Although surgical intervention to obtain tissue diagnosis is an established component of therapy for the management of intracranial neoplastic disease, controversy persists concerning what impact the extent of resection for high-grade gliomas may have on patient outcome. Attempts to relate outcome to type of surgical intervention (stereotactic biopsy, subtotal resection, or gross-total resection) have produced conflicting results. Some studies have found no significant correlation between the extent of resection and outcome in patients with high-grade gliomas. Other studies have revealed an inverse relationship between residual tumor volume and both the patient’s quality of life and length of survival.

An accurate assessment of the influence of residual tumor on patient outcome is dependent on a correct determination of residual tumor volume. Early studies relied solely on the assessment of the operating surgeon to determine the presence and extent of residual tumor, whereas recent studies show that postoperative imaging has become the standard. Because tumor response to adjuvant treatment is also assessed by computerized tomography (CT) and magnetic resonance (MR) imaging, these modalities have become increasingly important in the management of neurooncological disease. Appropriate evaluation of postoperative neuroimaging necessitates an accurate understanding of the effects of neurosurgical intervention on all intracranial contents. These changes have not been clearly defined with only a few studies published that describe postoperative MR imaging. Furthermore, early postoperative MR differentiation of residual tumor enhancement and enhancement of injured brain parenchyma is often difficult.

In this prospective clinical investigation, we obtained MR images in patients 1 postoperative day after they had undergone temporal lobectomies for epilepsy. The images were reviewed to determine postoperative changes in the nonneoplastic parenchyma, dura, and leptomeninges. The images were evaluated to assess the extent of tumor resection.
Clinical Material and Methods

Patient Population and Preoperative MR Imaging

Eleven patients (six female and five male) ranging in age from 12 to 55 years (median age 36 years) underwent temporal lobectomies for medically intractable epilepsy. Lesions with signal characteristics consistent with cavernous angiomas were present in two patients’ preoperative MR images, and a lesion consistent with a hamartoma appeared in one other. Eight patients had no structural lesion on preoperative MR imaging. The only parenchymal contrast enhancement observed was found in the center of the two cavernomas. Contrast enhancement was not observed in the pia-arachnoid or dura in any of the patients preoperatively.

Surgical Procedure

Each patient received a course of dexamethasone (4 mg every 6 hours beginning the night prior to surgery). General anesthesia was used in four operations and local anesthesia in seven. Standard temporal lobectomy techniques, including functional mapping and electrocorticography, were performed in all cases.29,38 The temporal lobe was resected in the subpial plane using an ultrasonic aspirator. The three preoperatively identified lesions were incorporated into the temporal lobe resection. Hemostasis of the resection bed was accomplished by lining the transected parenchyma and exposed pia-arachnoid with Surgicel.

Postoperative MR Imaging. Postoperative MR images were obtained the 1st day after surgery (range 17–28 hours after completion of surgery). Standard spin-echo T1-weighted (repetition time (TR)/echo time (TE) 480–800 msec/14–22 msec) and T2-weighted (TR/TE 2300–4600 msec/90 msec) images were followed by intravenous administration of 0.1 mmol/kg gadolinium diethylenetriamine pentaacetic acid (Magnevist; Berlex, Wayne, NJ). Postcontrast T1-weighted (TR/TE 800–960 msec/22 msec) images were obtained in a similar plane as the noncontrast images and in at least one other perpendicular plane. Other technical factors included a slice thickness of 4 or 5 mm; a 5- or 6-mm interslice gap; and one excitation. Five patients underwent scanning with a 1.0-tesla and six with a 1.5-tesla superconductive magnet (Magnetom; Siemens, Erlangen, Germany). A neuroradiologist (C.J.M.), blinded to the patients’ history, reviewed the postoperative images. The operative site, the meninges, and the extracerebral spaces at the craniotomy site were evaluated. The operative site was evaluated for parenchymal enhancement and, if present, was characterized as linear or nodular. The meninges were separated into the pia-arachnoid and the dura. Each was evaluated near the operative site and remote from the site. In evaluating the pia-arachnoid, an infratentorial location or a site contralateral to the operation was considered remote. Hemostasis of the resection bed parenchyma was accomplished by lining the transected parenchyma and exposed pia-arachnoid with Surgicel.

Results

Histological evaluation of the resected tissue confirmed the absence of neoplastic cells in all patients. The preoperative diagnosis of cavernous angioma was verified histologically in two patients as was a hamartoma in the third. Extraxial fluid, gas, and/or blood were present in all patients. These extraxial fluid collections occurred predominantly within the resection bed, did not appear enhanced, and displayed heterogeneous signal characteristics. Enhancement of the resection bed parenchyma occurred in seven (64%) of 11 patients (five linear, one linear and nodular, and one nodular; Fig. 1). In three of the remaining four patients, determination of parenchymal enhancement was obscured by extraxial fluid collections. Dural enhancement occurred adjacent to the resection site in all patients and remotely in 73%. Images in eight (73%) of 11 patients demonstrated enhancement of the pia-arachnoid of the ipsilateral cerebral convexity. Images in six patients (55%) demonstrated remote contrast enhancement of the pia-arachnoid: four overlying the cerebellum and two over the opposite cerebral convexity.

Discussion

Operative intervention for tumor resection profoundly alters the intracranial milieu and, consequently, complicates MR differentiation of tumor from nonneoplastic tissue. Accurate determination of residual tumor on postoperative images necessitates a detailed understanding of the effect of neurosurgical intervention on the normal intracranial contents. Efforts have been made to define these
changes and their evolution over time but findings have been inconsistent. Nevertheless, postoperative imaging has become the standard for determining the presence and extent of postoperative residual tumor.

**Magnetic Resonance Imaging Versus the Surgeon’s Estimation to Determine the Extent of Surgery**

Albert, et al., compared the presence of residual tumor based on the surgeon’s estimation to the presence of residual tumor as determined by postoperative MR imaging. The authors found that MR images revealed areas of enhancement consistent with residual tumor three times more often than predicted by the surgeons. Subsequent growth of tumor from areas of enhancement in 78% of recurrent cases confirmed the superiority of MR accuracy. Because tumor response to adjuvant therapy is also assessed by CT and MR imaging, these modalities have become integral to the postoperative standard of care management of neurooncological disease.

**Magnetic Resonance Imaging Versus Computerized Tomography to Determine the Extent of Surgery**

Magnetic resonance imaging affords greater spatial resolution than CT, and comparison studies have established that MR imaging has a higher resolution of enhancement as well. Runge and associates compared CT and MR contrast enhancement in a canine brain abscess model and determined that MR imaging was 20 times more sensitive to gadolinium (based on moles/kilogram of agent) than CT was to iodinated contrast media. For these reasons MR imaging has become the imaging study of choice for postoperative assessment and surveillance of patients with brain tumors.

**Obscuration of the Postoperative MR Image**

The two components of the postoperative image that are most likely to hinder accurate diagnosis of residual tumor are extraaxial fluid collections within the surgical bed and enhancement of normal brain following surgical trauma. Previous attempts to evaluate postoperative nonneoplastic enhancement have been confounded by residual nonneoplastic enhancement. By evaluating postoperative images of patients with histologically proven nonneoplastic disease we were able to avoid the additional variables introduced by residual tumor or peritumoral changes in brain adjacent to tumor.

**Etiology of MR Imaging Contrast Enhancement**

It has been established that areas that are enhanced following contrast administration on preoperative images of intracranial neoplastic disease generally correspond to areas of gross tumor. Breakdown of the blood-brain barrier, luxury perfusion (altered vascular autoregulation), and hypervascularity (neovascularity) are pathophysiological changes that have been implicated as causes of tumor contrast enhancement. Histopathological correlation has shown that contrast enhancement corresponds to densely cellular, hypervascular tumor tissue and does not appear to occur in the zone of microscopic tumor infiltration that surrounds many high-grade gliomas. The surrounding zone of tumor-infiltrated parenchyma corresponds to the nonenhancing high signal regions seen on $T_2$-weighted images. Although breakdown of the blood-brain barrier with intratumor extravasation of contrast material does occur, preoperative tumor enhancement appears to be caused primarily by hypervascularity. Each of the proposed mechanisms for contrast enhancement appears to be involved in the production of contrast enhancement postoperatively.

Jeffries, et al., performed partial parietooccipital lobectomies on dogs using a bipolar scalpel technique and documented postoperative changes with serial CT scans and histopathological examination. Contrast enhancement of the resection margin occurred approximately 7 days postoperatively, coincident with the appearance of neovascularity. After 4 weeks, both the enhancement and the neovascularity resolved. This temporal and spatial correlation supports the contention that contrast enhancement represents increased vascularity. The authors did not observe early postoperative enhancement and therefore recommended that postoperative scans be obtained prior to Day 7. The discrepancy between the findings of this report and our findings may be due in part to the authors’ use of a bipolar scalpel and our use of a ultrasonic aspirator. Cairncross and coworkers examined the postoperative CT scans of patients who had undergone partial resection or lobectomy for neoplastic disease. Although they reported no enhancement of the lobectomy resection margin, they did observe enhancement of the partial resection surgical bed after 5 days. Enhancement that was visible prior to postoperative Day 7 was attributed to residual neoplasm. These authors, like Jeffries, et al., recommended early postoperative imaging to avoid the confounding effect of benign enhancement from nonneoplastic hypervascularity. Others have reported contrast enhancement by CT as early as Day 3 postoperatively.

Laohaprasit, et al., studied serial CT scans in patients who underwent lobectomies for nonneoplastic disease. These authors found contrast enhancement of the resection bed on postoperative Day 3 in the absence of neoplastic pathology. Contrast enhancement persisted at postoperative Day 7 but not at Day 30.

Elster and DiPersio studied contrast-enhanced MR images in 46 patients who had undergone intracranial surgery for neoplastic and nonneoplastic pathology. The time from operation to MR imaging ranged from 1 day to 40 years. The authors observed dural enhancement in all patients in whom images were obtained within the 1st postoperative year and pial or brain enhancement in four of six patients in whom images were obtained in the 1st month. Because the authors were attempting to define enhancement of nonneoplastic tissue, areas of “contrast enhancement at the operative site immediately adjacent to the tumor bed” were not included in the results. They did, however, report finding brain enhancement at the surgical site in two patients in whom images were obtained at 18 and 72 hours postoperatively and hypothesized that this represented extravasation or leakage of contrast material from the margin of the parenchymal incision.

Albert, et al., examined the postoperative MR images of patients who had undergone resection of high-grade gliomas. Differentiation between benign enhancement and contrast enhancement of residual tumor was based on the spatial configuration of the contrast enhancement (that...
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is, linear vs. nodular) and on the subsequent appearance of follow-up images. Using these criteria, these authors determined that 12% of the contrast-enhancing areas was not representative of residual tumor. Nontumor contrast enhancement was generally linear; it usually appeared during the 2nd postoperative week but was seen as early as 4 days postoperatively in some cases. Enhancement of the parenchyma prior to postoperative Day 4 was not observed.

Leptomeningeal Enhancement

Profound and widespread dural and leptomeningeal enhancement also appears in the immediate postoperative period.1 Albert, et al.,2 analyzed postoperative MR images in 60 patients who had undergone resection of high-grade gliomas. The authors did not separate the dura from the pia-arachnoid and observed meningeal enhancement in 20% of the patients and enhancement at the site of resection in 70%. We observed dural enhancement on MR images obtained in all of our patients and enhancement of the pia-arachnoid in more than 70%. The etiology of this early enhancement of the pia-arachnoid and dura may include extravasation of contrast at the operative site, but the widespread distribution makes this less likely. The separation of the leptomeninges from the small vessels within the sulci can pose difficulties in MR imaging. The possibility that this is a similar phenomenon to that described by Elster and Moody16 in cerebral infarction as the “meningeal enhancement sign” should also be considered. As the enhancement seems to be greatest near the operative site and the least farther away, the possibility of mechanical causes (for example, compressive effects caused by surgery or postoperative extracerebral fluid collections) should be considered. That both of the patients in whom leptomeningeal enhancement was observed over the convexity opposite the temporal lobectomy had some mass effect at the time of scanning supports this possibility. Another possibility is that the contrast agent remains within blood vessels and the enhancement is due to slowed blood flow. Confronting this possibility is the close approximation of the increased signal to the gyral surface. Enhancement was observed on several contiguous slices, which would mitigate against the serpentine course of the blood vessels. Another alternative, particularly in situations in which the contrast enhancement is quite thick, is cortical enhancement. From the absence of neurological dysfunction we can infer that this is not the case.

In our study, the absence of neoplastic disease allowed us to evaluate benign contrast enhancement without the confounding enhancement of residual tumor or peritumoral brain. We found enhancement of brain adjacent to the resection during the immediate postoperative period in over 60% of cases. Although thin and linear in most cases, enhancement was nodular in two instances. Our results, in light of previously reported findings, lead us to suggest that postoperative contrast enhancement of normal brain results from a series of pathophysiological changes. Contrast enhancement of the parenchymal incision in the immediate postoperative period occurs well before angiogenesis and, as suggested by Elster and DiPersio,13 most likely represents the extravasation or leakage of contrast agent at the resection margin. Neovascularization of the resection bed produces parenchymal contrast enhancement which appears during the 2nd postoperative week.2,6 Parenchymal enhancement occurring between postoperative Days 4 and 7 may represent a combination of extravasation and hyperemia.

Based on their findings, Albert, et al.,2 recommended postoperative imaging during the first 3 postoperative days to avoid benign contrast enhancement that occurred no sooner than Day 4. Our results indicate that benign parenchymal contrast enhancement actually occurs as early as 17 hours postoperatively. Extensive dural and leptomeningeal enhancement also appears in the early postoperative period. Although exogenous steroids reduce the degree of tumor contrast enhancement,6,11,25 our results indicate that perioperative steroid administration does not prevent early benign postoperative enhancement. Nevertheless, we agree that early postoperative MR imaging affords the best opportunity to differentiate benign contrast enhancement from residual tumor.2,14,39 Once angiogenesis has begun in the resection bed, differentiation of tumor hypervascularity from parenchymal hypervascularity can be determined radiographically only by serial MR images. Benign contrast enhancement from vascularization of the parenchymal incision can thicken and become nodular but, unlike residual tumor, it remains localized to the resection margin and usually resolves after several weeks, concurrent with formation of the glial scar.2,6,14,39

Magnetic Resonance Imaging of Postoperative Extraaxial Fluid

Extraaxial fluid collections were noted in the resection bed in each case reviewed in our series. These collections were thought to represent a mix of extravasated blood, cerebrospinal fluid containing proteins and/or blood, and Surgicel. DiChiro and coworkers4 examined changes in the CT appearance and MR signal characteristics of stagnant blood in vivo and in vitro. Serial images of blood injected intraparenchymally in a primate model revealed increased attenuation within 2 hours on CT, with gradual return to normal brain density by approximately 10 days. Using MR imaging, the hematomas appeared dark on T1- and bright on T2-weighted images at 2 hours. Between 24 and 48 hours postinjection, the clot became hypointense to isointense on T1-weighted images and hypointense with a bright surrounding halo on T2-weighted images. Although the hematoma did not become hyperintense on T2-weighted images until postoperative Day 6, by postoperative Day 10 it had become bright on T2-weighted images as well. Changes in signal characteristics were attributed to degradation of hemoglobin to the more paramagnetic metahemoglobin. Signal characteristics of clots maintained in vitro displayed comparable time-dependent changes and chemical analysis confirmed a correlation between changes in relaxation times and metahemoglobin concentration. Although intraparenchymal hemorrhage per se was not seen in our postoperative images, each study revealed extraaxial fluid collections within the operative site. Signal characteristics differed significantly from those described by DiChiro and coworkers. The fluid col-
lections were heterogeneous; however, each displayed areas of high signal intensity on both $T_1^*$ and $T_2^*$-weighted images as early as 17 to 28 hours after operation. Other authors have noted an early high intensity signal within the postoperative site.\(^2\)\(^\text{26}\) We infer from the data that these areas represent accelerated methemoglobin formation secondary to use of hemostatic oxidizing agents.\(^2\)\(^\text{26}\) Although these extraaxial fluid collections were not enhanced after contrast administration, there was obscuration of the resection bed in three of 11 cases.

**Conclusions**

Contrary to previous reports, contrast enhancement of nonneoplastic human brain parenchyma can occur as early as 17 hours postoperatively. Benign parenchymal contrast enhancement is usually, but not always, linear in appearance. Nonneoplastic dural and leptomeningeal enhancement can be profound both adjacent to and distant from the surgical site. Extraaxial fluid collections can display signal characteristics consistent with methemoglobin within the first 28 hours postoperatively and can hinder radiological evaluation of the resection bed. Based on our findings, we suggest that postoperative MR imaging be obtained within 28 hours of surgery (prior to the development of neovascularization). However, even early images should be interpreted with caution, bearing in mind that MR changes can be seen by 17 hours postoperatively.

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**J. Neurosurg. / Volume 84 / February, 1996**
Early postoperative magnetic resonance imaging


Manuscript received February 21, 1995.
Accepted in final form July 18, 1995.
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