Limitations of stereotactic biopsy in the initial management of gliomas[1,2]

Robert J. Jackson, Gregory N. Fuller, Dima Abi-Said, Frederick F. Lang, Ziya L. Gokaslan, Wei Ming Shi, David M. Wildrick, and Raymond Sawaya[3]

Departments of Neurosurgery (R.J.J., D.A.-S., F.F.L, Z.L.G., W.M.S., D.M.W., R.S.) and Pathology (G.N.F.), The University of Texas M. D. Anderson Cancer Center, Houston, TX 77030

Stereotactic biopsy is often performed for diagnostic purposes before treating patients whose imaging studies highly suggest glioma. Indications cited for biopsy include diagnosis and/or the "inoperability" of the tumor. This study questions the routine use of stereotactic biopsy in the initial management of gliomas. At The University of Texas M. D. Anderson Cancer Center, we retrospectively reviewed a consecutive series of 81 patients whose imaging studies suggested glioma and who underwent stereotactic biopsy followed by craniotomy/resection (within 60 days) between 1993 and 1998. All relevant clinical and imaging information was reviewed, including computerized volumetric analysis of the tumors based on pre- and postoperative MRI. Stereotactic biopsy was performed at institutions other than M. D. Anderson in 78 (96%) of 81 patients. The majority of tumors were located either in eloquent brain (36 of 81 = 44%) or near-eloquent brain (41 of 81 = 51%), and this frequently was the rationale cited for performing stereotactic biopsy. Gross total resection (>95%) was achieved in 46 (57%) of 81 patients, with a median extent of resection of 96% for this series. Diagnoses based on biopsy or resection in the same patient differed in 40 (49%) of 82 cases. This discrepancy was reduced to 30 (38%) of 80 cases when the biopsy slides were reviewed preoperatively by each of three neuropathologists at M. D. Anderson. Major neurologic complications occurred in 10 (12.3%) of 81 surgical patients and 3 (3.7%) of 81 patients undergoing biopsy. Surgical morbidity was probably higher in our series than it would be for glioma patients in general because our patients represent a highly selected subset of glioma patients whose tumors present a technical challenge to remove. Stereotactic biopsy is frequently inaccurate in providing a correct diagnosis and is associated with additional risk and cost. If stereotactic biopsy is performed, expert neuropathology consultation should be sought. *Neuro-Oncology 3, 193–200, 2001 (Posted to Neuro-Oncology [serial online], Doc. 01-001, June 5, 2001. URL <neuro-oncology.mc.duke.edu>)*

Stereotactic biopsy is a procedure frequently performed for diagnostic purposes in patients with brain tumors. Proponents advocate the low risk, diagnostic accuracy, and minimally invasive nature of this procedure (Apuzzo et al., 1987; Kim and Gildenberg, 1998). Stereotactic biopsy is particularly well suited for lesions that are highly suspected of having a nonneoplastic origin, such as infectious, inflammatory, or demyelinating disease in which diagnosis may allow for specific medical treatment (Whiting et al., 1992). Stereotactic biopsy may also be useful in the diagnosis of lesions that are small or deeply located, such as in the brain stem (Coffey and Lunsford, 1985), or for those brain tumors that are diffusely infiltrative. Tumors that are considered particularly radio- or chemosensitive, such as germ-cell tumors or lymphomas, are also excellent candidates for stereotactic biopsy.

Received 2 January 2001, accepted 14 March 2001.

[1]Supported in part by the Bill Doré Fund for Neurological Research.

[2]This study was presented in part at the annual meeting of the Society for Neuro-Oncology, Scottsdale, AZ, in November 1999 (Sawaya et al., 1999).

[3]Address correspondence and reprint requests to Raymond Sawaya, Department of Neurosurgery, Box 442, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030.

[4]Lacroix, M., Abi-Said, D., Gokaslan, Z.L., Shi, W.M., McCutcheon, I.E., DeMonte, F., Lang, F.F., Holland, E.C., Hassenbusch, S.J., Michael, C.B., Miller, D., and Sawaya, R. (1999) Influence of tumor resection on time of survival in patients with GBM. Annual Conference of American Association of Neurological Surgeons. (Abstract)

[5]Abbreviation used is as follows: KPS, Karnofsky performance scale.

It is generally accepted that the extent of tumor resection, tumor histology, and the patient's age are major prognostic factors for patients with gliomas (Abi-Said et al., 1999; Danks et al., 1995; Devaux et al., 1993; Iacoangeli et al., 1993; Janny et al., 1994; Levin et al., 1995; Nitta and Sato, 1995; Piepmeier et al., 1996; Pollack et al., 1995; Rostomily et al., 1994; Vecht et al., 1990; Winger et al., 1989).[4] Extent of resection is the only one of these key variables that neurosurgeons can affect. In the case of patients suffering from gliomas that exert significant mass effect, there is general agreement that decompression by resection is necessary before radiation therapy or other treatment can be given, even among those not favoring cytoreductive surgery (Kreth et al., 1993; Lunsford et al., 1995). Despite this, stereotactic biopsy is frequently performed on patients harboring large gliomas that are exerting significant mass effect, even though resection might be more appropriate and produce a more favorable result. Other patients often undergo a "staged" procedure, that is, biopsy followed by resection at a later date. Indications cited for the initial stereotactic biopsy include diagnosis and/or the "inoperability" of the tumor. With modern neurosurgical techniques, many lesions are currently considered operable with minimal morbidity. The present study reviews the limitations of stereotactic biopsy in the initial management of gliomas and is by no means intended to address the role of surgery on survival in patients with glioma.

Materials and Methods

Patients who underwent surgical treatment or biopsy for gliomas before surgery at The University of Texas M. D. Anderson Cancer Center between the years 1993 and 1998 were identified in our neurosurgical database. These patients' charts were retrospectively reviewed, and all patients who had undergone stereotactic biopsy within 60 days of craniotomy/resection were included in the study. All patients who had an open biopsy or who had a stereotactic biopsy more than 60 days before craniotomy were excluded. The 60-day cutoff was used to minimize differences between histologic diagnoses based on stereotactic biopsy and surgical resection that were, in fact, caused by differentiation or progression of the tumor.

Presenting symptoms and signs, KPS[5] score, type of institution performing stereotactic biopsy (and method used), biopsy complications, and interpretation of histologic diagnosis of biopsied specimen by institutions outside our own were recorded for all patients. Biopsy slides prepared outside our institution were reviewed (independently) by three experienced neuropathologists at M. D. Anderson. The modified Ringertz classification system was used to grade astrocytomas (Fuller, 1996). Oligodendrogliomas were graded according to the 3-tiered system of Smith et al. (1983) (low grade, A; intermediate grade, B-C; anaplastic grade, D). Patients then underwent a craniotomy performed by any of six neurosurgeons, with the assistance of neurosurgical residents or fellows, in an attempt to resect as much tumor as was safely possible. Intraoperative ultrasound was used during all operations, whereas the intraoperative microscope, cortical mapping, image guidance systems, functional MRI, and awake craniotomy were used selectively as needed. Postoperative length of hospital stay, KPS score, and all complications that occurred within 30 days after surgery were recorded for each patient. Our neuropathologists' histologic diagnosis based on the surgical specimen was then compared with their interpretation of the histologic diagnosis of the biopsied specimen and to that of the outside institutions' interpretation of the biopsied specimen.

All of these patients underwent preoperative and postoperative MRI performed with computer-assisted volumetric analysis of the tumor (Shi et al., 1998). MRI evaluation and scoring were done prospectively with the reviewer unaware of the treatment. According to its location, each tumor was given a functional grade based on proximity to eloquent brain areas (I, noneloquent; II, near-eloquent; III, eloquent) as described by Sawaya et al. (1998). For each tumor, pre- and postoperative volume, location, percentage resected, amount of mass effect, and amount of edema were recorded. All postoperative MRI was performed within 72 h of surgery, in most cases within 24 h of surgery.

Results

Patient Characteristics

A total of 81 consecutive patients (49 men, 32 women) underwent 82 stereotactic biopsies within 60 days of undergoing craniotomy/resection for tumors. One patient underwent two temporally separate biopsy procedures at the same institution. Most of these biopsies (79 of 82, 96%) were performed at institutions outside M. D. Anderson, including university-affiliated medical centers (27 of 82, 33%) and nonuniversity-affiliated hospitals (55 of 82, 67%). The average age of our patients was 48 years (range, 15-81 years). Patient characteristics are listed in Table 1. Patients were referred from neuro-oncologists or outside neurosurgeons or were self-referrals.

The indications given for performing stereotactic biopsy were clearly stated in the medical records of only 39 of 81 (48%) patients. There were essentially two categories of stated indications. Some surgeons recommended biopsy for diagnostic purposes before treatment that could involve chemotherapy, radiation therapy, and/or surgical resection. Others recommended biopsy because the lesion was deemed "unresectable" or to be in an area that was "too dangerous" for surgery. Frame-based, CT-guided biopsy was the most common method of biopsy identified in our patient population, although some underwent frame-based and frameless MRI-guided biopsies. The average number of biopsy tissue samples obtained was 5 (range, 1-16).

Most tumors were located in either eloquent (36 of 81, 44%) or near-eloquent (41 of 81, 51%) brain, which frequently was the rationale cited for performing stereotactic biopsy. Patients with tumors located in noneloquent brain numbered only 4 of 81 (5%) of this series. Moderate-to-severe tumor mass effect was recorded preoperatively in 27 of 81 (33%) patients. Moderate-to-

Table 1. Characteristics of patients who underwent sterotactic biopsy within 60 days after craniotomy/resection for tumors between 1993 and 1998

No. of patients	81
Sex (M/F)	49/32
Mean age (yrs)	48 (range, 15-81)
Presentation	
Symptom	No. of patients
Seizure	46
Headache	28
Visual changes	20
Motor	19
Speech	17
Memory	10
Sensory	9
Personality	6
Coma	1
Incidental	1
Tumor location	
Eloquent brain	(44% of patients)
Site	No. of patients
Motor/sensory cortex	14
Speech center	11
Basal ganglia	4
Internal capsule	3
Hypothalamus/thalamus	2
Visual center	1
Brain stem	1
Near-eloquent brain	(51% of patients)
Site	No. of patients
Near speech center	17
Near motor/sensory cortex	15
Near calcarine fissure	5
Corpus callosum	3
Near brain stem	1
Noneloquent brain	(5% of patients)
Site	No. of patients
Frontal or temporal polar lesion	4
Right parietal occipital	0
Cerebellar hemisphere	0

severe tumor-related edema occurred in 25 of 81 (31%) patients. Patients not experiencing tumor mass effect were selected to proceed for further surgery. We wished to obtain a correct diagnosis, considering that many of these patients were symptomatic, many had large tumors, and we believe that functional survival improves after surgery in such patients. Gross total resection (>95%), as demonstrated by computer-assisted volumetric analysis, was achieved in 46 of 81 (57%) cases, with a median resection extent of 96% for this series. Subtotal (85%-95%) and partial (<85%) resections were achieved in 13 of 81 (16%) and 22 of 81 (27%) patients, respectively. The median length of hospital stay for patients undergoing craniotomy and resection in this series was 4 days (range, 3-20 days). The median KPS score remained at 90 after resection.

Biopsy-Based Versus Surgically Based Diagnosis

For each patient, the diagnosis based on the stereotactic biopsy was compared with that based on the surgically resected specimen, interpretations from outside institutions, and opinions of M. D. Anderson neuropathologists (Table 2). Diagnoses for each case were considered to be significantly different if the patient's prognosis and/or treatment would probably have been affected. We found a significant difference in 40 of 82 (49%) cases between the diagnosis obtained by stereotactic biopsy and that based on surgical resection. These 82 biopsies included those from 1 patient who had two temporally separate biopsies as well as those from 3 patients who had stereotactic biopsies performed at M. D. Anderson. The discrepancy between biopsy-based and surgically based diagnoses was calculated separately for university-affiliated hospitals (11 of 27, 41%) and for nonuniversity-affiliated hospitals (29 of 55, 53%); these discrepancy rates were not found to be significantly different ($P = 0.31$; Pearson chi-square test).

This discrepancy in biopsy-based versus surgically based diagnosis probably would have affected treatment in 27 of 82 (33%) and prognosis in 40 of 82 (49%) cases (82 temporally separate biopsies in a total of 81 patients). The significant difference in biopsy-based versus surgically based diagnosis was reduced from 49% (40 of 82) to 38% (30 of 80) when the specimens obtained by biopsy were reviewed preoperatively by each of three neuropathologists from our institution. Two specimens from an outside institution were not reviewed by neuropathologists from our institution. A significant discrepancy between biopsy-based and surgically based diagnosis occurred with both of these specimens. Overall, the discrepancy between the diagnosis made by M. D. Anderson neuropathologists based on stereotactic biopsy specimens and that based on surgically resected tumor material would probably have affected treatment in 21 of 80 (26%) instances and prognosis in 30 of 80 (38%) cases (Table 2).

The finding of glioblastoma multiforme by stereotactic biopsy was confirmed in 34 of 35 (97%) open surgical resections; anaplastic astrocytoma was upgraded to glioblastoma multiforme in 9 of 15 (60%) cases; and low- or intermediate-grade tumors were upgraded to malignant tumors in 12 of 19 (63%) cases (comparison of the diagnosis made by M. D. Anderson neuropathologists based on the stereotactic biopsy versus that based on the surgical specimen). Tissue from stereotactic biopsy from which a diagnosis could not be reached or was inconclusive was found to be malignant in 3 (3.7%) additional instances. Significant oligodendroglial components were identified by stereotactic biopsy in only 6 of 13 (46%) cases in which oligodendroglial components were identified in the surgical specimen.

Complications

All adverse medical conditions experienced by patients within 30 days of surgery were considered complications. Complications were divided into neurologic and systemic categories. Complications that required additional surgery, caused an increase in length of hospital stay, or

Table 2. Comparison of stereotactic biopsy-based and surgically based diagnoses for 81 patients with symptoms of glioma

No. of cases	Biopsy-based diagnosis by OI	Biopsy-based interpretation by MDA	Surgically based diagnosis by MDA	Discrepancy in treatment (T) or prognosis (P)[a]
30	GBM	GBM	GBM	
2	GBM	AA	GBM	P
1	GBM	AA	AA	
1	GBM	GBM	Gliosarcoma	
6	AA	AA	AA	
1	AA	Pleomorphic glioma	AA	T P
7	AA	AA	GBM	P
4	AA	GBM	GBM	
1	AA	Not reviewed	GBM	
2	AA	Infiltrating glioma	Oligo, anaplastic (grade D)	T P
1	AA	AA	Oligo, anaplastic (grade D)	T P
1	AA	Ganglioglioma	Ganglioglioma	
1	Astrocytoma, low grade	Infiltrating glioma	GBM	T P
1	Astrocytoma, low grade	Astrocytoma, low grade	AA	T P
1	Astrocytoma, low grade	Oligo, intermediate (grade B-C)	Oligo, intermediate (grade B-C)	
3	Astrocytoma, low grade	Infiltrating glioma	AA	T P
1	Astrocytoma, low grade	Not diagnostic	Oligo, anaplastic (grade D)	T P
1	Astrocytoma, low grade	Infiltrating glioma	Mixed oligo/astrocytoma	T P
1	Astrocytoma, low grade	AA	Mixed oligo/astrocytoma anaplastic	T P
1	Astrocytoma, low grade	Infiltrating glioma	Mixed oligo/astrocytoma anaplastic	T P
1	Astrocytoma, no grade	AA	AA	
1	Oligo	Oligo, low (grade A)	Oligo, anaplastic (grade D)	T P
2	Oligo	Oligo, intermediate (grade B-C)	Oligo, intermediate (grade B-C)	
1	Oligo, low grade	Oligo, intermediate (grade B-C)	Oligo, intermediate (grade B-C)	
1	Oligo, low grade	Oligo, intermediate (grade B-C)	Oligo, anaplastic (grade D)	T P
1	Mixed oligo/astrocytoma	Glial neoplasm	Oligo, anaplastic (grade D)	T P
1	Mixed oligo/ astrocytoma anaplastic	GBM	GBM	
1	Cerebellum	Cerebellum	JPA	T P
1	Gliosis	Not read	GBM	
1	Inconclusive	Gliosis	GBM	T P
1	Lymphoma	PNET	Gliosarcoma	T P
1	JPA	JPA	JPA	
1	Neuroblastoma	Malignant neuroectodermal tumor	GBM	T P
1	Pineocytoma	Pineal parenchymal tumor of intermediate differentiation	AA	T P

Abbreviations: OI, outside institution; MDA, The University of Texas M. D. Anderson Cancer Center; GBM, glioblastoma multiforme; AA, anaplastic astrocytoma; Oligo, oligodendroglioma; JPA, juvenile pilocytic astrocytoma; PNET, primitive neuroectodermal tumor.

[a]The discrepancy in treatment (T) or prognosis (P) reflects differences between the diagnosis made by MDA neuropathologists based on the stereotactic biopsy specimen and the surgical specimen. There was a greater concordance of the diagnosis based on the MDA interpretation of the stereotactic biopsy and that determined from the final surgical specimen than was seen with the interpretation by neuropathologists outside the institution.

that were potentially life threatening were considered major complications. Complications that did not significantly change the overall course of events and that did not increase the overall length of stay were considered minor complications.

After undergoing stereotactic biopsy, 3 patients (3.7%) had documented major complications, and 1 (1.2%) had minor neurologic complications. There were no deaths or systemic complications attributed to the biopsy. Major complications included intracerebral hemorrhage in 2 patients, causing aphasia and requiring craniotomy in 1 patient, and causing headache, nausea, vomiting, and increased length of hospital stay in the other patient. Another patient suffered from persistent hemiparesis following biopsy. Temporary unilateral leg weakness occurred in 1 patient after biopsy and was recorded as a minor neurological complication. Tissue that was nondiagnostic was obtained by stereotactic biopsy in 2 patients, which necessitated additional procedures and could also be considered a complication.

After surgery, 1 patient died due to an intracerebral hemorrhage. In addition, 10 patients experienced major

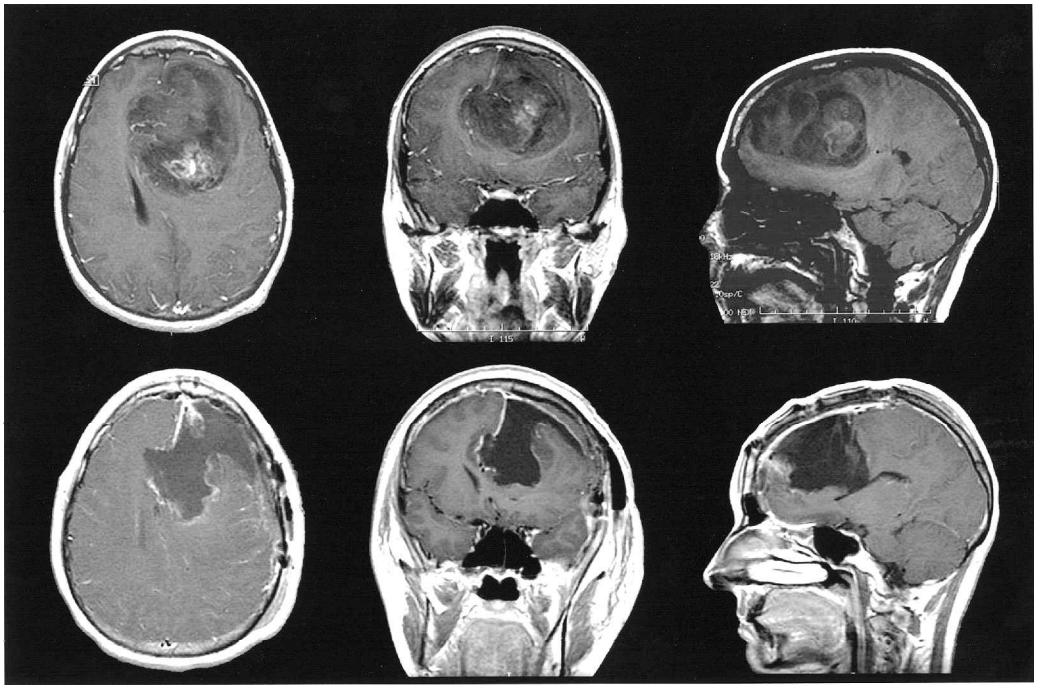

Fig. 1. Preoperative (top row) and postoperative (lower row) axial, coronal, and sagittal MRIs (gadolinium contrast-enhanced) demonstrating a left frontal brain tumor and the 97% resection. Preoperatively, functional grade was 3, mass effect grade was 3, edema grade was 1, and size was 160.99 cm^3. Postoperatively, the residual tumor volume was 5.39 cm^3.

neurologic complications, which included new hemiparesis in 5 patients, new hemiparesis and mild aphasia in 2 patients, new hemiparesis and increased aphasia in 1 patient, increased hemiparesis in 1 patient, and increased aphasia in 1 patient. There were 11 patients (13.7%) with minor neurologic complications that included increased weakness (in 4 patients), new mild weakness (in 2 patients), increased mild aphasia (in 3 patients), increased visual field deficits (in 2 patients), new visual deficit (in 1 patient), and increased upward gaze paresis (in 1 patient). There were 4 patients (4.9%) with major systemic complications that included 1 patient with a pulmonary embolus, 2 patients with deep venous thrombosis (1 of these patients also had new hemiparesis and is listed above), and 1 patient with cerebral salt wasting and atrial flutter. There were 3 patients (3.7%) with minor systemic complications that included facial cellulitis remote from the surgical wound, a urinary tract infection, and a mild rash thought to be secondary to phenytoin administration. There were no wound or craniotomy infections in this series. Major morbidity and mortality occurred in 13 (16%) patients and 1 (1.2%) patient, respectively, who underwent craniotomy and tumor resection in this series.

Illustrative Case

This 40-year-old chemical engineer presented with a 3-month history of headaches, nausea, vomiting, mild right hemiparesis, and word-finding difficulty. MRI revealed a large left frontal mass (Fig. 1). Stereotactic biopsy at an outside institution revealed a mixed oligoastrocytoma, low grade. She was subsequently referred to our institution for radiotherapy. Because of the significant mass effect of this tumor and the patient's progressive symptoms, we elected to resect (Fig. 1). Stereotactic biopsy was probably unnecessary considering the large size and significant mass effect of the tumor. In addition, the stereotactic biopsy-based diagnosis was inaccurate. Histologic examination of the surgical tissue revealed an anaplastic oligodendroglioma, grade D. There were no intraoperative or postoperative complications, and the patient was discharged home with an improved neurologic condition on postoperative day 3. Two months after her surgery and subsequent radiotherapy, she returned to work without neurologic deficits. She received chemotherapy and was alive and well without regrowth 15 months after her surgery.

Discussion

Stereotactic biopsy is a frequently performed diagnostic procedure in patients with brain tumors. Those who favor stereotactic biopsy point out its low risk, diagnostic accuracy, and minimally invasive nature (Apuzzo et al., 1987; Kim and Gildenberg, 1998). Stereotactic biopsy is a truly minimally invasive procedure associated with a low, but not negligible, risk. Review of 7 stereotactic biopsy studies (Apuzzo et al., 1987; Bernstein and Parrent, 1994; Hall, 1998; Mundinger, 1985; Ostertag et al., 1980; Sawin et al., 1998; Sedan et al., 1984), each containing more than 100 cases, revealed an average morbidity rate of 4.1% (range, 0.7%-7%) and a mortality rate of 0.9%

(range, 0.2%-2.3%). Stereotactic biopsy-associated morbidity occurred in 4 (4.9%) of 81 patients in this series. Stereotactic biopsy–associated complications may be underestimated in this series because most of the biopsies (79 of 82, 96%) were performed at outside institutions and were thus recorded in outside medical records that were not entirely available for all patients. Due to the design of this study, we saw no patients who had stereotactic biopsy–associated mortality.

Review of these same studies revealed an average of 5% (range, 0%-9%) acquisition of nondiagnostic tissue, which translates into a 95% diagnostic yield. Frequently, diagnostic accuracy is erroneously substituted for diagnostic yield. We must be careful to separate diagnostic yield from diagnostic accuracy. Diagnostic yield refers to the percentage of cases for which a diagnosis was given. This does not indicate the accuracy of the diagnosis.

Several studies have compared the immediate biopsy diagnosis, based on frozen sections or smears, with that of the permanent biopsy sections and have reported high accuracy (Apuzzo et al., 1987; Broggi et al., 1984; Gaudin et al., 1997; Kleihues et al., 1984; Ostertag et al., 1980; Revesz et al., 1993; Willems and Alva-Willems, 1984) or have concluded that the accuracy was high, based on survival studies (Gaudin et al., 1997; Revesz et al., 1993). However, only a few studies, using small sample sizes, have addressed the accuracy of diagnoses based on the biopsy specimen relative to those based on the resected surgical specimen (Broggi et al., 1984; Chandrasoma et al., 1989; Feiden et al., 1991; Kleihues et al., 1984; Scerrati and Rossi, 1984) (Table 3). Furthermore, none of these studies has specified or restricted the time interval between biopsy and subsequent surgical resection or autopsy.

Chandrasoma et al. (1989) compared the diagnosis based on stereotactic biopsy against that based on the resected surgical specimen in 30 patients; in 11 of 30 (37%) patients these diagnoses were found to be different. Moreover, in 6.7% of the patients, the discrepancy in diagnosis was found to be clinically significant with regard to treatment. We found a significant difference in 49% of the 82 diagnoses obtained by stereotactic biopsy compared with those based on surgical resection. This discrepancy was reduced to 38% when the specimens obtained by biopsy were reviewed preoperatively by neuropathologists at M. D. Anderson. Review of each sample by three M. D. Anderson neuropathologists allowed us to minimize interobserver variability in diagnosis, which is not infrequent with gliomas (Bruner et al., 1997; Mittler et al., 1996). In our series, discrepancy in diagnosis would be likely to affect prognosis or treatment in 38% and 26% of patients, respectively. Sampling error and the small quantity of tissue associated with the stereotactic biopsies were the most likely reasons for the discrepancies observed (Kepes, 1994).

Nearly one-half (40 of 82) of the stereotactic biopsy–based diagnoses were found to be discordant with those based on the surgically resected specimen, although this discrepancy was reduced to 38% (30 of 80) when the specimens obtained by biopsy were reviewed preoperatively by each of three neuropathologists at M. D. Anderson. There was a strong trend toward finding an increased level of malignancy based on specimens from open resection. Tumors classified by stereotactic biopsy as being of low or intermediate grade were found to be malignant by open surgical resection in 63% of cases; anaplastic astrocytomas were upgraded to glioblastomas multiforme in 60% of cases; and glioblastomas multiforme were confirmed as such 97% of the time. Moreover, open resection permitted diagnosis of tumors as malignant in three additional patients in whom stereotactic biopsy samples were not diagnostic, and it allowed detection of significant oligodendroglial components in more than twice as many tumors as did samples from stereotactic biopsy.

Precise histologic diagnosis is crucial in patient care for guiding appropriate treatment and for determining prognosis. Meaningful evaluation of experimental treatment protocols also requires an accurate histologic diagnosis (Fulling and Nelson, 1984). The grading of glial tumors by stereotactic biopsy may produce a significant underestimate of the degree of malignancy (Glantz et al., 1991) and may be invalid in some cases. Inaccurate diagnosis may lead to suboptimal therapy, incorrect prognosis, and misinterpretation of clinical trials.

In addition to providing adequate tissue for precise histologic diagnosis, surgical resection is often therapeutic. Many would agree that the extent of tumor resection, tumor histologic features, and the patient's age are key prognostic factors for patients with gliomas (Abi-Said et al., 1999; Danks et al., 1995; Devaux et al., 1993; Iacoangeli et al., 1993; Janny et al., 1994; Levin et al., 1995; Nitta and Sato, 1995; Piepmeier et al., 1996; Pollack et al., 1995; Rostomily et al., 1994; Vecht et al., 1990; Winger et al., 1989).[4] Even those less enthusiastic about the role of cytoreductive surgery agree that patients harboring tumors with significant mass effect should undergo resection prior to radiotherapy and/or

Table 3. Historical accuracy of stereotactic biopsy

Authors (yr)	Percentage of diagnostic accuracy	No. of biopsy patients with subsequent	
		Surgery	Autopsy
Broggi et al. (1984)	89	36 (surgery or autopsy)	
Kleihues et al. (1984)	85	33	19
Scerrati and Rossi (1984)	95	14	5
Chandrasoma et al. (1989)	63	30	0
Feiden et al. (1991)	89	38	9
Present study	62	81	0

additional treatment (Kreth et al., 1993; Lunsford et al., 1995). This is because mass effect in such patients, if left alone, will interfere with the completion of radiation therapy; if no debulking is performed, radiation therapy will lead to further edema, swelling, and even death. Nonetheless, patients harboring large gliomas with significant mass effect are frequently subjected to biopsy when resection may be indicated. Preoperatively, moderate-to-severe tumor mass effect and edema were recorded in 33% (27 of 81) and 31% (25 of 81) of patients, respectively, in this study. In this series, we retrospectively found that stereotactic biopsy was either performed inappropriately in patients with moderate-to-severe tumor-related mass effect or edema, or resulted in additional morbidity, and/or yielded an incorrect diagnosis in 75% (61 of 81) of patients. If one makes the decision to treat these patients, then in our opinion surgical resection and decompression, rather than stereotactic biopsy, is a better initial treatment option. Because modern neurosurgical techniques have rendered many tumors operable that were previously considered inoperable, gross total resection can now be achieved with acceptable morbidity and mortality (Fadul et al., 1988; Sawaya et al., 1998). Considering that 95% of the tumors in this series were located in eloquent or near-eloquent brain, that 62% were glioblastomas multiforme, and that 73% were resected to a level of 85% to 100% (median extent of resection, 96%), the surgical morbidity in this select group of patients was relatively low. Nevertheless, the surgical complication rate reported here should not be taken as typical of the entire population of glioma patients undergoing craniotomy for tumor resection; the complication rate we observed is probably higher than that for the general glioma patient population because our patients represent a subset deemed too technically challenging to be appropriate for open resection by the neurosurgeons outside M. D. Anderson who referred most of them to our institution.

In summary, stereotactic biopsy may be an additional, perhaps unnecessary, procedure in the management of patients with suspected glioma. The biopsy adds additional 0.9% and 4% risks of mortality and major morbidity, respectively, and leads to an inaccurate or imprecise diagnosis in one-third to one-half of cases. Frequently, patients who undergo stereotactic biopsy have tumors creating significant mass effect, which necessitates craniotomy for decompression. Whenever possible, surgical resection should be considered as the initial treatment in patients with suspected gliomas.

This study is limited by its retrospective nature and by referral patterns to a major cancer specialty hospital that caused the patient series analyzed here to represent a selected subset of glioma patients. Stereotactic biopsy may be preferred in cases in which inflammatory, demyelinating, or infectious disease etiologies are considered, or if the individual clinical situation makes craniotomy and resection less desirable. If stereotactic biopsy is performed, expert neuropathology consultation should be sought.

References

Abi-Said, D., Lacroix, M., Shi, W., Gokaslan, Z.L., Hess, K., DeMonte, F., Lang, F.F., McCutcheon, I.E., Hassenbusch, S.J., Michael, C., Miller, D., and Sawaya, R. (1999) Imaging-based necrosis and the survival of patients with glioblastoma multiforme. Neuro-Oncology [serial online], Doc. N1, September 29, 1999. URL http://neuro-oncology.mc.duke.edu. *Neuro-Oncol.* **1**, 294. (Abstract)

Apuzzo, M.L., Chandrasoma, P.T., Cohen, D., Zee, C.S., and Zelman, V. (1987) Computed imaging stereotaxy: Experience and perspective related to 500 procedures applied to brain masses. *Neurosurgery* **20**, 930-937.

Bernstein, M., and Parrent, A.G. (1994) Complications of CT-guided stereotactic biopsy of intra-axial brain lesions. *J. Neurosurg.* **81**, 165-168.

Broggi, G., Franzini, A., Giorgi, C., and Allegranza, A. (1984) Diagnostic accuracy and multimodal approach in stereotactic biopsies of deep brain tumors. *Acta Neurochir. Suppl.* **33**, 211-212.

Bruner, J.M., Inouye, L., Fuller, G.N., and Langford, L.A. (1997) Diagnostic discrepancies and their clinical impact in a neuropathology referral practice. *Cancer* **79**, 796-803.

Chandrasoma, P.T., Smith, M.M., and Apuzzo, M.L. (1989) Stereotactic biopsy in the diagnosis of brain masses: Comparison of results of biopsy and resected surgical specimen. *Neurosurgery* **24**, 160-165.

Coffey, R.J., and Lunsford, L.D. (1985) Stereotactic surgery for mass lesions of the midbrain and pons. *Neurosurgery* **17**, 12-18.

Danks, R.A., Chopra, G., Gonzales, M.F., Orian, J.M., and Kaye, A.H. (1995) Aberrant p53 expression does not correlate with the prognosis in anaplastic astrocytoma. *Neurosurgery* **37**, 246-254.

Devaux, B.C., O'Fallon, J.R., and Kelly, P.J. (1993) Resection, biopsy, and survival in malignant glial neoplasms: A retrospective study of clinical parameters, therapy, and outcome. *J. Neurosurg.* **78**, 767-775.

Fadul, C., Wood, J., Thaler, H., Galicich, J., Patterson, R.H., Jr., and Posner, J.B. (1988) Morbidity and mortality of craniotomy for excision of supratentorial gliomas. *Neurology* **38**, 1374-1379.

Feiden, W., Steude, U., Bise, K., and Gundisch, O. (1991) Accuracy of stereotactic brain tumor biopsy: Comparison of the histologic findings in biopsy cylinders and resected tumor tissue. *Neurosurg. Rev.* **14**, 51-56.

Fuller, G.N. (1996) Central nervous system tumors. In: Parham, D.M. (Ed.), *Pediatric Neoplasia: Morphology and Biology*. Philadelphia, Pa.: Lippincott-Raven. pp. 153-204.

Fulling, K.H., and Nelson, J.S. (1984) Cerebral astrocytic neoplasms in the adult: Contribution of histologic examination to the assessment of prognosis. *Semin. Diagn. Pathol.* **1**, 152-163.

Gaudin, P.B., Sherman, M.E., Brat, D.J., Zahurak, M., and Erozan, Y.S. (1997) Accuracy of grading gliomas on CT-guided stereotactic biopsies: A survival analysis. *Diagn. Cytopathol.* **17**, 461-466.

Glantz, M.J., Burger, P.C., Herndon, J.E., II, Friedman, A.H., Cairncross, J.G., Vick, N.A., and Schold, S.C., Jr. (1991) Influence of the type of surgery on the histologic diagnosis in patients with anaplastic gliomas. *Neurology* **41**, 1741-1744.

Hall, W.A. (1998) The safety and efficacy of stereotactic biopsy for intracranial lesions. *Cancer* **82**, 1749-1755.

Iacoangeli, M., Roselli, R., Prezioso, A., Scerrati, M., and Rossi, G.F. (1993) Staging of supratentorial hemispheric glioma using tumour extension, histopathological grade and extent of surgical resection. *Br. J. Surg.* **80**, 1130-1133.

Janny, P., Cure, H., Mohr, M., Heldt, N., Kwiatkowski, F., Lemaire, J.J., Plagne, R., and Rozan, R. (1994) Low grade supratentorial astrocytomas: Management and prognostic factors. *Cancer* **73**, 1937-1945.

Kepes, J.J. (1994) Pitfalls and problems in the histopathologic evaluation of stereotactic needle biopsy specimens. *Neurosurg. Clin. N. Am.* **5**, 19-33.

Kim, J.-H., and Gildenberg, P.L. (1998) Stereotactic biopsy. In: Gildenberg, P.L., and Tasker, R.R. (Eds.), *Textbook of Stereotactic and Functional Neurosurgery*. New York: McGraw-Hill. pp. 387-396.

Kleihues, P., Volk, B., Anagnostopoulos, J., and Kiessling, M. (1984) Morphologic evaluation of stereotactic brain tumour biopsies. *Acta Neurochir. Suppl. (Wien)* **33**, 171-181.

Kreth, F.W., Warnke, P.C., Scheremet, R., and Ostertag, C.B. (1993) Surgical resection and radiation therapy versus biopsy and radiation therapy in the treatment of glioblastoma multiforme. *J. Neurosurg.* **78**, 762-766.

Levin, V.A., Prados, M.R., Wara, W.M., Davis, R.L., Gutin, P.H., Phillips, T.L., Lamborn, K., and Wilson, C.B. (1995) Radiation therapy and bromodeoxyuridine chemotherapy followed by procarbazine, lomustine, and vincristine for the treatment of anaplastic gliomas. *Int. J. Radiat. Oncol. Biol. Phys.* **32**, 75-83.

Lunsford, L.D., Somaza, S., Kondziolka, D., and Flickinger, J.C. (1995) Survival after stereotactic biopsy and irradiation of cerebral nonanaplastic, nonpilocytic astrocytoma. *J. Neurosurg.* **82**, 523-529.

Mittler, M.A., Walters, B.C., and Stopa, E.G. (1996) Observer reliability in histological grading of astrocytoma stereotactic biopsies. *J. Neurosurg.* **85**, 1091-1094.

Mundinger, F. (1985) CT stereotactic biopsy for optimizing the therapy of intracranial processes. *Acta Neurochir. Suppl. (Wien)* **35**, 70-74.

Nitta, T., and Sato, K. (1995) Prognostic implications of the extent of surgical resection in patients with intracranial malignant gliomas. *Cancer* **75**, 2727-2731.

Ostertag, C.B., Mennel, H.D., and Kiessling, M. (1980) Stereotactic biopsy of brain tumors. *Surg. Neurol.* **14**, 275-283.

Piepmeier, J., Christopher, S., Spencer, D., Byrne, T., Kim, J., Knisel, J.P., Lacy, J., Tsukerman, L., and Makuch, R. (1996) Variations in the natural history and survival of patients with supratentorial low-grade astrocytomas. *Neurosurgery* **38**, 872-879.

Pollack, I.F., Claassen, D., al-Shboul, Q., Janosky, J.E., and Deutsch, M. (1995) Low-grade gliomas of the cerebral hemispheres in children: An analysis of 71 cases. *J. Neurosurg.* **82**, 536-547.

Revesz, T., Scaravilli, F., Coutinho, L., Cockburn, H., Sacares, P., and Thomas, D.G. (1993) Reliability of histological diagnosis including grading in gliomas biopsied by image-guided stereotactic technique. *Brain* **116**, 781-793.

Rostomily, R.C., Spence, A.M., Duong, D., McCormick, K., Bland, M., and Berger, M.S. (1994) Multimodality management of recurrent adult malignant gliomas: Results of a phase II multiagent chemotherapy study and analysis of cytoreductive surgery. *Neurosurgery* **35**, 378-388.

Sawaya, R., Hammoud, M., Schoppa, D., Hess, K.R., Wu, S.Z., Shi, W.M., and Wildrick, D.M. (1998) Neurosurgical outcomes in a modern series of 400 craniotomies for treatment of parenchymal tumors. *Neurosurgery* **42**, 1044-1056.

Sawin, P.D., Hitchon, P.W., Follett, K.A., and Torner, J.C. (1998) Computed imaging-assisted stereotactic brain biopsy: A risk analysis of 225 consecutive cases. *Surg. Neurol.* **49**, 640-649.

Scerrati, M., and Rossi, G.F. (1984) The reliability of stereotactic biopsy. *Acta Neurochir. Suppl.* **33**, 201-205.

Sedan, R., Peragut, J.C., Farnarier, P.H., Hassoun, J., and Sethian, M. (1984) Intra-encephalic stereotactic biopsies (309 patients/318 biopsies). *Acta Neurochir. Suppl.* **33**, 207-210.

Shi, W.-M., Wildrick, D.M., and Sawaya, R. (1998) Volumetric measurement of brain tumors from MR imaging. *J. Neurooncol.* **37**, 87-93.

Smith, M.T., Ludwig, C.L., Godfrey, A.D., and Armbrustmacher, V.W. (1983) Grading of oligodendrogliomas. *Cancer* **52**, 2107-2114.

Vecht, C.J., Avezaat, C.J., van Putten, W.L., Eijkenboom, W.M., and Stefanko, S.Z. (1990) The influence of the extent of surgery on the neurological function and survival in malignant glioma: A retrospective analysis in 243 patients. *J. Neurol. Neurosurg. Psychiatry* **53**, 466-471.

Whiting, D.M., Barnett, G.H., Estes, M.L., Sila, C.A., Rudick, R.A., Hassenbusch, S.J., and Lanzieri, C.F. (1992) Stereotactic biopsy of non-neoplastic lesions in adults. *Cleve. Clin. J. Med.* **59**, 48-55.

Willems, J.G., and Alva-Willems, J.M. (1984) Accuracy of cytologic diagnosis of central nervous system neoplasms in stereotactic biopsies. *Acta Cytol.* **28**, 243-249.

Winger, M.J., Macdonald, D.R., and Cairncross, J.G. (1989) Supratentorial anaplastic gliomas in adults: The prognostic importance of extent of resection and prior low-grade glioma. *J. Neurosurg.* **71**, 487-493.