ITH advancements in high-resolution CT scanning and magnetic resonance imaging over the past two decades, the use of stereotactic brain biopsy has become routine in the diagnosis and initial management of many newly identified or expanding intracranial mass lesions. The procedure and indications for stereotactic brain biopsy have been well established.1,3,5,10,20 The reported rates of stereotactic biopsy complications and case management recommendations have varied considerably. Reported hemorrhage rates have ranged from 1.2 to 59.8%.1,2,7,8,11,12,16,17,20,22 Most of these hemorrhages remain asymptomatic and most patients never require further evaluation or treatment. As a result, most neurosurgeons do not order postbiopsy imaging, unless their patients experience new symptoms. The timing of postbiopsy CT scanning is not consistent in previous studies and the risk factors associated with hemorrhages are not well characterized. To perform a systematic evaluation of the rate of hemorrhage that is detectable on imaging in our experience with stereotactic brain biopsy, we prospectively obtained intraoperative postbiopsy CT scans in all patients undergoing stereotactic brain biopsies between 1990 and 1999. All patients were observed overnight in the hospital to detect any delayed-onset neurological deficits. We performed multivariate analyses to detect other factors that might influence the risk of biopsy-related hemorrhage.

Clinical Material and Methods

Object. Stereotactic brain biopsy has played an integral role in the diagnosis and management of brain lesions. At most centers, imaging studies following biopsy are rarely performed. The authors prospectively determined the acute hemorrhage rate after stereotactic biopsy by performing immediate postbiopsy intraoperative computerized tomography (CT) scanning. They then analyzed factors that may influence the risk of hemorrhage and the diagnostic accuracy rate.

Methods. Five hundred consecutive patients undergoing stereotactic brain biopsy underwent immediate postbiopsy intraoperative CT scanning. Before surgery, routine preoperative coagulation studies were performed in all patients. All medical charts, laboratory results, preoperative imaging studies, and postoperative imaging studies were reviewed.

In 40 patients (8%) hemorrhage was detected using immediate postbiopsy intraoperative CT scanning. Neurological deficits developed in six patients (1.2%) and one patient (0.2%) died. Symptomatic delayed neurological deficits developed in two patients (0.4%), despite the fact that the initial postbiopsy CT scans in these cases did not show acute hemorrhage. Both patients had large intracerebral hemorrhages that were confirmed at the time of repeated imaging. The results of a multivariate logistic regression analysis of the risk of postbiopsy hemorrhage of any size showed a significant correlation only with the degree to which the platelet count was below 150,000/mm³ (p = 0.006). The results of a multivariate analysis of a hemorrhage measuring greater than 5 mm in diameter also showed a correlation between the risk of hemorrhage and a lesion location in the pineal region (p = 0.0086). The rate at which a nondiagnostic biopsy specimen was obtained increased as the number of biopsy samples increased (p = 0.0073) and in accordance with younger patient age (p = 0.026).

Conclusions. Stereotactic brain biopsy was associated with a low likelihood of postbiopsy hemorrhage. The risk of hemorrhage increased steadily as the platelet count fell below 150,000/mm³. The authors found a small but definable risk of delayed hemorrhage, despite unremarkable findings on an immediate postbiopsy head CT scan. This risk justifies an overnight hospital observation stay for all patients after having undergone stereotactic brain biopsy.

Abbreviations used in this paper: CI = confidence interval; CT = computerized tomography; EDH = epidural hemorrhage; ICH = intracerebral hemorrhage; IVH = intraventricular hemorrhage; SAH = subarachnoid hemorrhage; SDH = subdural hematoma.
brain biopsies at the University of Pittsburgh Medical Center. Each patient underwent prospective intraoperative postbiopsy CT scanning of the head within 15 minutes after completion of the procedure. Patients undergoing stereotactic cyst drainage only, stereotaxy for functional procedures, stereotactic Ommaya reservoir or ventriculoperitoneal shunt insertion, brachytherapy, or stereotactic craniotomy were excluded from the study.

**Biopsy Procedures**

All biopsies were performed by the senior authors (D.K. and L.D.L.), both of whom are experienced in stereotactic neurosurgical procedures. In all biopsies, the Leksell model G stereotactic frame system (AB Elekta Instruments, Stockholm, Sweden) was used with either magnetic resonance or CT image guidance for stereotactic lesion localization. Whenever possible, biopsy trajectories were designed to avoid both an entrance through a sulcus and any cortical arterial or venous structures. Biopsy trajectories were also chosen to minimize the number of ependymal and pial surfaces to be traversed.

Multiplanar reformatted imaging was used to plot the trajectories before the actual probe was positioned. The patient had been prepared by having the scalp cleaned with alcohol, the stereotactic frame was attached to the head, and sterile drapes were applied. The stereotactic coordinates were then set, a local anesthetic agent (lidocaine or marcaine) was administered, and a 4-mm twist-drill craniotomy was performed. The dura mater was punctured with the aid of a blunt-tip 1.9-mm-diameter probe (AB Elekta Instruments), after which the biopsy needle was advanced to the target through a single pial surface along a predetermined trajectory. In children and selected adult patients, intravenous sedation or general endotracheal anesthesia was induced before applying the stereotactic frame and planning stereotactic coordinates. Twenty-five patients underwent spiral-needle biopsies in 1990, whereas the remaining 475 patients underwent Sedan-type side-cutting aspiration biopsies, which were performed using 3- or 10-mm openings with 2.1- or 2.5-mm-diameter cannulas (Elekta Instruments, Inc., Atlanta, GA). All surgical procedures were performed in a stereotactic operating room that was equipped with a dedicated CT scanner (model 9800; General Electric Medical Systems, Milwauk ee, WI). Preoperative hematological studies were routinely performed, including those for platelet count, prothrombin time, and partial thromboplastin time.

**Computerized Tomography Scans**

All postbiopsy CT scans were reviewed by a neurosurgeon and a neuroradiologist. These scans were compared with prebiopsy images to distinguish and identify areas of true hemorrhage from those of residual extravasation of contrast agent. New hemorrhages were classified according to their location (intraparenchymal hemorrhage, IVH, SAH, SDH, or EDH) and size (maximum diameter for intraparenchymal bleeding and maximum thickness for SDH or EDH) as described by Kulkarni and colleagues.11

In each case, both electronic and hard-copy medical charts were reviewed, as well as laboratory results, to identify factors that may have increased the risk of postbiopsy intracranial hemorrhage and to identify patients who had symptomatic complications related to their stereotactic biopsy procedure. Factors evaluated included the following: the age and sex of the patient, location and type of lesion, number of biopsies obtained, use of medications that alter coagulation or platelet function (aspirin, warfarin, heparin, enoxaparin, clopidogrel, or ticlopidine), history of hypertension, prothrombin and partial thromboplastin times, and platelet count (Table 1).

**Results**

Postbiopsy intraoperative CT scans were obtained in all 500 patients. The location and distribution of the biopsy targets are listed in Table 2. The final neuropathological diagnoses and the percentages of representation in this series are listed in Table 3. In 460 patients (92%) there was no evidence of intracranial hemorrhage following the procedure. In the 40 patients in whom hemorrhage was detected after biopsy, there were 27 intraparenchymal hemorrhages (67.5%), five IVHs (12.5%), five SAHs (12.5%), and three SDHs or EDHs (7.5%). In 14 patients (2.8%) the diameter of the intraparenchymal hemorrhage was small-
er than 5 mm. Intraparenchymal hemorrhages were 5 to 10 mm in diameter in six patients (1.2%), 10 to 30 mm in five patients (1%), 30 to 40 mm in one patient (0.2%), and more than 40 mm in one patient (0.2%). In six patients (1.2%) hemorrhage-related neurological deficits developed after stereotactic biopsy. In two of these patients there was no evidence of significant hemorrhage on the immediate postbiopsy intraoperative CT scans. In both patients the neurological deficits developed within 48 hours after the procedure, and repeated CT scans revealed new ICH at the biopsy site (Fig. 1). One of these patients, who harbored a glioblastoma multiforme, ultimately died as a consequence of the ICH.

The results of the multivariate regression analysis of the risk of postbiopsy hemorrhage (for all intracranial hemorrhages) demonstrated a significant correlation with the degree to which the platelet count was lower than 150,000/mm³ (p = 0.006). The results of the multivari-
neal region) or brainstem biopsies (Table 4). Similarly, no increased risk for hemorrhage was found in patients undergoing biopsies of highly vascular lesions (Table 5).

The results of multivariate logistic regression analysis of obtaining a nondiagnostic specimen as the final pathological diagnosis demonstrated a significant correlation directly with the increased number of biopsy samples obtained (p = 0.0073) and inversely with patient age (p = 0.0263; Table 4). The risk of obtaining a nondiagnostic biopsy increased by a factor of 1.37 (95% CI 1.09–1.71) with each additional biopsy sample collected and decreased by a factor of 0.8 (95% CI 0.65–0.97) with every additional 10 years of patient age.

**Discussion**

Numerous studies have been published in which postoperative imaging was performed to evaluate the incidence of intracranial hemorrhage after a stereotactic procedure.1,2,7,9,11,12,14,17,20,25 Hemorrhage rates for the major published series of stereotactic brain biopsies are listed in Table 6. However, most series included nonbiopsy stereotactic procedures, such as stereotactic ventricular catheter placements or cyst or abscess aspirations. In each series, the timing of postbiopsy CT imaging was variable, not clearly stated, or inconsistently performed. These variations result in a wide range of calculated hemorrhage rates after stereotactic brain biopsy. In some series the researchers only obtained postbiopsy CT scans in patients with symptoms or in those in whom there was a high clinical suspicion of hemorrhage. Despite these inconsistencies, the authors of most series estimated a hemorrhage rate of 1 to 7%.10 In a recent series by Kulkarni and colleagues,11 102 consecutive patients underwent postbiopsy CT scanning. Sixty-one patients (59.8%) were found to have evidence of hemorrhage and six (5.9%) had no symptoms. When postbiopsy CT scanning had failed to detect a hemorrhage, no patient experienced a delayed neurological deficit. The authors concluded that, although the incidence of hemorrhage following a stereotactic biopsy is common, asymptomatic patients in whom there is no evidence of hemorrhage on postbiopsy CT scans can safely be discharged home on the day of their procedure.

In our prospective series, all postbiopsy CT scans were obtained within 15 minutes after the biopsy specimen had been obtained by using a dedicated intraoperative CT scanner. These scans were obtained while the stereotactic frame was still on the patient’s head. The postbiopsy CT scans were obtained at levels identical to those of the prebiopsy images to allow for an accurate comparison. All images were subsequently reviewed to distinguish areas of acute hemorrhage from areas of residual extravasation of contrast agent. All patients in our study remained in the hospital overnight. Any patient in whom a delayed neurological deficit developed during the observation period underwent emergency repeated CT scanning to evaluate the possibility of a delayed ICH. Unlike in the series conducted by Kulkarni and colleagues,11 in our series there were two patients (0.4%) who experienced delayed neurological deficits after an uncomplicated brain biopsy and a postbiopsy CT scan that failed to suggest acute hemorrhage. One patient became progressively lethargic as a result of a large occipitotemporal hemorrhage with intraventricular rupture (Fig. 1). She underwent emergency evacuation of the hemorrhage, but failed to improve and eventually died only days after biopsy. The second patient experienced a left hemiparesis and neglect syndrome 24 hours after discharge. Repeated CT scanning demonstrated a right frontotemporal intraparenchymal hematoma. This patient was treated conservatively at his local hospital and achieved partial recovery of motor function. Both patients harbored glioblastomas multiforme, and although such tumors have a propensity for spontaneous hemorrhage, the temporal relationship between the ICH and the diagnostic

![Fig. 2. Graph demonstrating platelet count plotted against the risk of any hemorrhage.](image-url)

**Table 4**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Any Detectable Hemorrhage (40 patients)</th>
<th>Hemorrhage ≥5 mm in Diameter (26 patients)</th>
<th>Nondiagnostic Findings (30 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>0.1819</td>
<td>0.1386</td>
<td>0.0263†</td>
</tr>
<tr>
<td>sex</td>
<td>0.7602</td>
<td>0.4780</td>
<td>0.4679</td>
</tr>
<tr>
<td>history of hypertension</td>
<td>0.6381</td>
<td>0.3259</td>
<td>0.7590</td>
</tr>
<tr>
<td>platelet count &lt; 150,000/mm³</td>
<td>0.0060†</td>
<td>0.0208†</td>
<td>0.9092</td>
</tr>
<tr>
<td>prothrombin time</td>
<td>0.8926</td>
<td>0.5473</td>
<td>0.7267</td>
</tr>
<tr>
<td>partial thromboplastin time</td>
<td>0.7526</td>
<td>0.8844</td>
<td>0.7715</td>
</tr>
<tr>
<td>anticoagulation or antiplatelet medications</td>
<td>0.8092</td>
<td>0.7909</td>
<td>0.5962</td>
</tr>
<tr>
<td>aspirin use w/in 1 wk of biopsy</td>
<td>0.9484</td>
<td>0.5227</td>
<td>0.9465</td>
</tr>
<tr>
<td>Coumadin use</td>
<td>0.4141</td>
<td>0.5436</td>
<td>0.4034</td>
</tr>
<tr>
<td>lesion location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>brainstem</td>
<td>0.5202</td>
<td>0.8294</td>
<td>0.2888</td>
</tr>
<tr>
<td>pineal</td>
<td>0.0607</td>
<td>0.0086†</td>
<td>0.5887</td>
</tr>
<tr>
<td>periventricular</td>
<td>0.7303</td>
<td>0.2325</td>
<td>0.7037</td>
</tr>
<tr>
<td>no. of specimens collected</td>
<td>0.5302</td>
<td>0.4426</td>
<td>0.0073†</td>
</tr>
</tbody>
</table>

* Comparison between platelet count below 150,000/mm³ (value 150) and platelet count of 150,000/mm³ (value 0) or higher.
† Statistically significant (p < 0.05).
Assessment of outcomes after stereotactic brain biopsy

stereotactic brain biopsy in these cases makes the likelihood of such an occurrence improbable. Although the risk is low, on the basis of these two cases, we believe that nondiagnostic findings on a CT scan obtained immediately after stereotactic brain biopsy are insufficient to justify discharging a patient on the day of the procedure.

Factors Associated With an Increased Hemorrhage Risk and Nondiagnostic Biopsy Findings

In this study, we evaluated several factors that potentially increase the risk of hemorrhage after stereotactic brain biopsy. Specifically, we analyzed the following: 1) use of anticoagulation or antiplatelet agents; 2) presence or absence of preoperative or intraoperative hypertension; 3) number of biopsy specimens collected; 4) patient age; 5) patient sex; and 6) location of the lesion, especially the relationship between the lesion and pial, ependymal, or vascular structures.

Coagulation and Platelet Effects. Although authors of most reports recommend that patients have a platelet count higher than 100,000/mm³ at the time of stereotactic biopsy, in no study has a statistical relationship between the risk of hemorrhage and platelet count been shown. Using multivariate logistic regression analysis, we found a significant risk for hemorrhage after stereotactic biopsy in patients with a platelet count less than 150,000/mm³. The risk of a hemorrhage greater than 5 mm in diameter statistically correlated with a platelet count of less than 150,000/mm³ (Fig. 2). These observations support the need for normal platelet volume and, presumably, function before a stereotactic biopsy. Normal platelet count should be restored in patients before a biopsy is performed.

No statistical correlation was found between prothrombin or partial thromboplastin time and the risk of hemorrhage. However, we generally took steps to correct potential coagulation abnormalities before surgery. All patients were asked to discontinue their use of antplatelet drugs 5 to 7 days before biopsy, and subcutaneous heparin administration was withheld 24 to 48 hours before the procedure. As a result, we performed stereotactic biopsies on very few patients with abnormal coagulation profiles. Surprisingly, although a platelet count less than 150,000/mm³ increased the risk of hemorrhage from a stereotactic biopsy, oral ingestion of aspirin within 1 week of surgery did not increase the risk of hemorrhage.

Effect of Hypertension. In our series, 105 patients (21%) exhibited either intraoperative hypertension (systolic blood pressure > 150 mm Hg) or a history of chronic hypertension at the time of biopsy. Perioperatively, all patients were treated for systolic blood pressure that was greater than 150 mm Hg with oral or intravenous antihypertension medications. Postbiopsy CT scanning revealed acute hemorrhages in nine (8.57%) of the patients with hypertension, but only one of these patients had a hemorrhage larger than 10 mm in diameter. No patient with a tendency to experience hypertension required surgical clot removal. Although we detected no statistically significant increased risk for hemorrhage in this population (p = 0.6381), we aggressively managed perioperative blood pressure to keep the systolic level at 150 mm Hg or lower during hospitalization because authors of previous studies have shown a correlation between perioperative hypertension and intracranial hemorrhage after brain surgery.

Relationship of Hemorrhage to Number of Collected Biopsy Specimens. The number of biopsies per patient in our series ranged from one to more than five (Table 7). The literature contains various recommendations concerning the number of biopsies that are safe and necessary when trying to obtain adequate diagnostic tissue. Kelly recommended judicious lesion sampling during stereotactic biopsy in an attempt to maximize diagnostic yield and accuracy. Kondziolka, et al., warned that increasing the number of biopsy specimens collected may increase the risk for hemorrhage and is unlikely to increase the likelihood of preventing a nondiagnostic or misdiagnostic biopsy significantly, if the target is selected carefully. We found no statistically increased risk for hemorrhage with increased biopsy number. Interestingly, we found an inverse relationship between the number of samples taken and the diagnostic yield: as the number of samples increased, the number of diagnoses made decreased. This finding seemed surprising at first, but actually reflected the nature of our stereotactic biopsy protocol.

At our center, axial stereotactic images of 3- to 5-mm slice thickness are preferred to visualize the target and surrounding brain structures. If the target demonstrates contrast enhancement, we obtain specimens from the area of...
In our experience, the risk of hemorrhage following biopsy of a tumor located in the pineal region can be reduced by ensuring that only small samples within the tumor mass are obtained and that the trajectory moves through the low frontal region, inferior to the internal cerebral vein. Pineocytomas and pineoblastomas are very vascular, which may contribute to the risk of hemorrhage in this region. However, these lesions were not independently evaluated based on their pathological characteristics and risk for hemorrhage in our series. As a result, to minimize the risk of intraventricular hemorrhage, one should not perform a biopsy of the capsule, which abuts the third ventricle.

Conclusions

Stereotactic brain biopsy at our center was associated with a low likelihood of postbiopsy hemorrhage-related neurological deficit. The risk of hemorrhage increased significantly in patients in whom the platelet count was less than 150,000/mm³ and in patients harboring a lesion located in the pineal region. Normalization of coagulation rates and blood pressure control are methods to reduce complications. Although the increased number of biopsy samples did not increase the risk of hemorrhage, the diagnostic yield was not enhanced by more specimens. The small but significant risk of hemorrhage occurring more than 12 hours after biopsy warrants an initial in-hospital period of observation for all patients undergoing stereotactic biopsy.

TABLE 7
Number of specimens obtained after stereotactic brain biopsy in 500 patients

<table>
<thead>
<tr>
<th>No. of Specimens</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28</td>
<td>5.6</td>
</tr>
<tr>
<td>2</td>
<td>130</td>
<td>26.0</td>
</tr>
<tr>
<td>3</td>
<td>187</td>
<td>37.4</td>
</tr>
<tr>
<td>4</td>
<td>88</td>
<td>17.6</td>
</tr>
<tr>
<td>≥5</td>
<td>67</td>
<td>13.4</td>
</tr>
</tbody>
</table>

and emesis developed in two patients and mild photophobia in one patient. No patient required cerebrospinal fluid diversion as a result of the hemorrhage and none experienced signs or symptoms that were indicative of a major venous injury to the great vessels of the pineal region.

References

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