Comparing the risks of frameless stereotactic biopsy in eloquent and noneloquent regions of the brain: a retrospective review of 284 cases

Clinical article

ELLEN L. AIR, M.D., PH.D.,1 JAMES L. LEACH, M.D.,2,3 RONALD E. WARNICK, M.D.,1,4 AND CHRISTOPHER M. McPHERSON, M.D.1,4

Departments of 1Neurosurgery and 2Radiology, Brain Tumor Center at the University of Cincinnati Neuroscience Institute and University of Cincinnati College of Medicine; 3Department of Radiology, Cincinnati Children’s Hospital Medical Center; and 4Mayfield Clinic, Cincinnati, Ohio

OBJECT. Frameless stereotactic biopsy has been shown in multiple studies to be a safe and effective tool for the diagnosis of brain lesions. However, no study has directly evaluated its safety in lesions located in eloquent regions in comparison with noneloquent locations. In this study, the authors determine whether an increased risk of neurological decline is associated with biopsy of lesions in eloquent regions of the brain.

METHODS. Medical records, including imaging studies, were reviewed for 284 cases in which frameless stereotactic biopsy procedures were performed by 19 neurosurgeons at 7 institutions between January 2000 and December 2006. Lesion location was classified as eloquent or noneloquent in each patient. The incidence of neurological decline was calculated for each group.

RESULTS. During the study period, 160 of the 284 biopsies predominately involved eloquent regions of the brain. In evaluation of the complication rate with respect to biopsy site, neurological decline occurred in 9 (5.6%) of 160 biopsies in eloquent brain areas and 10 (8.1%) of 124 biopsies in noneloquent regions; this difference was not statistically significant (p = 0.416). A higher number of needle passes was associated with the presence of a postoperative hemorrhage at the biopsy site, although not with a change in the result of neurological examination.

CONCLUSIONS. Frameless stereotactic biopsy of lesions located in eloquent brain regions is as safe and effective as biopsy of lesions in noneloquent regions. Therefore, with careful planning, frameless stereotactic biopsy remains a valuable and safe tool for diagnosis of brain lesions, independent of lesion location. (DOI: 10.3171/2009.3.JNS081695)

KEY WORDS • complications • eloquent brain • neurological deficit • frameless stereotactic biopsy

Frameless stereotactic needle biopsy, an often-used neurosurgical tool for the diagnosis of brain lesions, provides a minimally invasive means of establishing a tissue diagnosis to guide subsequent therapies.5,6,18 A number of studies evaluating the efficacy and risk of this procedure have found high diagnostic yields ranging from 85 to 98% and low complication rates ranging from 2 to 6.5%.1–3,10–12,17,19,30 Frameless stereotactic biopsy is particularly useful for deep-seated lesions or lesions located in or near eloquent areas of the brain. In these regions, however, resection carries a much higher risk of causing neurological dysfunction,22 and thus biopsy is often performed to guide noninvasive therapies in lieu of lesion resection. Although a general belief is that the small amount of tissue disruption associated with stereotactic biopsy does not pose significant risk of neurological deficit even when eloquent tissue is involved, this assumption has not been documented in the literature.

In this retrospective review, we aimed to define the risk of using a frameless stereotactic needle in the biopsy of lesions in eloquent and noneloquent regions of the brain. Specifically, we tested the hypothesis that frameless stereotactic needle biopsy of lesions in eloquent regions does not confer a higher risk of neurological decline compared with noneloquent regions. In our series of 284 consecutive frameless stereotactic biopsies, we directly compared neurological deficits that occurred after biopsy of lesions in eloquent and noneloquent regions.
Risk of stereotactic biopsy in eloquent brain regions

Methods

The billing records of the Mayfield Clinic were reviewed to identify patients who underwent stereotactic brain biopsy from January 1, 2000, through December 31, 2006; surgeries were performed by 19 neurosurgeons at 7 area hospitals. Our search included CPT Codes 61750, 61751, and 61795. Electronic medical records were reviewed, specifically for the operative record, pathology reports, postoperative notes/discharge summary, and radiology reports; the paper chart was reviewed when the electronic record was insufficient or lacking information. After abstracted data were entered into a password-protected database accessible only by the authors, all identifying information was then deleted and files containing protected health information were destroyed. Excluded were cases for which data were incomplete, cases in which surgery was converted into an open resection, and open biopsies in which stereotactic localization was used. This study was completed with approval of the institutional review boards of the University of Cincinnati (no. 06–08–15–03-EE) and TriHealth (no. 06108–0806–064).

Data collected from the records of 284 biopsies included the number of stereotactic needle passes performed during surgery, complications developing intra- and postoperatively, and diagnosis, location of the lesion, and whether it involved eloquent brain. Samples were defined as nondiagnostic when identified as such by the pathologist or when reported as normal brain tissue, gliosis, or cerebritis without underlying cause. Complications were defined as neurological deficits (including documented worsening of those deficits already present), seizures, symptomatic hemorrhage, or death. Asymptomatic hemorrhages documented by head CT were also recorded. Lesions were classified as eloquent or noneloquent based on the radiology report, in conjunction with the dictated report of the attending neurosurgeon. Eloquent regions were defined as lesions of the brainstem, basal ganglia, corpus callosum, dominant frontal operculum, hypothalamus, insula, motor cortex, dominant posterior temporal lobe, sensory cortex, thalamus, and visual cortex. The percentage of biopsies for lesions located in eloquent brain, relative rates of complications, and diagnostic yield were then calculated. To identify factors that may have contributed to the adverse event, cases involving complications were then compared with those without complications.

Although some variability existed among surgeons, the standard method for frameless stereotactic biopsy at all institutions was based on fiducial MR images obtained within 48 hours before surgery. Images were then loaded into a frameless navigation system and registered to the patient. Several types of navigation systems were used during this 7-year period. Generally, a linear incision was made over the entrance point identified by the surgeon. The dura and pia mater were coagulated and opened. The guide needle then was calibrated and the distance to the target calculated using the offset feature of the imaging system. The depth was marked on the guide needle and then inserted, together with the sample needle, into the brain. The tissue sample was withdrawn, leaving the guide needle in place; additional samples were generally taken in quadrants. One trajectory was defined as 1 pass of the guide needle. Postoperative CT scans were not uniformly acquired.

Statistical Analysis

Statistical analysis was performed using Microsoft Excel software. Differences between groups were assessed using the Student t-test and z-ratio for proportions, as appropriate.

Results

Clinical Characteristics

During our screening of the Mayfield Clinic billing records (2000–2006), we identified 320 cases of frameless stereotactic biopsy. Of the 36 cases excluded from this study, 11 cases were open biopsies or those converted to open resection (5 of which were in eloquent regions), 1 was a skull biopsy, and 1 was aborted because of venous bleeding before needle insertion; information was incomplete for 23 cases. The remaining 284 cases were included in the analysis. Patients ranged in age from 17 to 90 years (mean 57 years) at the time of surgery. The most common presenting symptoms were seizure, weakness, and mental status changes. Eighty-seven percent of the procedures represented an initial biopsy. The most common diagnosis was glioblastoma multiforme (31%), followed by a lower-grade glial tumor (27%). Other diagnoses are shown in Table 1.

| TABLE 1: Summary of patient characteristics by lesion location* |
|---------------------------------|-----------------|-----------------|-----------|
| Characteristic                  | Eloquent (%)    | Noneloquent (%) | p Value   |
| no. of patients                 | 160             | 124             |           |
| mean age in yrs (range)         | 56.8 (17–90)    | 57.2 (18–87)    | 0.863     |
| male (%)                        | 80 (50)         | 66 (53.2)       | 0.59      |
| initial biopsy (%)              | 144 (90)        | 104 (84)        | 0.124     |
| diagnosis                       |                 |                 |           |
| glioblastoma multiforme         | 70              | 19              |           |
| glial tumor                     | 48              | 29              |           |
| lymphoma                        | 16              | 17              |           |
| metastasis                      | 1               | 12              |           |
| abscess                         | 4               | 9               |           |
| nonabscess infection            | 1               | 7               |           |
| radiation necrosis              | 2               | 3               |           |
| nonglial tumor                  | 0               | 5               |           |
| demyelination                   | 2               | 2               |           |
| PTLD                            | 2               | 1               |           |
| hemorrhage                      | 3               | 0               |           |
| stroke, vasculitis              | 1               | 1               |           |
| nondiagnostic (%)               | 10 (6.25)       | 19 (15.3)       | 0.012     |
| adverse events (%)              |                 |                 |           |
| asymptomatic hemorrhages        | 22 (13.8)       | 14 (11.3)       | 0.537     |
| neurological decline            | 9 (5.6)         | 10 (8.1)        | 0.416     |

* PTLD = posttransplant lymphoproliferative disorder.
Diagnostic Yield

The overall diagnostic yield was 89.8% for the 284 biopsies. Non-diagnostic findings were more likely for lesions located in a noneloquent region. Samples were non-diagnostic in 19 (15.3%) of 124 biopsies in noneloquent regions and 10 (6.25%) of 160 biopsies in eloquent regions; this difference was statistically significant (p = 0.012, Table 1).

The majority of lesions biopsied (234 [82.4%] of 284) were considered unresectable by the surgeon, and > 50% were located in eloquent regions. Additional reasons for lesions being considered unresectable were the presence of multiple other lesions, a deep location, or the nature of the lesion (for example, herpes encephalitis or demyelinating disease). Patients with lesions considered resectable typically underwent biopsy because of their age or health, or uncertainty in likely diagnosis (for example, radiation necrosis vs recurrent tumor).

Adverse Neurological Events

When adverse neurological events were considered, the complication rate was 6.7% for 284 biopsies. Of the 19 patients with complications, 3 developed hematomas that required operative evacuation, and in 1, malignant edema of the tumor developed and the lesion was resected within 24 hours of biopsy. Of these 19 patients, 11 significantly improved or returned to their prior baseline status and 2 improved minimally. The remaining 6 patients experienced neurological decline following biopsy, and the decision to forego additional treatment was made by the family; these 6 cases represented the 30-day mortality rate of 2%. Only 2 of these 6 patients suffered a biopsy-associated hemorrhage.

In evaluating the complication rate with respect to biopsy site, we observed neurological decline in 9 (5.6%) of 160 biopsies in eloquent brain areas and 10 (8.1%) of 124 biopsies in noneloquent regions (Table 1); this difference was not statistically significant (p = 0.416). When particular areas of the brain were analyzed, no correlation was found between location and complications. Specifically, we observed no increased incidence of neurological decline in patients whose lesions were in the thalamus, basal ganglia, or deep structures compared with patients whose lesions were in superficial structures.

The average number of trajectories, and therefore passes of the guide needle, made by the surgeon ranged from 1 to 4 (average 1.24). Surgeons made significantly more needle passes for biopsies deemed nondiagnostic (1.58 passes) compared with diagnostic (1.20 passes) (p = 0.0006). The number of trajectories was 1.49 in cases in which an asymptomatic hemorrhage was noted compared with 1.20 in cases in which no bleeding was identified (p = 0.006). No differences were observed in the average number of needle passes made in patients who suffered (1.26) and those who did not suffer (1.24) neurological decline, regardless of whether the biopsy was in an eloquent or noneloquent region (p = 0.852, Table 2).

Discussion

In examining a large cohort of patients treated in a 7-year period, our study demonstrates the safety and efficacy of frameless stereotactic biopsy of lesions in eloquent brain regions. Among the 160 biopsies performed in eloquent brain regions, neurological decline occurred in 5.6%, and this incidence did not statistically differ from that in noneloquent brain regions (8.1%). Stereotactic biopsy has been established as a safe procedure with a low risk of complication3,5,8,12 and has been used in challenging and dangerous locations, such as the cavernous sinus9 and brainstem24 while yielding a low morbidity rate. However, insufficient data exist to specifically address whether patients whose lesions are in eloquent location may face a higher risk of biopsy-related neurological decline. To the best of our knowledge, this is the first study to specifically evaluate whether an eloquent location confers an increased risk of neurological deficit after stereotactic needle biopsy.

Previous work has suggested that lesion location influences the risk of neurological decline. In a multivariate regression analysis of 270 frame-based and frameless stereotactic biopsies, McGirt et al.17 found an increased morbidity rate associated with lesions located in the basal ganglia or thalamus. Because all eloquent regions were not evaluated, it is unclear whether this morbidity was due to the eloquent nature or deep location of the region. The 5 symptomatic complications that occurred in our study—after biopsies of thalamic and basal ganglia lesions—were proportionate to the total number of biopsies performed in these regions. As there was no higher incidence of complications noted for basal ganglia and thalamic lesions, all deep locations were compared with superficial locations, although no difference in complication rates was seen (7.8 vs 5.3%, respectively; p = 0.4).

The overall rate of neurological complications in our study is similar, although in the higher range, to that seen in other studies (6.7 vs 2–6.5%).1,3,5,10,12,19,30 Six of our patients experienced a neurological decline of subacute onset that prompted evaluation and eventual biopsy. Postoperatively, status in these patients continued to decline and their families requested no further intervention or treatment. All patients who died within 30 days exhibited the features of this clinical scenario. These patients contributed significantly to the complication rate.

The rate of asymptomatic hemorrhages in our study is consistent with that in previously published work from this and other institutions. During the study period, we documented an asymptomatic intracerebral hemorrhage in

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**Table 2: Effect of number of trajectories on adverse events**

<table>
<thead>
<tr>
<th>Location</th>
<th>Asymptomatic Hemorrhage</th>
<th>Neurological Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>all</td>
<td>1.49</td>
<td>1.20</td>
</tr>
<tr>
<td>eloquent</td>
<td>1.48</td>
<td>1.14</td>
</tr>
<tr>
<td>noneloquent</td>
<td>1.50</td>
<td>1.27</td>
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* With the exception of p values, data represent the mean number of needle trajectories made intraoperatively.
12.7% (36) of all 284 cases. However, because postoperative head CT scans were not routinely obtained by all the surgeons, this rate of asymptomatic hemorrhages is most likely underestimated. A wide range of incident rates for asymptomatic hemorrhages have been documented in the literature (3–59%). These hemorrhages are typically small, and the literature has shown that without clinical symptoms, the morbidity associated with such episodes is minimal.

In the absence of a correlation between biopsy location and complication rate, additional factors that may have contributed to adverse events were assessed. A significant correlation was found between the number of needle trajectories and rates of complications. However, this was specific to the development of asymptomatic hemorrhages because the average number of needle passes did not differ between patients in whom neurological status did and did not decline. These findings emphasize the importance of careful surgical planning to optimize the targeting of high-yield areas, thus keeping the need for additional needle trajectories to a minimum.

The patients evaluated in this study represent a population drawn from a large practice area and the broad range of patients referred to Mayfield Clinic. Patient characteristics and diagnostic yield in this study of 89.2% are comparable to those previously reported (range 85–98%). Many of the patients, in whom a diagnosis could not be established, presented with neurological symptoms but indistinct MR imaging findings. In these patients, the surgeon typically targeted noneloquent regions of the brain, accounting for the higher nondiagnostic rate in noneloquent regions. Greater numbers of needle trajectories were used as well in an effort to establish a diagnosis. Because of the greater difficulty in targeting ill-defined lesions, adjunctive tools (such as PET imaging and MR imaging spectroscopy) have been advocated. Although these modalities are now increasingly used at our institution, they were not yet common during the study period. The distribution of pathological findings is also consistent with previous reports. These findings indicate the applicability of this study to the broader neurosurgical patient population.

**Study Limitations**

The limitations of our study are its retrospective design and its reliance on operative records and imaging reports to classify lesion and biopsy locations. Lesions were classified by their inclusion of eloquent territory because a hemorrhage or other biopsy-related complication likely would affect the entire region of the tumor. Also, classification was based on lesion location, rather than biopsy trajectory, because the stereotactic trajectory plans were not available. Prospective evaluation with multiple independent reviews of preoperative imaging could provide a more accurate assessment of risk. Another limitation is the lack of information in the literature as to the true relationship between individual types of lesions and functional pathways. Lesions may largely or entirely displace rather than infiltrate functional pathways. This displacement may explain the contrast between the lack of increased risk in this cohort and the clear increased risk associated with tumor resection.

Although tumors considered infiltrative in nature, such as lymphoma, have been associated with an increased risk of complication in previous work, we did not observe this risk in our study. Future studies that involve functional MR imaging as a surgical adjunct may help to assess the risk of biopsy and resection in patients with brain tumors. Functional MR imaging has been applied in the preoperative planning for surgical treatment of brain tumors to aid in the localization of primary motor, sensory, and speech areas. While its application remains under investigation, in conjunction with other modalities, functional MR imaging has aided localization, and its use is now being validated by electrocortical mapping and clinical outcome in patients with brain tumors.

**Conclusions**

In our retrospective review of 284 frameless stereotactic biopsies, we found no evidence of increased risk of neurological decline from biopsy of lesions located in eloquent compared with noneloquent regions. However, the increased risk associated with multiple needle trajectories emphasizes the importance of surgical planning to optimize both the entry and the target in terms of both location and imaging characteristics. When multiple lesions or possible trajectories are present with similar likelihood of diagnostic yield, a noneloquent location is still favored. When necessity indicates biopsy of a lesion located in an eloquent location, our comparison indicates that the biopsy can be performed safely without increased risk over standard biopsy of noneloquent lesions. However, we do recommend preoperative planning to limit the number of needle passes and samples taken. Frameless stereotactic biopsy should be considered a safe and effective procedure for the diagnosis of lesions located in eloquent brain.

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**Disclaimer**

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

**References**


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Address correspondence to: Christopher M. McPherson, M.D., c/o Editorial Office, Department of Neurosurgery, University of Cincinnati College of Medicine, P.O. Box 670515, Cincinnati, Ohio 45267-0515. email: editor@mayfieldclinic.com.