

Complications in 622 Cases of Frame-Based Stereotactic Biopsy, a Decreasing Procedure

Paul N. Kongkham, Eva Knifed, Mandeep S. Tamber, Mark Bernstein

ABSTRACT: Background: Frame-based stereotactic brain biopsy has played an important role in the management of patients with suspected neoplastic intracranial lesions over the last three decades. We reviewed the surgical experience of one surgeon to determine the nature and frequency of complications associated with this procedure. **Methods:** Records were reviewed for 858 patients undergoing frame-based stereotactic procedures from January 1986 to May 2006. Data on each case were prospectively collected by the senior author. Procedures for Ommaya reservoir placement, brachytherapy, stereotactic craniotomy flap localization, shunt placement, or treatment of previously-diagnosed intracranial cystic lesions were excluded, leaving 614 patients in whom a total of 622 procedures were performed for purely diagnostic purposes. Complication rates and their association with clinical variables were sought. **Results:** Morbidity and mortality rates were 6.9% (43/622) and 1.3% (8/622), respectively. The risk of symptomatic hemorrhage (intracerebral hemorrhage [ICH], subarachnoid hemorrhage [SAH], intraventricular hemorrhage [IVH]) was 4.8%. The risks of transient or permanent neurological deficits were 2.9% (18/622) and 1.5% (9/622), respectively. Biopsy of deep-seated lesions was associated with increased overall complication rate, while biopsy of Glioblastoma Multiforme (GBM) was associated with perioperative mortality. **Conclusions:** Overall, complication rates were comparable with those in previous reports. The subgroup of patients with deep-seated lesions or a histologic diagnosis of GBM may possess an elevated risk of overall complications or mortality, respectively, compared to other patients undergoing frame-based stereotactic brain biopsy.

RÉSUMÉ: Complications observées chez 622 patients qui ont subi une biopsie avec cadre stéréotaxique, une intervention de moins en moins pratiquée. Contexte : Au cours des trente dernières années, la biopsie du cerveau avec cadre stéréotaxique a joué un rôle important dans l'évaluation des patients chez qui on soupçonnait la présence de lésions néoplasiques intracrâniennes. Nous avons revu l'expérience d'un chirurgien afin de déterminer la nature et la fréquence des complications associées à cette intervention. **Méthodes :** Les dossiers de 858 patients ayant subi cette intervention entre janvier 1986 et mai 2006 ont été révisés. Les données concernant chaque patient ont été recueillies de façon prospective par l'auteur principal. Les dossiers de patients qui avaient subi une intervention pour mettre en place un réservoir d'Ommaya, une brachythérapie, la localisation stéréotaxique d'un volet osseux, la mise en place d'une dérivation ou le traitement de lésions kystiques intracrâniennes dont le diagnostic était déjà posé ont été exclus. Il restait donc 614 dossiers de patients qui avaient subi au total 622 interventions à des fins diagnostiques. Nous avons déterminé le taux de complications et leur association à des variables cliniques. **Résultats :** Les taux de morbidité et de mortalité étaient respectivement de 6,9% (43/622) et 1,3% (8/622). Le risque d'hémorragie symptomatique (HIC, HSA, HIV) était de 4,8%. Le risque de déficits neurologiques transitoires ou permanents était respectivement de 2,9% (18/622) et 1,5% (9/622). La biopsie de lésions profondes était associée à un taux de complications plus élevé alors que la biopsie de glioblastomes multiformes (GBM) était associée à la mortalité périopératoire. **Conclusions :** En général, les taux de complications étaient comparables à ceux rapportés antérieurement. Le sous-groupe de patients ayant des lésions profondes présenterait un risque accru de complications et le sous-groupe chez qui un diagnostic histologique de GBM a été posé aurait un risque accru de mortalité par rapport aux autres patients qui subissent une biopsie cérébrale stéréotaxique avec cadre.

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Frame-based image-guided stereotactic biopsy for intracranial mass lesions has served as a vital tool in the neurosurgical armamentarium over the last three decades. The rationale for its use has relied on the importance of obtaining a histologic tissue diagnosis for intrinsic brain lesions, in order to help guide further rational therapy. Due to the perceived low risk of the procedure, as well as the ability it provided to access almost any point in the intracranial space, this biopsy technique rapidly acquired many indications, including obtaining tissue from lesions that were small, deeply-located, diffusely infiltrating, multifocal, located

in or adjacent to eloquent cortex, or from patients unable to tolerate open resection. Despite many advances in anatomic, functional and physiologic imaging modalities, accurate non-

From the Division of Neurosurgery, University of Toronto, Toronto, ON, Canada.

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Reprint requests to: Mark Bernstein, Toronto Western Hospital, 4W415 399 Bathurst Street, Toronto, Ontario, M5T 2S8, Canada

invasive diagnosis is not yet feasible based on imaging studies alone, and as such needle biopsy for intracranial lesions remains a vital tool for the practicing neurosurgeon. In recent years, however, frameless stereotaxy has largely supplanted frame-based systems. It has been estimated that approximately 80% of biopsy cases previously performed using frame-based techniques may be done with equivalent safety and accuracy using frameless stereotaxy.¹ As a result, frame-based biopsy has become increasingly reserved for cases involving lesions located in perceived high-risk areas, such as the brainstem or pineal region. It is unlikely that future generations of neurosurgeons will amass an extensive experience using frame-based biopsy techniques. In fact, the senior author (MB) has personally converted completely to frameless guidance for biopsies and therefore no longer teaches this frame-based technique to residents. Therefore, we felt it timely to summarize the experience using this technique in 622 cases over the last two decades. This paper focuses on highlighting the complications encountered using frame-based stereotactic biopsy in a large single-surgeon series. Moreover, we identify risk factors associated with biopsy-related morbidity and mortality, and compare these with risk factors previously reported in the literature.

MATERIALS AND METHODS

Patient population

Data regarding patient clinical variables and perioperative morbidity and mortality for patients undergoing all frame-based stereotactic biopsy procedures were prospectively collected and maintained in a database. Data were collected immediately as they became available (i.e.: surgical details, complications, pathology) by the senior author and subsequently entered into a computer database (Microsoft Access). This database, along with the medical records for 858 consecutive patients who underwent frame-based stereotactic surgery at the Toronto Western Hospital (University Health Network, University of Toronto) during the period from January 1986 to May 2006 by the senior author were reviewed. Patients undergoing procedures for Ommaya reservoir placement, brachytherapy, stereotactic craniotomy flap localization, shunt placement, or treatment of previously-diagnosed intracranial cystic lesions were excluded from the analysis, leaving 614 individual patients in whom a total of 622 procedures were performed for purely diagnostic purposes. Overall complication, neurologic deficit, hemorrhage, and mortality rates were determined. Clinical variables assessed included patient age, lesion size, location, and histology. The various pathologies biopsied in this series of cases are summarized in Table 1.

Surgical technique

On the morning of surgery, patients underwent pre-operative contrast-enhanced computed tomography (CT) scanning of the brain, following the placement of the stereotactic frame base ring and localizer under local anesthetic. Either the Brown-Roberts-Wells or Cosman-Roberts-Wells frame systems (Radionics, Burlington MA) were used. Biopsy trajectories were planned which avoided transgression of multiple ependymal/pial surfaces, eloquent cortex, and minimized the distance from entry point to the target. Target localization and trajectory planning

Table 1: Summary of pathologic diagnoses for biopsied lesions

Lesion Category	Lesion Subtype	Number	Percentage
Neoplastic		528	84.89
Glial		379	60.93
	Pilocytic Astrocytoma	4	0.64
	LGG	88	14.15
	Anaplastic Astrocytoma	71	11.41
	Anaplastic Oligodendroglioma	9	1.45
	Anaplastic Oligoastrocytoma	3	0.48
	GBM	201	32.32
	Astroblastoma	1	0.16
	Gliosarcoma	1	0.16
	Choroid Plexus Papilloma	1	0.16
Neuronal		5	0.80
	Ganglioglioma	2	0.32
	Medulloblastoma	2	0.32
	sPNET	1	0.16
Pineal Region		7	1.13
	Pineocytoma	4	0.64
	Germ Cell Tumor	3	0.48
Secondary		76	12.22
	Metastasis	75	12.06
	LMC	1	0.16
Miscellaneous		61	9.81
	PCNSL	54	8.68
	Meningioma	1	0.16
	Atypical Meningioma	1	0.16
	Craniopharyngioma	4	0.64
	Ependymoma	1	0.16
Non-Neoplastic		83	13.34
Infectious		46	7.40
	Pyogenic Abscess	24	3.86
	Tuberculoma	2	0.32
	Fungal	4	0.64
	Viral (including PML)	10	1.61
	Toxoplasmosis	5	0.80
	Cysticercosis	1	0.16
Miscellaneous		37	5.95
	Inflammatory lesion NS	11	1.77
	Sarcoidosis	1	0.16
	Demyelination	3	0.48
	Infarct	4	0.64
	Necrosis	6	0.96
	Hematoma	7	1.13
	Thrombosed AVM	1	0.16
	Glial Cyst	1	0.16
	Gliosis	1	0.16
	Reactive Astrocytosis	2	0.32
Non-Diagnostic		10	1.61

NS = not specified, GBM = glioblastoma multiforme, PCNSL = primary CNS lymphoma, AVM = arteriovenous malformation, LGG = low-grade glioma, sPNET = supratentorial primitive neuroectodermal tumor, PML = progressive multifocal leukoencephalopathy, LMC = leptomeningeal carcinomatosis

were verified on a phantom base unit in the operating room. Stereotactic biopsy was performed by the senior author under light neurolept anesthesia. The cranium was penetrated using a twist drill, and the biopsy performed using a side-cutting Sedan needle. Typically, only a single biopsy core was obtained, unless

this was deemed non-diagnostic upon quick-section analysis by an experienced neuropathologist. Following the completion of the procedure, patients were observed for several hours in the post-anesthetic care unit. Since late 1996, the majority of cases were performed on an out-patient basis, with patients discharged home after additional observation in the day-surgery unit and re-examination by the neurosurgeon before discharge.² Post-biopsy CT scanning was done routinely, for the purposes of confirming the accuracy of biopsy targeting (i.e.: biopsy site hemorrhage or air) as well as excluding a potentially clinically important hemorrhage. Final histopathologic diagnosis was performed by an experienced neuropathologist according to the World Health Organization (WHO) criteria.³

Statistical analysis

Logistic regression analysis was used to explore the univariate associations between certain patient (age) and lesion-related (location, maximal lesion diameter, and histopathologic subtype) characteristics and the occurrence of perioperative complications, namely the risk of any complication (overall morbidity and mortality), hemorrhage and death. Patient age and lesion diameter were analyzed as continuous variables, while lesion location (deep versus lobar/cortical) and histopathologic subtype were assessed as categorical variables. Due to the limited absolute numbers of complication events, multivariate logistic regression analysis was not feasible. When assessing hemorrhagic complications, only clinically symptomatic hemorrhage was deemed significant, excluding punctate, biopsy-site hemorrhage seen only on routine post-operative imaging.⁴ A Bonferroni correction was employed, using a nominal p-value of 0.05, and adjusting for multiple comparison analysis in order to minimize the risk of discovering false associations.

RESULTS

Complications

Complications observed in this series of 622 frame-based stereotactic biopsy procedures are summarized in Table 2. Overall morbidity and mortality rates were 6.9% (43/622) and 1.3% (8/622), respectively. The risk of symptomatic intracranial hemorrhage was 4.8% (30/622). Specifically, the incidence of intracerebral hemorrhages (ICH) was 3.4% (21/622), while subarachnoid hemorrhage (SAH) and intraventricular hemorrhage (IVH) occurred in 1.0% (6/622) and 1.0% (6/622), respectively. One patient suffered an ischemic event (0.16%). In total, neurologic deficits were incurred in 4.3% (27/622) of cases. The risks of transient or permanent neurological deficits were 2.9% (18/622) and 1.5% (9/622), respectively. Of the transient neurologic deficits, 27.8% (5/18) occurred without evidence of intracranial hemorrhage, while 72.2% (13/18) were associated with hemorrhage. Transient deficits incurred without evidence of hemorrhage were thought to be due to post-biopsy edema. Permanent neurologic deficits were associated with intracranial hemorrhage in 88.9% (8/9) of cases. Additional morbidity observed in our series included postoperative seizures (0.5%, 3/622), and non-diagnostic biopsy (1.6%, 10/622).

Association between complications and clinical variables

Among the various clinical variables available, we examined patient age, lesion location, lesion size (maximal cross-sectional

Table 2: Summary of observed complications

Complication	Number of Patients	Percentage
Perioperative Mortality	8	1.3
Overall Morbidity	43	6.9
Symptomatic Intracranial Hemorrhage	30	4.8
- ICH	21	3.4
- SAH	6	1.0
- IVH	6	1.0
Infarction	1	0.2
Neurologic Deficit	27	4.3
- Transient (total)	18	2.9
- with hemorrhage	13	2.1
- without hemorrhage	5	0.8
- Permanent (total)	9	1.4
- with hemorrhage	8	1.3
- without hemorrhage	1	0.2
Seizures	3	0.5
Non-diagnostic Biopsy	10	1.6

ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage, IVH = intraventricular hemorrhage

diameter), and histopathologic subtype (based on final pathologic diagnosis) for their possible association with risk for any complication (combined morbidities and mortality), intracranial hemorrhage, or death. No significant univariate associations between increasing patient age and overall complication rate (Odds Ratio [OR] 0.98, 95% confidence interval [CI] 0.97, 1.00), hemorrhage risk (OR 0.99, 95% CI 0.97, 1.01) or death (OR 0.99, 95% CI 0.96, 1.03) were observed. Similarly, increasing lesion size did not correlate with either overall complication rate (OR 1.01, 95% CI 0.84, 1.21) or hemorrhagic complication rate (OR 1.05, 95% CI 0.83, 1.33). Lesion size was associated with risk of perioperative mortality on univariate analysis (OR 1.60, 95% CI 1.04, 2.45). Biopsy of a deep lesion location showed a significant association with overall complication rate in comparison with lobar/cortical lesions (OR 1.82, 95% CI 1.01, 3.25), but not specifically with hemorrhage rate (OR 2.03, 95% CI 0.96, 4.32), or death (OR 1.81, 95% CI 0.42, 7.66). Regarding lesion histopathology, a final diagnosis of GBM was significantly associated with risk of perioperative mortality. On univariate analysis by logistic regression, the odds of perioperative mortality following biopsy for GBM was 15.04 compared to non-GBM pathology (95% CI 1.84, 123.10). In addition, if one considers only those cases where complications occurred, the odds of the complication proving fatal if the lesion biopsied was GBM compared to other pathology was 36.00 (95% CI 3.81, 340.30).

DISCUSSION

Frame-based stereotactic biopsy-related morbidity and mortality

Frame-based stereotactic biopsy is a well-established surgical technique providing the neurosurgeon with the ability to accurately access almost any region of the intracranial space, and

the capability to obtain tissue for histologic diagnosis on newly discovered intracranial mass lesions. It has generally been regarded as a safe procedure, with minimal associated morbidity and mortality as compared to other cranial surgical procedures. Numerous authors have previously published on their experience using this procedure, and their observed complication rates. Table 3 summarizes the overall morbidity and mortality rates for series reporting on at least 100 cases, published over the last two and a half decades.⁵⁻³⁷ Reported overall morbidity rates for frame-based stereotactic diagnostic brain biopsy ranges between 0.4-17.2%, with the average being approximately 4.9%.⁵⁻³⁷ Published mortality rates range from 0-3.3%.⁵⁻³⁷ The overall morbidity rate (6.9%) and mortality rate (1.3%) observed in our series is in keeping with those previously published. The overall risk of symptomatic intracranial hemorrhage in our series was 4.8%. Intracranial hemorrhage rates from 0-9% have been reported in the literature.^{4-7,9,11,12,14,15,17,19-23,26,28,30-32,34,35,37} Our center has previously identified overall post-biopsy hemorrhage rates as high as 59.8%, based on post-operative CT imaging.⁴ When asymptomatic hemorrhage was excluded, however, the symptomatic hemorrhage rate was 8.8%.⁴

Table 3: Summary of published overall morbidity and mortality rates for stereotactic brain biopsy procedures. Only series with at least 100 cases are included

Author	Year	Cases	Morbidity (%)	Mortality (%)
Ostertag et al	1980	302	3.3	2.3
Edner	1981	345	2.9	0.9
Lobato et al	1982	109	0.9	0.0
Lunsford et al	1984	102	5.9	0.0
Sedan et al	1984	318	4.7	0.6
Munding	1985	815	3.0	0.6
Apuzzo et al	1987	500	1.0	0.2
Davis et al	1987	439	0.4	0.2
Blaauw et al	1988	243	4.1	0.4
Niizuma et al	1988	121	6.6	0.0
Kelly	1989	226	9.3	0.4
Thomas et al	1989	300	4.7	0.3
Wild et al	1990	200	6.0	1.0
Kelly	1991	547	2.9	0.3
O'Neill et al	1992	259	6.5	3.3
Voges et al	1993	338	1.2	0.6
Bernstein et al	1994	300	4.7	1.7
Grunert et al	1994	200	3.0	1.0
Regis et al	1996	370	7.3	1.3
Nicolato et al	1997	200	17.2	2.4
Hall	1998	134	0.7	0.7
Kulkarni et al	1998	102	12.7	2.0
Lunsford	1998	240	4.6	0.0
Sawin et al	1998	225	4.9	0.4
Yu et al	2000	550	7.8	0.0
Field et al	2001	500	9.6	0.2
Kreth et al	2001	345	3.1	0.0
Ulm et al	2001	200	2.5	0.0
Kim et al	2003	300	3.9	0.6
Grossman et al	2005	355	NS	0.6
Heper et al	2005	130	0.7	0.0
McGirt et al	2005	270	13.0	1.0
Smith et al	2005	139	5.0	0.0
Ferreira et al	2006	170	2.9	1.2
Kongkham et al	2007	622	6.9	1.3
Mean Values Based on Available Literature:			4.9	0.7

NS = not specified.

Risk factors associated with operative morbidity and mortality

Despite the numerous publications reporting complication rates associated with stereotactic brain biopsy, relatively few have systematically tried to identify clinical or radiological variables associated with increased risk.^{11,12,18,19,23,30} Variables that have been assessed for a possible association with increased risk of operative complications include patient factors such as age, sex, Karnofsky score, pre-biopsy radiation therapy and comorbid disease (such as hypertension, diabetes mellitus, or extracranial malignancy).^{11,12,18,19,23,30} Chronic steroid use, preoperative antiplatelet use, and thrombocytopenia have also been examined for their association with adverse outcomes.^{11,19,30} Procedure-related variables examined have included the number of biopsy specimens obtained and the biopsy instrument used.^{11,12,18,19,23,30} Lesion characteristics investigated include lesion histology, location, size, and associated mass effect or edema seen on imaging studies.^{11,12,18,19,23,30}

Among the patient-related variables mentioned above, no significant association between patient sex, Karnofsky score, hypertension, extra-cranial malignancy or prior radiation therapy and adverse outcome has thus far been demonstrated.^{11,12,18,19,23,30} Conflicting evidence exists for the association between diabetes mellitus (DM) and increased complications. Sawin et al, specifically reviewed their experience with 225 cases in an attempt to identify factors that conferred increased risk with frame-based stereotactic biopsy, and found no association between co-morbid DM and increased risk.³⁰ Conversely, McGirt et al recently reported that the odds ratio for having an adverse event if the patient was diabetic was 3.73 compared to non-diabetics (95% CI 1.37,10.17), based on their review of 270 frame-based and frameless stereotactic biopsies.²³ In their study, Sawin et al did identify pre-operative chronic corticosteroid use (>3 months duration) as well as perioperative use of antiplatelet agents as being significantly associated with increased biopsy risk ($p < 0.05$).³⁰ Specifically, they reported a 35-fold increased operative risk associated with antiplatelet agent use.

In their study of 500 consecutive patients undergoing frame-based stereotactic biopsy, Field et al recently identified thrombocytopenia as a risk factor, with biopsy risk increasing as platelet counts decreased below 150,000/mm³ based on multivariate analysis ($p = 0.006$).¹¹ Interestingly, use of antiplatelet agents was not associated with increased biopsy risk in this study.¹¹ Of these patient-related risk factors, only patient age was examined for its association with adverse events in our study. Based on univariate logistic regression analysis, age was not found to be significantly associated with overall complication rate, hemorrhage rate, or mortality in our study. In their study of 308 cases in 300 patients, Kim et al found advanced patient age to be associated with increased risk of complications following stereotactic biopsy, based on univariate analysis alone. Age did not remain significant with multivariate analysis, however.¹⁸

Procedural factors such as the number of biopsy specimens taken, and the instrumentation employed, were not examined directly in our study. In our study, however, all patients were subject to a standardized technical approach, in which one surgeon either performed the procedure himself or directly supervised residents doing the procedure. This partially

eliminated inter-operator variability as a factor and minimized the effect of surgeon, technique, and criteria for patient selection on the random error term in the logistic model. In addition, all biopsies were obtained using the same needle instrument (side-cutting Sedan type instrument). Finally, patients in this series in general were biopsied using typically one pass of the biopsy needle. Reports in the literature provide equivocal evidence for the role of increasing biopsy specimens and complication risk. Sawin et al. observed that the subgroup of patients that suffered morbidity following biopsy had a higher mean number of biopsy attempts (mean = 22), compared to the subgroup of patients without operative morbidity (mean = 11).³⁰ Of note, the number of biopsy attempts in both groups is significantly greater than the standard of practice at our institute. McGirt et al found an association between increased biopsy attempts and neurologic deficit, but only in the subgroup of patients with deep-seated (basal ganglia or thalamic) lesions.²³ Others have found no relationship between the number of biopsy attempts, or the instrument used, and adverse events.^{11,12,18,19}

Lesion-related characteristics specifically examined in our study included lesion size (maximal cross-sectional diameter), lesion location (cortical/lobar versus deep), and final histopathology. Lesion size did not show any significant association with either overall complication rate or hemorrhage risk. Increased lesion size was associated with perioperative mortality based on univariate logistic regression analysis (OR 1.6, 95% CI 1.04, 2.45). Due to insufficient numbers, we were not able to confirm whether lesion size remained significantly associated with mortality on multivariate analysis. In their recent report, McGirt et al found no association between the size of the lesion biopsied and adverse outcomes.²³

Lesion location has been suspected to be important in conferring differential risk with stereotactic biopsy. Sawin et al reported that biopsy of deep lesions (basal ganglia or thalamic lesions) was associated with increased complication risk.³⁰ Similar findings have been reported by McGirt et al.²³ In their study, biopsy of thalamic lesions (OR 4.06, 95% CI 1.63, 10.11) and basal ganglia lesions (OR 3.29 95% CI 1.05, 10.25) were associated with increased operative risk. Kim et al also found biopsy of deep-seated lesions to be associated with increased risk, on univariate and multivariate analysis.¹⁸ In a retrospective review of 355 cases, Grossman et al reported increased complication rates for biopsies involving brainstem lesions.¹² Field et al reported an increased risk of hemorrhage for biopsies in the pineal region.¹¹ Their series only included 19 cases of pineal region pathology, however, and other authors have shown pineal region biopsies to carry no greater risk than biopsies elsewhere within the cranium.²⁹ In our series of cases, the biopsy of a deep-seated lesion was associated with a slightly increased risk of incurring any complication (OR 1.82, 95% CI 1.02, 3.25). The specific risks of hemorrhage or death were not significantly associated with the biopsy of a deep lesion, however.

Over a decade ago the senior author (MB) published a review on his series of 300 patients who underwent frame-based stereotactic biopsies for intracranial lesions, specifically reporting the associated morbidity and mortality of this procedure.⁶ At that time, it was suggested that biopsy of specific pathologies (eg: GBM, lymphoma) may be associated with an increased risk of either hemorrhage or severe edema, due to the

abnormal neovasculature of these tumors.⁶ Since that time, several other investigators have examined the role specific lesion pathology plays in conferring increased operative risk, generating conflicting data. Sawin et al identified malignant glioma pathology (anaplastic astrocytoma or GBM) to be associated with a 4-fold increased risk of morbidity, particularly from hemorrhage.³⁰ Of the nine patients who suffered from intracranial hemorrhage, six had a diagnosis of malignant glioma. Kim et al also found malignant glioma pathology to be significantly associated with morbidity, following both univariate and multivariate analysis.¹⁸

Two studies have identified high-grade glioma pathology to be associated significantly with increased risk of silent hemorrhage, but not with symptomatic bleeding.^{19,23} In contrast to these studies, Grossman et al found no association between lesion pathology and complication rates.¹² This conflicting data may be a reflection of the fact that, overall, complication rates for frame-based stereotactic brain biopsy are low. Existing series may lack sufficient numbers of cases to consistently demonstrate an association between a specific pathology and complication rates. In our current study of 622 cases, we found no association between lesion pathology and either overall complication rate or hemorrhage risk. We did, however, identify an association between biopsy of GBM pathology and mortality, on univariate analysis. Patients harboring a GBM were found to have an odds ratio of 15.04 (95% CI 1.84, 123.10) for perioperative mortality following biopsy, compared to patients with non-GBM pathology. This association between GBM pathology and mortality may be more plausible, compared to that between lesion size and mortality, due to the associated abnormal tumor neovasculature and theoretically increased risk of post-biopsy hemorrhage or malignant cerebral edema.

As complication rates for this procedure are typically low, an interesting statistic to consider may be the risk of a complication proving to be fatal, once it has occurred. In the subgroup of patients who suffered from any post-operative morbidity, the odds of the complication being fatal were 36.0 for patients with GBM versus non-GBM patients (95% CI 3.81, 340.30). We, and others, have reported on the tendency for the biopsy of high-grade gliomas to produce asymptomatic hemorrhage.^{4,19,23} Post-biopsy intracranial hemorrhage accounted for the majority of perioperative mortalities in our study. Uncontrollable cerebral edema following biopsy also contributed to mortality in our series.

CONCLUSIONS

In conclusion, we have examined the complications observed in the treatment of 614 patients undergoing a total of 622 frame-based stereotactic diagnostic brain biopsies. The biopsy of deep-seated lesions was found to be associated with a slight increase in overall complication risk. This report is the first to identify specific risk factors (increased lesion size and GBM pathology) to be associated with mortality following frame-based stereotactic brain biopsy. Due to the small number of mortality events, however, the confidence intervals on the point estimates of the OR for the association between lesion size or GBM pathology and mortality are relatively wide, making it difficult to estimate the degree of increased risk conferred by these two variables. Although this association has been suggested for

frame-based procedures, we suspect that the same association will be true for any intracranial biopsy procedure, as this risk factor is inherent in the type lesion biopsied as opposed to the technique employed. This is important, as stereotactic biopsy (frame-based or frameless) of intracranial mass lesions is a technique that will likely continue to play an important role in diagnosis and management of this patient population. When the lesion to be biopsied is suspected to be GBM, knowledge of this potential increased mortality risk will assist the neurosurgeon to appropriately counsel the patient and their family regarding procedural risks. Irrespective of the suspected pathology, stereotactic biopsy can occasionally produce devastating complications, of which both the operator and the patient must be mindful. These complications will continue to be seen with frameless stereotactic biopsies (i.e. those done with surgical navigation systems guiding the biopsy instrument) as these procedures replace frame-based procedures.

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