Hemorrhage after Stereotactic Biopsy from Intra-Axial Brain Lesions: Incidence and Avoidance

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Abstract

Background With the introduction of stereotactic surgery in humans by Spiegel and Wycis in 1947 and the great advances in neuroimaging, image-guided stereotactic brain biopsy is the mainstay for diagnosis of intrinsic deep-seated brain lesions. Stereotactic biopsy is usually safe, and the reported rate of complications is minimal, with mortality being reported in less than 1% and significant morbidity occurring in less than 5%. The complication most often encountered after stereotactic biopsy is hemorrhage.

Patients and Methods A total of 150 patients (84 male and 66 female) with the mean age of 52.8 years having intra-axial brain lesions were included in the study. Image-guided (114 computed tomography [CT] and 36 magnetic resonance imaging [MRI]) stereotactic biopsy were performed by a specialized stereotactic neurosurgeon. Routine preoperative coagulation studies were performed in all patients. A workstation with multiplanar trajectory planning software was used. Serial biopsies were done with Sedan-type side cutting needle. Any detectable bleeding was analyzed by CT within 4 hours after procedure. All medical charts, laboratory results, preoperative imaging studies, and postoperative imaging studies were reviewed.

Results A conclusive histopathological diagnosis was achieved in 147 patients (98%). In 7 patients (4.7%), hemorrhage was detected in post-biopsy CT scan (3.3% asymptomatic and 1.4% symptomatic). Hemorrhage occurred in patients with highly malignant tumors. There was no mortality.

Conclusion Using multiplanar image-guided trajectory planning and a small biopsy needle decreases the incidence of post-biopsy hemorrhage. Neurologically intact patients with no hemorrhage in post-biopsy CT scan could safely be discharged home at the same operative day.

Introduction

With recent advances in high-resolution computed tomography (CT) scanning and magnetic resonance imaging (MRI) over the past two decades, the use of stereotactic biopsy has become routine in the diagnosis and management of many brain lesions. Treatment of intracranial mass lesions must be based on accurate diagnosis. In spite of their sophistication, new imaging modalities are still unable to establish tissue diagnosis. Stereotactic biopsy offers a highly accurate method of approaching intrinsic deep-seated brain lesions, lesions located nearby eloquent areas of the brain, or multiple lesions.

Stereotactic biopsy is today the most frequently performed stereotactic procedure. Since its introduction, a large number of series have been published that document its relative safety. The reported mortality rate is below 1% and the morbidity rate is less than 5%. It is possible for the neurosurgeons and other physicians, as well as patients, to
Hemorrhage rates have ranged from 1.2 to 59.8%. Over-night hospitalization to monitor for neurological changes is not evidenced to be useful or cost-effective.

Despite the proven safety of stereotactic brain biopsy, reasonable attempt should be made to diagnose a lesion before an invasive procedure is undertaken. Consideration should also be given to how a biopsy diagnosis can influence the course of therapy for the patient. The procedures and indications for stereotactic brain biopsy have been well established.

Stereotactic biopsy may be accompanied with certain complications such as hemorrhage, neurological deficit, fits, and infection. Death following stereotactic biopsy is very rare as a result of either increased cerebral edema or intracranial hemorrhage. The complication most often encountered after stereotactic biopsy is hemorrhage.

Hemorrhage after stereotactic biopsy has been classified on one hand either into intratumoral hemorrhage (biopsy related) or hemorrhage along the needle track (trajectory related). On the other hand, it can be classified into symptomatic when it causes a new neurological deficit or results in deterioration of a pre-existing neurological deficit and into asymptomatic or silent when only discovered in routine post-biopsy CT images without clinical change. Furthermore, hemorrhage could be classified by location into intrallesional hemorrhage, intraparenchymal extralesional hemorrhage, intraventricular hemorrhage (IVH), subarachnoid hemorrhage (SAH), subdural hemorrhage (SDH), and epidural hemorrhage (EDH). Most neurosurgeons do not perform post-biopsy imaging unless their patients experience new symptoms. The timing of post-biopsy CT scanning is not consistent in previous studies. We prospectively obtained post-biopsy CT scans for all patients undergoing stereotactic brain biopsies between September 2005 and November 2010. All patients were observed overnight in the hospital to detect any neurological deficits of delayed onset.

Clinical Materials and Methods

Patients’ Population and Preoperative Preparation
At the Department of Neurosurgery, Tanta University Hospital, between September 2005 and November 2010, 150 stereotactic frame-based, image-guided brain biopsies were done in 150 patients (84 males and 66 females) with the mean age of 52.8 years (range 5 to 72 years). Patients on oral anticoagulant drugs stopped drug intake 5 to 7 days before biopsy. Subcutaneous heparin was stopped 1 to 2 days before the procedure. Systolic blood pressure greater than 150 mmHg has been treated by antihypertensive drugs. Platelet count should not have been less than 80,000/mm³. Prothrombin concentration was kept above 70% (Table 1).

<table>
<thead>
<tr>
<th>Cases</th>
<th>Age</th>
<th>Sex</th>
<th>Image</th>
<th>Anesthesia</th>
<th>Site</th>
<th>IOB</th>
<th>Pathology</th>
<th>Symptoms</th>
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<tbody>
<tr>
<td>Case 1</td>
<td>55</td>
<td>M</td>
<td>CT</td>
<td>Local</td>
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<td>Yes</td>
<td>Astrocytoma III</td>
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<td>Case 2</td>
<td>57</td>
<td>M</td>
<td>CT</td>
<td>Local</td>
<td>Parietal</td>
<td>Yes</td>
<td>Metastatic Br. carcinoma</td>
<td>Yes</td>
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<tr>
<td>Case 3</td>
<td>62</td>
<td>F</td>
<td>CT</td>
<td>Local</td>
<td>Basal ganglia</td>
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<td>GBM</td>
<td>No</td>
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<tr>
<td>Case 4</td>
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<td>F</td>
<td>CT</td>
<td>General</td>
<td>Basal ganglia</td>
<td>Yes</td>
<td>GBM</td>
<td>Yes</td>
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<tr>
<td>Case 5</td>
<td>70</td>
<td>M</td>
<td>CT</td>
<td>Local</td>
<td>Frontal</td>
<td>Yes</td>
<td>Metastatic melanoma</td>
<td>No</td>
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<td>Case 6</td>
<td>59</td>
<td>M</td>
<td>MRI</td>
<td>Local</td>
<td>Corpus callosum</td>
<td>No</td>
<td>GBM</td>
<td>No</td>
</tr>
<tr>
<td>Case 7</td>
<td>60</td>
<td>M</td>
<td>MRI</td>
<td>General</td>
<td>Basal ganglia</td>
<td>Yes</td>
<td>GBM</td>
<td>No</td>
</tr>
</tbody>
</table>

M, male; F, female; CT, computerized tomography; IOB, intraoperative bleeding; GBM, glioblastoma multiformis; Br., bronchogenic.
probe was slowly removed. No further biopsy samples were taken.

**Post-biopsy Computerized Tomography Scans**

All post-biopsy CT scans were obtained 4 hours after biopsy and reviewed by a neurosurgeon and a neuroradiologist. These scans were compared with pre-biopsy images to distinguish and identify areas of true hemorrhage from those of residual extravasation of the contrast agent. A hemorrhagic complication was defined when a parenchymal hematoma at or around the biopsy site was seen on postoperative CT scan, with or without a new neurological deficit. Punctate hemorrhage seen at the site of biopsy was not considered a hemorrhagic complication.

New hemorrhages were classified by location (intrasional, intraparenchymal extrasional, IVH, SAH, SDH, or EDH), and by clinical symptoms and signs (symptomatic and silent). Intratumoral hemorrhage or bleeding in the vicinity of the tumor was regarded as biopsy related. Otherwise, the bleeding was classified as trajectory related.

In each case, medical charts were reviewed, as well as laboratory results, to identify factors that may have increased the risk of post-biopsy intracranial hemorrhage and to identify patients who had symptomatic hemorrhages. Factors evaluated included age and gender of the patient, location and type of lesion, number of biopsies obtained, use of medications that alter coagulation or platelet function (acetylsalicylic acid, warfarin, heparin, enoxaparin, clopidogrel, or ticlopidine), history of hypertension, prothrombin and partial thromboplastin times, and platelets count.

**Results**

A conclusive histopathological diagnosis was achieved in 147 patients (98%).

In 143 patients (95.3%), there was no evidence of intracranial hemorrhage following the procedure. In 7 patients (4.7%), hemorrhage was detected in post-biopsy CT scan. All hemorrhages were intraparenchymal (→**Figs. 1 and 2**) except in 1 patient who had intraparenchymal hemorrhage with intraventricular extension (→**Fig. 3**). In 5 patients (3.3%), the hemorrhage was asymptomatic and discovered only in post-biopsy CT scan, and in 2 patients (1.4%), the hemorrhage was symptomatic. A subdural or epidural hemorrhage was not detected.

One of the two symptomatic patients suffered from a new hemiparesis on the left side that improved after days of medical treatment by steroids and dehydrating measure, such as lasix and mannitol. Finally, the patient fully recovered. The other patient lost consciousness and the post-biopsy CT scan showed a large intraparenchymal hemorrhages. The patient was transferred to intensive care unit and managed medically for 10 days until he regained consciousness. A residual weakness was seen. Serial follow-up CT scans showed resolution of hematoma and surrounding edema.

In 6 of the 7 patients that had hemorrhage in the post-biopsy CT scan (85.7%), intraoperative bleeding occurred. This bleeding was managed by continuous and patient irrigation with saline, as described before. The age of the 7 patients with post-biopsy hemorrhage ranged from 55 to 72 years with an average of 62.1 years.

The pathological diagnoses associated with hemorrhage were glioblastoma multiforme (GBM; 4 patients [57.1%]), anaplastic astrocytoma (1 patient [14.3%]), and metastatic "bronchogenic carcinoma and melanoma" (2 patients [28.6%]). The average number of needle biopsy samples taken per case was 3.4 (range 2 to 16). There is no difference in average number of samples between the patients with and without hemorrhagic complications. The overall biopsy-related morbidity and mortality rate was 1.4% and 0%, respectively.

**Discussion**

Numerous studies have been published in which postoperative imaging was performed to evaluate the incidence of intracranial hemorrhage after a stereotactic procedure. Hemorrhage rates in the major published series of stereotactic brain biopsies are listed in →**Table 2**. The
authors of most series estimated a hemorrhage rate of 1 to 7%. Voges et al found eight postoperative hemorrhages in a series of 338 patients (2.4%), with three (0.9%) being asymptomatic. Levin reported 3 (3.4%) asymptomatic hemorrhages in 87 stereotactic biopsies. Niizuma et al reported 4 (3.3%) cases of asymptomatic hemorrhage in a series of 121 biopsies. In the series of Grossman et al, 25 of 355 patients (7%) experienced a hemorrhagic complication, 12 (3.4%) of them were asymptomatic (Table 2).

In the study of Smith et al four (2.9%) out of 139 patients had postoperative hemorrhagic complication. In the series of Heper et al, three (2.3%) of 130 patients had postoperative hemorrhagic complication. Of those three cases, two (1.5%) had silent hemorrhage and one case (0.8%) was symptomatic.

The only prospective study was conducted by Kulkarni et al, in which 102 consecutive patients underwent post-biopsy CT scanning. Sixty-one patients (59.8%) were found to have evidence of hemorrhage in post-biopsy CT scan, which is one of the highest rates of bleeding complication after stereotactic biopsy. Based on these prospective data, it was concluded that the true risk of the frame-based stereotactic biopsy is significantly higher than it has been reported in the literature so far. However, suboptimal planning of the biopsy (a workstation for surgical simulation was not used), the use of three different frames by multiple neurosurgeons, and the low frequency of biopsies per year possibly have significantly increased the risk of hemorrhage as reported by the authors.

A very important finding in our study was that in patients who had no new neurological deficit after biopsy and whose initial CT scan showed no evidence of hemorrhage, there were no delayed deterioration. The negative predictive value, therefore, was 100%. This fact does, indeed, suggest a possibly useful role for routine postoperative CT scanning. If the CT scan shows no hemorrhage 4 hours after the biopsy in a neurologically well patient, the patient may be safely discharged home that day. The financial implications are obvious. In these days, with an increasing trend toward outpatient-based medical care, any investigation that can save a hospital admission while maintaining a high degree of medical safety would be of great value. It appears that

Fig. 2 Left: Stereotactic post-contrast CT demonstrating left ganglionic mass lesion. Right: Post-biopsy CT revealing small left intraparenchymal hemorrhage at the biopsy site.

Fig. 3 Left: Stereotactic post-contrast CT demonstrating left thalamo-ganglionic mass lesion. Right: Post-biopsy CT showing intraparenchymal hemorrhage with intraventricular extension.
Table 2: Review of literature for hemorrhagic complications detected after stereotactic brain biopsy procedures

<table>
<thead>
<tr>
<th>Authors and year</th>
<th>No. of cases</th>
<th>Hemorrhage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ostertag et al, 1980</td>
<td>302</td>
<td>2.9</td>
</tr>
<tr>
<td>Lunsford &amp; Martinez, 1984</td>
<td>102</td>
<td>2.0</td>
</tr>
<tr>
<td>Apuzzo et al, 1987</td>
<td>500</td>
<td>0.4</td>
</tr>
<tr>
<td>Kelly, 1991</td>
<td>547</td>
<td>0.9</td>
</tr>
<tr>
<td>Voges et al, 1993</td>
<td>338</td>
<td>2.4</td>
</tr>
<tr>
<td>Bernstein &amp; Parrent, 1994</td>
<td>300</td>
<td>5.3</td>
</tr>
<tr>
<td>Kulkarni et al, 1998</td>
<td>102</td>
<td>59.8</td>
</tr>
<tr>
<td>Sawin et al, 1998</td>
<td>225</td>
<td>3.6</td>
</tr>
<tr>
<td>Yu et al, 1998</td>
<td>310</td>
<td>1.6</td>
</tr>
<tr>
<td>Kreth et al, 2001</td>
<td>345</td>
<td>10.5</td>
</tr>
<tr>
<td>Field et al, 2001</td>
<td>500</td>
<td>8.0</td>
</tr>
<tr>
<td>Hertel et al, 2005</td>
<td>155</td>
<td>2.6</td>
</tr>
<tr>
<td>Grossman et al, 2005</td>
<td>355</td>
<td>7.0</td>
</tr>
<tr>
<td>Present study</td>
<td>150</td>
<td>4.7</td>
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</tbody>
</table>

post-biopsy CT, if routinely requested, may well meet these criteria.

Kulkarni et al.15 showed that when post-biopsy CT scanning had failed to detect a hemorrhage in neurologically intact patients, no patient experienced a delayed neurological deficit. The authors concluded that although the incidence of hemorrhage following stereotactic biopsy is common, asymptomatic patients in whom there is no evidence of hemorrhage on post-biopsy CT scans can safely be discharged home on the day of their procedure.

In Grossman et al’s study, an important finding was that in six patients who had no neurological deficit after biopsy and whose immediate postoperative CT scan showed no evidence of hemorrhage, there was a delayed clinical deterioration due to a parenchymal hematoma. In four patients, the clinical deterioration occurred after several hours following the biopsy, whereas in the other two patients, the complication occurred within days after the procedure. Based on their results, the current practice at their institution is to keep all patients undergoing a biopsy overnight.

In the present series, hemorrhage-related complications following biopsy were significantly lower than in the published prospective series of Kulkarni et al 15 and the retrospective studies of Bernstein and Parrent6 and Sawin et al.14 There was no mortality. The favorable results could be interpreted as the result of a complex interaction between technology (multiplanar image-guided planning) and biopsy device (small biopsy needle with a diameter of 1 mm). It was obvious that complex preoperative surgical planning was not used in the Kulkarni et al,15 Bernstein and Parrent,6 and Sawin et al.14 studies, which might explain, in part, the significantly higher symptomatic bleeding rates of these series.

Voges et al.12 have considered additional preoperative cerebral angiography and intraoperative Doppler investigation as being extremely useful for increasing the safety of stereotactic biopsy. Hertel et al.18 have also concluded that despite the overall high security of stereotactic biopsy, the use of intraoperative micro-Doppler may lead to an additional reduction of the risk of biopsy-related bleeding without enormous expense.

In our study, the pathological conditions associated with hemorrhage were GBM (four patients), anaplastic astrocytoma (one patient), and metastatic melanoma (two patients). So all patients with hemorrhagic complications had highly malignant lesions.

Among the most common pathological conditions, it appeared that high-grade astrocytomas, metastases, and lymphoma had the greatest tendency to bleed. Although the overall numbers are too small to make any definite conclusions, it would appear intuitively that highly malignant lesions with the increased presence of vascular proliferation would have a greater tendency to bleed after biopsy. In fact, all of the hemorrhages were associated with highly malignant lesions.15 Patients with malignant lesions were identified to be at higher risk for hemorrhage-related complications in the study of Sawin et al.14 Bernstein and Parrent6 reported that malignant lesions with neovascularization and/or abnormal blood vessels were prone to postoperative bleeding.

Cortical involvement, lesions located in eloquent areas, or the pre-existing signs and symptoms of elevated intracranial pressure may also be associated with an increased incidence of hemorrhages. However, Grossman et al’s study did not support these assumptions because none of the evaluated variables appeared to contribute significantly to the occurrence of hemorrhagic complications. Similar findings have been reported by Field et al.10 The only risk factor found in their analysis was an increased bleeding tendency when the platelet count fell below 150,000/mm3.

One of the major reasons cited to explain the wide range of the published complication rates has been the variability in surgical judgment, experience, and skill. Important considerations for the surgeon performing the biopsy include selection of the patient, the target, the trajectory, and the biopsy device. Knowledge, experience, and intellectual interest in stereotactic neurosurgery and/or neuro-oncology can influence the success of the procedure significantly.6,7

Recommendations

- Normalization of the coagulation state and blood pressure are important factors to reduce the risk of post-biopsy hemorrhage
- Choosing the best trajectory to avoid an entrance through any arterial or venous structure that is achieved by using multiplanar reconstruction software that lowers the rate of trajectory related hemorrhage
- Verification of the target coordinates by means of a phantom base
- Careful dealing with any intraoperative hemorrhage
- The presence of neovascularization and abnormal blood vessels in malignant tumors increases the incidence of post-biopsy hemorrhage and/or cerebral edema resulting in neurological deficit
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- A CT scan brain 4 hours after biopsy to detect any post-biopsy clot and assess its size
- Neurologically intact patients with no hemorrhage in post-biopsy CT scanning could be safely discharged home the same operative day
- Patients with hemorrhage in post-biopsy CT scans should be admitted to inpatient department for follow-up

Conflict of Interest
None

References