Evaluation of factors predicting accurate resection of high-grade gliomas by using frameless image-guided stereotactic guidance

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Object. Frameless image-guided stereotaxy is often used in the resection of high-grade gliomas. The authors of several studies, however, have suggested that brain shift may occur intraoperatively and result in inaccurate resection. To determine the usefulness of frameless stereotactic image-guided surgery of high-grade gliomas, the authors correlated factors predictive of brain shift, such as tumor size, periventricular location, and patient age (as an indicator of brain atrophy) with the extent of resection.

Methods. Inclusion criteria included the following: 1) stereotactic volumetric craniotomy for resection of tumor; 2) histologically proven high-grade glioma; 3) preoperative magnetic resonance (MR) imaging demonstration of an enhancing portion of tumor; 4) postoperative MR imaging within 48 hours to assess the extent of resection; and 5) preoperative intention to perform gross-total resection of the enhancing tumor. Fifty-four patients met these criteria between September 1997 and November 2002. Accurate resection was considered to be indicated by a lack of nodular enhancement on postoperative Gd-enhanced MR images obtained within 48 hours of surgery.

Frameless stereotactic image-guided surgery resulted in the successful resection of 46 (85%) of 54 high-grade gliomas. Accurate resection was significantly more likely with tumors less than 30 ml in volume than with those greater than 30 ml (93 and 58%, respectively [$p < 0.05$]). In addition, small periventricular tumors were associated with significant less successful resection compared with nonperiventricular tumor (77 and 96%, respectively [$p = 0.5$]). Patient age did not affect the likelihood of successful resection.

Conclusions. Frameless image-guided stereotactic techniques can be reliably used for accurate resection of high-grade gliomas when the tumor is less than 30 ml in volume and not adjacent to the ventricular system. In cases involving tumors larger in volume or located near the ventricles, intraoperative ultrasonography or MR imaging updates should be considered.

KEY WORDS • image-guided neurosurgery • malignant gliomas • stereotaxy • brain shift

High-grade gliomas are the most common primary brain tumors in adults and cause significant morbidity and mortality.[30] Conventional treatment of these lesions includes resection when technically feasible, followed by external-beam radiotherapy and adjuvant treatment.[4] Although still debated among neurosurgeons, evaluation of the recent literature suggests that aggressive resection of malignant astrocytomas, as assessed by postoperative MR imaging, is associated with improved survival and functional status.[1,2,14,18]

Over the past decade, advances in computer software have allowed the widespread use of stereotactic volumetric resection within the neurosurgical community. The use of frameless modalities for resection of intraparenchymal brain lesion, including malignant gliomas, has been proven to facilitate surgical planning, allow minimally invasive craniotomies, and facilitate microsurgical dissection avoiding eloquent structures.[7–10,25] One of the current limitations of stereotactic volumetric technology for resection of high-grade gliomas, however, is the phenomenon referred to as intraoperative brain shift. Brain shift during open neurosurgical procedures occurs as the brain “relaxes,” and this is related to different causes, including the use of mannitol, opening of the dura mater, cisterns, ventricles which caused cerebrospinal fluid diversion, and surgical debulking of large masses. When brain shift occurs, intraoperative guidance based on preoperatively acquired images may prove inaccurate. In several studies the authors have elegantly quantified intraoperative brain shift by using optical techniques[12,27,28] and intraoperative MR imaging.[19,21,22] In these studies, the brain surface shifted up to 2.4 cm during surgery; the amount and direction of shift depended on many factors, most importantly the volume of tissue resected. To date, however, there has been no clinical study conducted to correlate tumor size, location, and atrophy to the extent of resection in malignant gliomas.

Abbreviations used in this paper: GBM = glioblastoma multiforme; MR = magnetic resonance.

The purpose of this retrospective study was to determine if certain factors predict brain shift and unsuccessful gross-total resection of the enhancing portion of the tumor during frameless stereotactic resection of malignant gliomas. In particular tumor size, periventricular location, and patient age (as an indicator of brain atrophy) were correlated with success of resection based on postoperative MR imaging.

CLINICAL MATERIAL AND METHODS

Patient Population

All medical records of patients with histopathologically confirmed high-grade gliomas at Mount Sinai Medical Center were included in this retrospective study for the period between September 1997 to November 2002. Internal review board approval was obtained prior to initiating this study in accordance with Mount Sinai School of Medicine guidelines. High-grade gliomas included GBM, anaplastic astrocytoma, anaplastic oligoastrocytoma, and anaplastic oligodendroglioma. Inclusion criteria for this study were: 1) stereotactic volumetric craniotomy for tumor resection; 2) histologically proven high-grade glioma; 3) preoperative MR imaging demonstration of an enhancing portion of tumor; 4) postoperative MR imaging performed within 48 hours to assess the extent of resection; and 5) preoperative intention to perform gross-total resection of the enhancing tumor. Fifty-four patients met the aforementioned entry criteria.

Surgical Techniques

All patients underwent preoperative contrast-enhanced MR imaging the day of the surgery after skin-adhering fiducial markers were placed. The preoperative MR imaging study was acquired using a conventional frameless protocol (axial T_1-weighted sequences, 2 mm thick, 0-mm interval). Patients were then brought to the operating room and anesthesia induced.

The StealthStation (Medtronic SNT, Louisville, CO) was used in all cases for frameless guidance. In cases in which the tumor was located near eloquent cortex, intraoperative electrophysiological mapping was also performed. In patients undergoing postirradiation reoperation for recurrent tumor, frozen tissue sections were obtained to distinguish tumor from radiation necrosis. All patients were treated perioperatively with dexamethasone, antibiotic, and antiseizures medications. Table 1 provides a summary of the techniques used to minimize brain shift.

TABLE 1

*Techniques for minimizing brain shift during resection of high-grade gliomas**

Technique
hyperventilation until tumor debulking begins
avoid mannitol & other diuretics
avoid CSF diversion
delineate tumor margin in the x, y, and z dimensions before debulking
avoid penetration of tumoral cyst

* CSF = cerebrospinal fluid.

Magnetic Resonance Imaging Evaluation

Preoperative and postoperative tumor size was measured using the modified ellipsoid method described previously and validated for intracerebral hematomas.[6,17] Residual tumor demonstrated on postoperative MR images was considered an area of nodular, nonlinear enhancement after administration of Gd; nodular enhancement, but not smooth linear enhancement, around the postoperative tumor bed has been documented to predict tumor regrowth in prospective studies.[1,3] We considered tumor resection to be accurate if no nodular enhancement was present on postoperative MR images obtained 48 hours after the surgery. In addition, cases in which the surgeon had noted that a small percentage (5%) of the tumor was deliberately not resected because of intraoperatively acquired information, which was confirmed on postoperative MR images, were also classified into the accurate resection group. These included 15 patients: a cuff of tumor was intentionally left against the ventricular wall to avoid opening of the ventricular system in 10 cases, intraoperative mapping revealed that a small portion of the tumor was invading the eloquent cortex in two cases, and examination of an intraoperative frozen section revealed the presence of radionecrosis and not recurrent tumor in a small deep part of the lesion in three cases.

A tumor was defined as periventricular when partially touching the ventricular wall. Preoperative assessment of brain atrophy was difficult because significant mass effect and edema on preoperative imaging studies was demonstrated in most patients. Therefore, we used age as a predictor of brain atrophy and divided patients into two groups: greater than 70 and less than 70 years of age.

Statistical Analysis

Statistical analysis was performed using commercially available software (Stat View 4.5.1; Abacus Concepts, Berkeley, CA). A statistical value of p less than 0.05 was considered significant.

RESULTS

Small Tumor Size: Predictor of Successful Resection

Frameless image-guided stereotaxy resulted in successful resection of 46 (85%) of 54 high-grade gliomas. To assess the impact of lesions volume on extent of resection, tumors were divided into three groups: less than 15 ml, 15 to 30 ml, and greater than 30 ml in volume. We found that 29 (94%) of 31 tumors less than 15 ml in volume and 10 (91%) of 11 tumors of 15 to 30 ml in volume were successfully resected. This difference was not statistically significant. On the other hand, only seven (58%) of 12 tumors greater than 30 ml in volume were successfully resected, a statistically significant difference ($p < 0.05$) (Fig. 1).

Periventricular Tumor Location: Predictor of Unsuccessful Resection

Fourteen (61%) of 23 periventricular tumors were successfully resected, whereas 92% of tumors located away from the ventricles were successfully resected ($p < 0.05$).

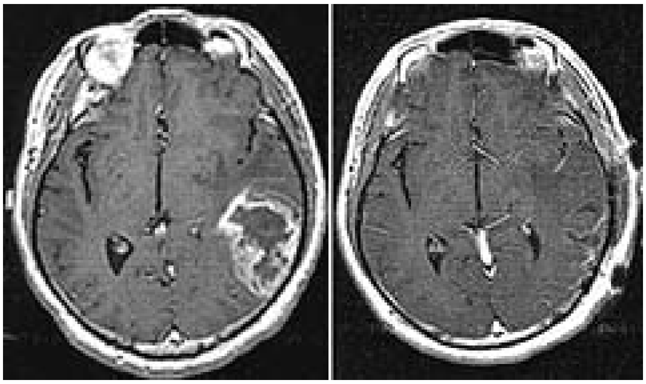

Fig. 1. Gadolinium-enhanced MR images obtained before *(left)* and 24 hours after surgery *(right)* in a 55-year-old man who presented with progressive receptive dysphasia. The large left temporal GBM was successfully resected using frameless image guidance. Postoperatively the patient experienced significant improvement of his symptoms.

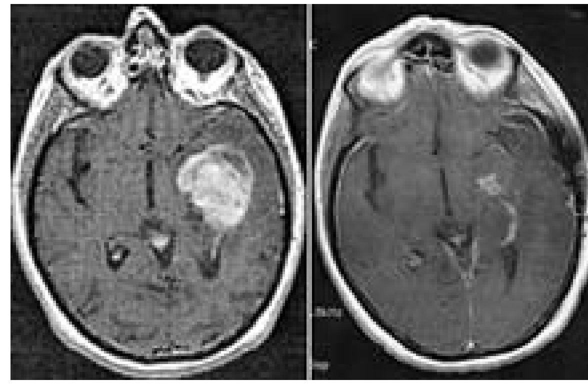

Fig. 2. Gadolinium-enhanced MR images obtained before *(left)* and 24 hours after surgery *(right)* in a 65-year-old woman who presented with mild receptive dysphasia. The postoperative image reveals a residual small nodule *(right)* after resection using frameless image guidance. The patient's symptoms remained unchanged postoperatively.

In our study, however, periventricular tumors were significantly larger than nonperiventricular (mean volumes 29 and 14 ml, respectively [$p < 0.05$]). We therefore compared the rate of successful resection for periventricular and nonperiventricular tumors separately for those greater than 30 ml and less than 30 ml in volume. When comparing tumors less than 30 ml in volume, nonperiventricular lesions were associated with a significantly greater rate of successful resection than periventricular tumors (91 and 77%, respectively [Fig. 2]). For tumors greater than 30 ml this difference was not statistically significant.

Patient Age: Not a Predictor of Extent of Tumor Resection

We hypothesized that in older patients with atrophic brains successful tumor resections would be less likely because of the greater amount of brain shift. We therefore compared rates of successful resection in patients younger than 70 and 70 years of age or older. Age was not found to have an impact on extent of resection: 81% of 49 patients younger than 70 years of age underwent successful resection compared with 100% of five patients age 70 years or older, a difference that was not statistically significant.

DISCUSSION

The use of volumetric resection for gliomas was introduced by Kelly approximately 20 years ago.[16] Advances in computer software and hardware have encouraged the widespread use of frameless image-guided computer-assisted technology in the neurosurgical community in the past decade.[8] Because frameless image-guided stereotactic equipment has become user friendly and relatively affordable, it is used in academic and community hospitals for various neurosurgical procedures.[10,25] Its advantages are well described in the literature and include assistance in accurate and minimally invasive resections, decreased morbidity rates, and shorter hospitalization.[9,26] Nonetheless, for resection of supratentorial glioma this technology seems to be limited by potential intraoperative error due to brain shift. The movement of the intracranial contents such that they do not match their perspective positions on preoperative images has long being documented.[5,12,20] In most image-guided computer-assisted technology the procedure is based on preoperatively acquired images. Thus, if brain shift occurs, the feedback delivered to the surgeon may be erroneous. In this study we found that accurate resection of supratentorial gliomas with volumes less than 30 ml was achieved in 93% of the cases. On the other hand, the overall accuracy was fund to be 85%. Thus, a tumor volume less than 30 ml should reassure the surgeon that brain shift may not interfere significantly during tumor resection.

Techniques to minimize brain shift have been described and are worth following when using frameless image-guided stereotactic equipment.[15] In our practice we do not administer mannitol or other diuretics to induce brain relaxation prior to opening of the dura. Hyperventilation with end tidal PCO_2 in the range of 20 to 25 torr is usually sufficient to allow safe opening of the dura. As the tumor debulking proceeds, hyperventilation is discontinued. Prior to beginning the tumor removal, we use the frameless probe to map the anteroposterior and mesiolateral extent of the tumor by depositing a silk thread on the brain surface to delineate the tumor perimeter. In addition, we insert cottonoid at the interface between the area of tumor enhancement and the adjacent brain by using a picket fencing technique, as previously described.[15] Despite these meticulous maneuvers, in our study we found that accurate resection of large tumor was achieved only in 58% of the cases. Thus, in cases involving these tumors the use of intraoperative image-updating technology, such as ultrasonography or MR imaging, should be considered when clinically indicated. We have successfully used intraoperative ultrasonography interfaced with frameless image-guided stereotactic equipment for resection of tumors.[10] By digitizing the video output of the intraoperative ultrasonography, these images can be overlapped with the preoperative MR images, allowing for real-time update.[11,13,23,24,29]

CONCLUSIONS

We found that frameless image-guided stereotaxy can be successfully used to assist in the resection of supratentorial malignant glioma (< 30 ml), if precautions to minimize brain shift are respected. In cases involving larger tumors and tumors located periventricularly, the use of intraoperative imaging to update data in real time is desirable to increase resection accuracy.

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