticulous planning of target, entry point, and trajectory could not be stressed more to achieve successful biopsies. The target is essentially chosen from areas of the lesion with contrast enhancement as this results in better diagnostic yield.[8] The trajectory of the biopsy needle is carefully delineated in a computer software that allows 3D viewing and a Probe's eye view. Studies have described the importance of trajectory planning in deep brain stimulation and stereoelectroencephalography (SEEG) where precision is of utmost importance.[9,10] Selecting a needle path that avoids the ventricles, sulcus, and important neurovascular structures with the shortest distance to the target is imperative.

Frame and Coordinates

The frame-based biopsy has been considered by many to be the "gold standard" of accurate biopsies.[8,11] However, the frame bulkiness and inherent technicalities pose a disadvantage to this method. The performing surgeon needs to be extremely familiar with the choice of frame or frameless system that is used. If a stereotactic frame is used, all the parts and screws should be checked as a faulty part or a loose screw can cause geometrical distortions, which would affect accuracy. The frames in our center, the CRW and AW frames, have phantoms to check the target and trajectory coordinates. We also strongly advocate the double checking of frame coordinates by two or more surgeons and the review of the planned target and trajectory again with the frame fixed on the patient to detect any gross inaccuracy, particularly on the side (right or left) of biopsy.

Corticosteroids and Methods to Minimize Brain Shift and Trajectory Deviation

Classical teaching advices against the use of corticosteroids in suspected cases of primary CNS lymphoma. The reduction in diagnostic yield of these lesion with a pretreatment of corticosteroids has been challenged by multiple studies.[12,13] Nonetheless, numerous studies have demonstrated the difficulty in reaching an objective and consistent histopathological and immunohistochemical finding with patients having administered steroids.[14,15] Primary CNS lymphoma accounted for the largest proportion of cases in our previous biopsy analysis, and we have refrained from using corticosteroids for lesions planned for stereotactic biopsy to reduce the possibility of a negative yield.[6] A sufficiently sized burr hole that is centered on the planned entry point is a simple but often neglected detail that could cause the biopsy needle to skirt or be obstructed by the outer or inner table of the skull. This would inadvertently result in a deviation in the trajectory. The loss of CSF would prove costly in biopsies with a small margin of error. The resultant shift in brain structures causes inaccuracies, which have been reported in cases of deep brain stimulation.[16] These cortical and subcortical shifts also stem from the postural changes of intracranial structures under the influence of gravity, pneumocephalus, and distortion of the cortical and

Table 2 Baseline comparison and analysis of diagnostic yield and accuracy between groups 1 and 2

Variables	Group 1 ($n = 50$) Frequency (%)	Group 2 ($n = 33$) Frequency (%)	*p*-value
Gender			
Male	31 (62)	21 (64)	0.88
Female	19 (38)	12 (36)	
Age (mean)	48.3	54.5	0.14
Lesion location			
Deep	29 (58)	24 (73)	0.24
Superficial	21 (42)	9 (27)	
Lesion size			
$>$ **10** mL	20 (40)	19 (58)	0.07
$<$ 10 mL	30 (60)	14 (42)	
Biopsy method			
Frameless	40 (80)	5 (15)	0.01[a]
Frame-based	10 (20)	28 (85)	
Overall complications	6 (12)	5 (15)	0.74
Radiological accuracy	44 (88)	32 (97)	0.15
Positive histopathological yield	38 (76)	32 (97)	0.01[a]

Note: Group 1 includes cases done before the year 2020 prior to the introduction of new stereotactic biopsy criteria/pre-requisites and group 2 includes cases done after the year 2020.
[a]Statistically significant.

Table 3 Frame-based versus frameless method, lesion size $>$10 versus $<$10 mL, and diagnostic yield

Variable	Positive yield Frequency (%)		Negative yield Frequency (%)	*p*
Overall				
Frame based	35 (50)		3 (23)	0.07
Frameless	35 (50)		10 (77)	
Group 1				
Frame based	7 (18)		3 (25)	0.62
Frameless	31 (82)		9 (75)	
Group 2				
Frame based	28 (88)		0 (0)	0.15
Frameless	4 (12)		1 (100)	
Lesion size				
$>$ 10 mL	37 (53)		2 (15)	0.01*
$<$ 10 mL	33 (47)		11 (85)	
	Positive yield			
	Group 1	**Group 2**		
$>$ 10 mL	18 (47)	19 (59)		0.3
$<$ 10 mL	20 (53)	13 (41)		

Note: *Statistically significant.

subcortical structures with the advancing biopsy needle. Thus, care must be taken when durotomy is performed to minimize CSF egress, and needless to say excessive suctioning of CSF is not recommended. The use of fibrin sealant has been advocated by some authors in regard to this.[17]

Sampling Techniques and Examination of Acquired Sample

The method of acquiring a tissue sample during the biopsy is subject to a wide inter-user variability depending on the surgeons' common practice and preference. The technique of

sampling consistently used at our center after the year 2020 is the "negative-pressure and rotation" technique. The needle is advanced with a closed window into the brain and upon reaching the target, the window is opened and the needle is rotated 360 degrees. This achieves separation of the tissue through the cutting by the longer window edge.[18] Subsequently, the window is closed and the needle is removed. The addition of a vacuum pressure through the aspiration of the syringe connected to the biopsy needle has been shown to increase the quality, size, and mass of samples.[18,19] The biopsy sample should be examined for color and weight to be deemed satisfactory. Clot-laden samples and buoyant specimens without significant mass are deemed suboptimal.

These criteria and prerequisites when applied to all stereotactic biopsies in unison are bound to improve the accuracy and diagnostic yield as per the review above.

Conclusion

Simple and small details in routine surgical practice, although often underestimated and overlooked, still remain important in improving the precision and efficiency of surgical procedures as demonstrated in this study.

Limitations

The limitations of this study arise from its retrospective and prospective nature, which limits the opportunity to adequately match and randomize patients into groups and control. This is also contributed by the fact that the number of biopsy cases is not large, which may have affected the statistical significance of the study. In a high-volume center, a randomized or case control study would possibly improve the statistical value of the study.

Authors' Contributions

K.V, B.L.L., and A.S.H.W. have given substantial contributions to the conception and the design of the manuscript. S.S.L. and D.L.N. have contributed in providing the samples and designing the methodology. K.V, B.L.L., and D.K. have contributed to acquisition, analysis, and interpretation of the data. All the authors participated in drafting the manuscript, and author A.S.H.W. revised it critically. All the authors contributed equally to the manuscript and read and approved the final version of the manuscript.

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Conflict of Interest

None declared.

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