Neuronavigation

INTRAOPERATIVE COMPENSATION FOR BRAIN SHIFT

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BACKGROUND
Tumor removal, brain swelling, the use of brain retractors, and cerebrospinal-fluid drainage all result in an intraoperative brain deformation that is known as brain shift. Thus, neuronavigation systems relying on preoperative image data have a decreasing accuracy during the surgical procedure. Intraoperative image data represent the correct anatomic situation, so their use may compensate for the effects of brain shift.

METHODS
In a series of 16 brain tumor patients, we used intraoperative magnetic resonance (MR) imaging to obtain 3-D data, which were then transferred to the microscope-based neuronavigation system. With the help of bone fiducial markers these images were registered intraoperatively, updating the neuronavigation system.

RESULTS
In all patients the updating of the neuronavigation system with the intraoperative MR data was successful. It led to reliable neuronavigation with high accuracy; the mean registration error of the update procedure in all patients was 1.1 mm. The updating procedure added about 15 minutes to the operation time. In all patients the area suggestive of remaining tumor was reached and the additional tumor could be resected, resulting in a complete tumor removal in 14 patients. In the remaining patients extension of the tumor into eloquent brain areas prevented a complete excision.

CONCLUSIONS
The update of a neuronavigation system with intraoperative MR images reliably compensates for the effects of brain shift. This method allows completion of tumor removal in some difficult brain tumors.

KEY WORDS
Accuracy, brain shift, intraoperative imaging, intraoperative magnetic resonance imaging, intraoperative ultrasound, neuronavigation.

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It is a well-known fact that the accuracy of neuronavigation systems decreases during the surgical procedure. This is caused by different factors, all summarized by the so-called brain shift, an intraoperative deformation of the brain during surgical manipulation that depends on a variety of factors, mainly gravity (i.e., patient positioning), brain swelling, and the different surgical maneuvers [4,6,15,19].

The extent of brain shift, first described by Kelly et al [17], who observed a displacement of small steel balls in tele-radiography, has been evaluated by different methods in the last years. Navigation systems have been used to measure the extent of brain shift, relying on pointer-based [6,15], mechanical arm-based [29], or autofocus/laser-based techniques [26]. On the other hand, intraoperative imaging has led to a clear delineation of the extent and distribution of brain shift. Ultrasound examinations [4,16] and later the intraoperative use of magnetic resonance imaging (MRI) [8,19] also allowed the first quantitative analyses of the behavior of subsurface structures which were not accessible by the navigation systems that evaluate only the deformation of the brain surface. In particular, the comparison of pre- with intraoperative volume datasets obtained by MR imaging allowed evaluation of the extent of brain shift for the whole brain [23]. In this series of 64 patients the shift of the cortical surface was up to 23.8 mm and the shift of the deep tumor margin varied between a movement toward the cortical surface of up to 30.9 mm and a sinking of up to 7.9 mm. All results proved the marked interindividual variability of the extent of brain shift.

Recently, mathematical models have been developed that try to describe the behavior of the brain during surgery [7,14,21,22,25,27]. Up to now, no reliable prediction of brain shift is possible. Intraoperative imaging is the most useful method of demonstrating the 3-D anatomic structure of the brain during surgery. This information allows the

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1 Overview of Patients (n = 16) in Whom an Intraoperative Update of Neuronavigation Was Performed

Patient No.	Age [years], Gender	Diagnosis (WHO grade) Location	Navigation Microscope	Functional Navigation Modalities	MRE [mm]	Further Tumor Removal	Complete Resection
1	45, M	Oligodendroglioma (II) rt precentral	NC4	MEG & fMRI	1.2	ø	yes
2	50, F	Astrocytoma (III) rt frontal	NC4	ø	1.3	+	yes
3	8, M	Oligodendroglioma (II) rt parietal	MKM	ø	0.39	+	yes
4	68, M	Glioblastoma (IV) rt precentral	MKM	MEG	0.79	+	no
5	31, F	Glioblastoma (IV) lt precentral	MKM	MEG & fMRI	1.5	+	yes
6	51, F	Oligodendroglioma (III) lt frontal	NC4	MEG	1.1	ø	yes
7	21, F	Astrocytoma (I) rt postcentral	NC4	MEG & fMRI	1.1	+	yes
8	27, M	Astrocytoma (I) lt frontal	MKM	ø	0.80	+	yes
9	45, M	Astrocytoma (III) lt precentral	MKM	MEG	2.3	+	yes
10	37, M	Astrocytoma (II) rt precentral	MKM	MEG	2.0	+	yes
11	26, F	Neurocytoma lateral ventricles	MKM	ø	0.90	+	yes
12	34, F	Astrocytoma (II) rt precentral	NC4	MEG	0.94	+	yes
13	52, M	Oligodendroglioma (II) lt temporal	NC4	ø	0.57	+	yes
14	42, M	Astrocytoma (II) rt postcentral	NC4	MEG	0.90	+	yes
15	32, M	Glioblastoma (IV) lt frontal	MKM	ø	0.77	ø	yes
16	26, M	Oligoastrocytoma (III) rt postcentral	MKM	MEG	2.1	+	no

F, female; M, male; rt, right; lt, left; WHO, world health organization; MKM/NC4, navigation microscopes; MEG, magnetoencephalography; fMRI, functional magnetic resonance imaging; MRE, mean registration error.

surgeon to compensate for the effects of brain shift, using the intraoperative 3-D MR data as a basis for re-referencing the neuronavigation system, resulting in an "update" of the neuronavigation system [33].

We performed intraoperative MR imaging in a group of patients undergoing craniotomy for brain tumor surgery. In case of remaining tumor or an intraoperative finding being suggestive of remaining tumor, a "second look" was performed. We analyzed the feasibility of the neuronavigation update procedure, how it could be integrated into the surgical workflow, and whether it resulted in completion of the tumor removal.

Patients and Methods

In 16 patients (10 male, 6 female, age range 8–68 years, mean: 37.2 years) an intraoperative update of neuronavigation data was performed (Table 1). The results of the histopathological examination are given in Table 1. These 16 patients were part of a lesser group of 145 patients undergoing craniotomy for tumor resection (mainly glioma patients) in which intraoperative imaging was used in combination with a microscope-based neuronavigation system. Of these, in 35 patients intraoperative imaging resulted in a finding that was suggestive of remaining tumor that was at least partially removable so that the surgeon decided to continue surgery. An update of the navigation system was performed only in those patients in whom it seemed likely that the suspicious area would not be reliably located again in the surgical field.

Neuronavigation

For intraoperative imaging, the patient's head was fixed in an MR-compatible ceramic headholder (Brandis Medizintechnik, Weinheim, Germany). All surgical procedures were performed under general anesthesia. The local ethics committee had approved intraoperative MR imaging including intraoperative patient transport, and all patients signed a consent form.

The preoperative 3-D MR datasets (see below) were registered with the patient by 8 to 10 skin-attached fiducials using the autofocus system of the neuronavigation microscope. Two different microscopes were used: the MKM and the NC4 microscope (both: Zeiss, Oberkochen, Germany). When the MKM microscope was used, intraoperative patient transport was necessary for intraoperative imaging, because the MKM cannot be operated in the magnetic field of the MR scanner and because it would severely disturb intraoperative MR imaging [30]. Just before scanning, the patient, lying on an air-cushioned OR table, was moved a distance of about 4 m from the adjacent conventional operating theater, where the MKM is placed, into the center of the MR scanner within the radiofrequency-shielded OR. Starting in May 1999, we used the NC4 microscope, which can be placed in the low magnetic field of the scanner near the 5 gauss line. The patient was lying on the movable table of the MR scanner; for imaging this table could be moved into the center of the scanner in less than half a minute.

Functional data from either magnetoencephalography (MEG) or functional MR imaging (fMRI) to identify eloquent brain areas such as the motor cortex, the sensory cortex, speech related areas, and the visual cortex were integrated in 10 of the 16 patients in their preoperative 3-D MR image data. Details of these techniques have been published previously [9,24].

IMAGING

Pre- and intraoperative MR imaging was performed with a 0.2 Tesla Magnetom Open scanner (Siemens AG, Erlangen, Germany) which is located in the radiofrequency-shielded part of our 'twin operating theater' [30, 32]. MR volume data were measured using a T1-weighted 3-D FLASH gradient echo sequence (FLASH: fast low angle shot, TE: 7.0 ms, TR: 16.1 ms, flip angle: 30°, slab 168 mm, 112 slices, FOV: 250 mm, matrix: 256 × 256).

If the tumor showed enhancement on the preoperative images, MR contrast agent (20 mL Gadolinium-diethylenetriamine pentaacetic acid) was given i.v. just before the scanning procedure. The 3-D image data were used to evaluate the extent of tumor resection. In the glioma patients a more extensive imaging protocol (not part of this study) was applied. It included T2-weighted and inversion recovery sequences, allowing a better detection of tumor remnants and giving further information in cases of contrast media leakage at the resection border or diffuse spreading of contrast enhancement because of surgical manipulations.

Five MR-visible bone fiducials (Howmedica-Leibinger, Freiburg, Germany) were placed around the craniotomy opening as a prerequisite for intraoperative updating of the navigation system.

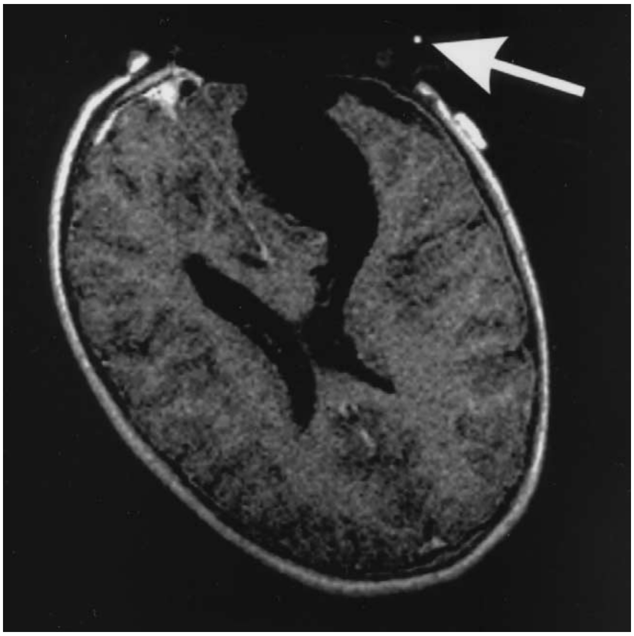
For imaging the head position was not changed compared to the placement at the site of surgery, and the scalp remained retracted by MR-compatible titanium hooks. We avoided the use of hemostatic material in the resection cavity before imaging, which could have generated artifacts. After irrigating the resection cavity, the craniotomy was covered by sterile draping and the patient was moved into the center of the scanner for imaging. The use of brain retractors was kept to a minimum in our patients; when applied they had to be removed before imaging. When they were needed after the update of the neuronavigation they were repositioned only under microscope view to ensure, that the segmented area of interest was not moved by the placement of the retractors.

UPDATE OF NEURONAVIGATION

If intraoperative MR imaging showed remaining tumor and further resection was possible, an update of the neuronavigation system was performed. The intraoperative 3-D MR image data were transferred via ethernet to the neuronavigation system (MKM/NC4). The intraoperative reference markers (bone fiducials) were identified on the intraoperative images with standard navigation software (STP 4.0, Zeiss, Oberkochen, Germany). In addition, the suspicious area was segmented and the approach was planned. Then, registration with these markers completed the navigational update. As an estimate of the accuracy of the updated neuronavigation the mean registration error, a technical measure calculated by the navigation software using the fiducial coordinates (root mean square error) was documented. Furthermore, the accuracy was checked by repeated landmark verifications; that is, it was verified whether the position of fiducial or anatomic landmarks that could be easily identified with the autofocus pointer of the microscope was depicted correctly by the MR image data.

Results

In all patients it was possible to perform an intraoperative update of the neuronavigation system. In two patients (no. 5 & 16) the bone fiducials (Figure 1) were not clearly visible on the intraoperative MR images. In these two patients skin fiducials, which



1 Display of a bone fiducial (arrow) in the intraoperative images (patient 3), which is used for referencing the intraoperative MR images. A skin fiducial is also visible.

were attached to the patient's skin a day before surgery for registration of the preoperative image data, could be used also for the intraoperative referencing. The intraoperative registration resulted in neuronavigation with high accuracy. The calculated individual mean registration error was between 0.39 and 2.3 mm (mean: 1.1 ± 0.55 mm) (see Table 1).

The time required for the different steps of intraoperative imaging and the neuronavigation update is summarized in Table 2. The update procedure added about 15 minutes to the operating time, mainly needed for segmentation and re-referencing. Depending on which neuronavigation microscope was used, intraoperative imaging required 35 (MKM) or 16 minutes (NC4). In cases in which further imaging studies were conducted (e.g., T2-weighted sequences) additional time was needed for these measurements.

The updated neuronavigation reliably guided the surgeon in all cases to the area that was suspected to contain remaining tumor. In three patients (no. 1, 6, and 15) the histopathological examination of this area revealed no tumor. Complete tumor removal was confirmed by early scanning in all three of them. In patient 15 intraoperative contrast media extravasation mimicked remaining tumor; in patients 1 and 6 edematous changes on the intraoperative T2-weighted images at the resection border were interpreted as tumor remnants.

The intraoperative update of the neuronavigation system with continued tumor removal led to macroscopically complete tumor removal in 14 out of the 16 patients. In two patients an extension of the tumor into eloquent brain areas prohibited complete removal. As an illustrative example, Figure 2 depicts the intraoperative update in a 42-year-old male patient (No. 14) with a right postcentral astrocytoma (WHO grade II).

In one patient (12) an aggravation of the neurological deficit occurred. Because of the resection of the supplementary motor area she developed a nearly complete paresis of her left arm, which resolved nearly completely in the following four weeks. We did not encounter a wound infection or rebleeding in this small group of patients.

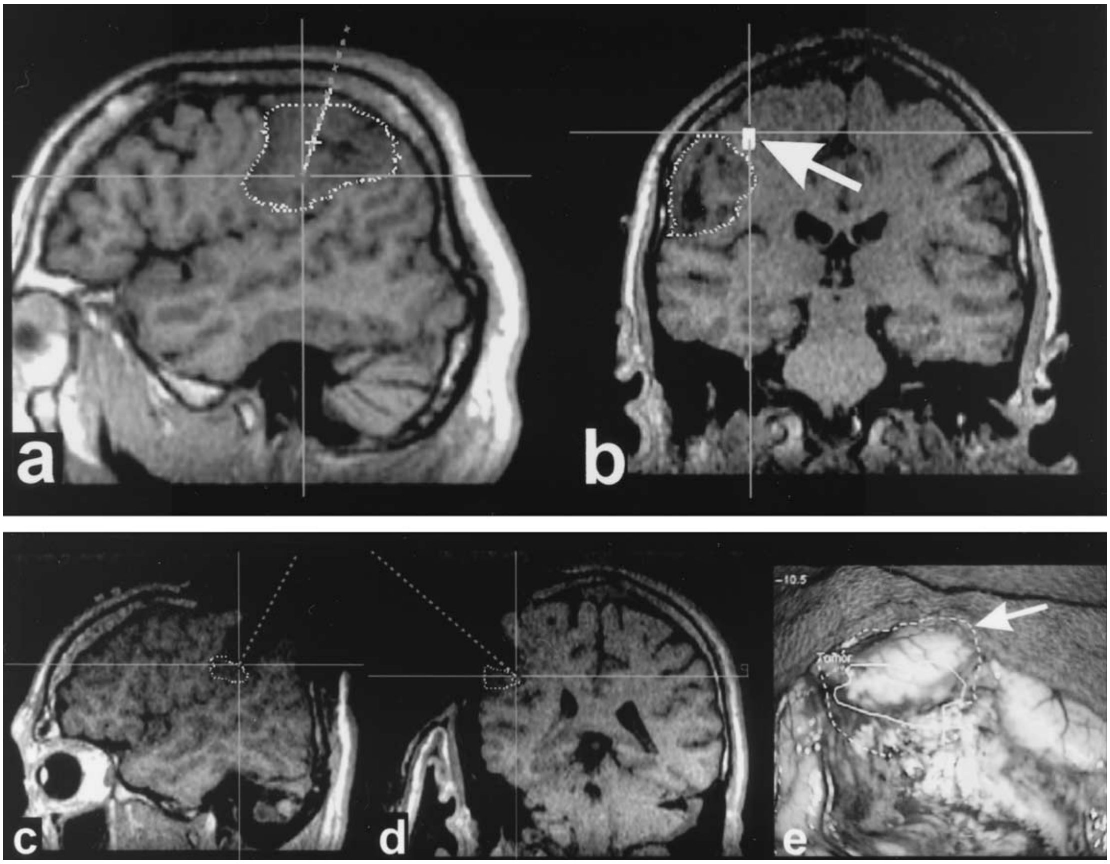
Discussion

The intraoperative update of the neuronavigation system with intraoperative MR image data are a reliable way to compensate for the effects of brain shift [33]. In all patients it resulted in a high degree of accuracy. The area suggestive of remaining tumor was easily found in all cases. Histopathological examination revealed tumor tissue in 13 patients, which was further removed. A macroscopic complete tumor removal was finally achieved in 14 of 16 patients. In three patients intraoperative imaging suggested residual tumor, but the histology was

2 Intraoperative Workflow and Average Time Needed for Intraoperative Imaging and Neuronavigation Update in Relation to the Applied Navigation System (MKM or NC4)

	Navigation System	
Procedural Step	MKM	NC4
1. Placement of bone fiducials	2 min	2 min
2. Patient transport into the scanner	10 min	0.5 min
3. Intraoperative scanning (3-D MR dataset)	15 min	15 min
4. Patient transport to the operating position	10 min	0.5 min
5. Data transfer MR scanner→ neuronavigation system	2 min	2 min
6. Definition of reference points, segmentation of suspicious area	5 min	5 min
7. Intraoperative re-referencing	5 min	5 min
Time needed for neuronavigation update (1+5+6+7)	14 min	14 min
Total time	49 min	30 min

Steps 2 to 4 are required for intraoperative imaging (italic).



2 42-year-old male patient (14) with a right postcentral astrocytoma (WHO grade II). **A**,**B:** sagittal and coronal views of the navigation screen displaying the preoperative images. In the coronal plane a white square (arrow) depicts the localization of the functional information from magnetoencephalography (somatosensory evoked fields) integrated in the preoperative images. **C**,**D:** sagittal and coronal view of the navigation screen after the intraoperative update of the navigation system. The remaining tumor is segmented. **e:** intraoperative view, the dotted line (arrow) delineates the maximum extension of the remaining tumor perpendicular to the viewing axis. The white line delineates the extension in the focal plane.

negative. In one of them contrast media leakage into the resection cavity mimicked remaining tumor. In the two other patients surgically induced edematous changes at the resection border were interpreted as remaining tumor on the T2-weighted sequences. The comparison of pre- with intraoperative scans (Figure 2 **A**,**B** with **C**,**D**), which were obtained with the same scanner, shows a reduction of intraoperative image quality. This is because of external artifacts from the electrical anesthesia equipment, artifacts from the surgical field as described above, and the need to use a separable MR coil for intraoperative imaging, which results in lower image quality compared to the coil used in preoperative scanning. Intraoperative image quality was sufficient to delineate the extent of the resection in the majority of cases.

Nevertheless, intraoperative imaging with neuronavigation update is a complex, expensive, and also time-consuming procedure, which should be restricted to certain situations. In our opinion, it is not necessary to perform the update procedure if intraoperative imaging shows a remaining tumor that is easily accessible and that can be identified in the surgical field without difficulty.

If intraoperative imaging is available and the combination of neuronavigation with intraoperative imaging is favored, it is the most elegant method to compensate for the effects of brain shift. There are two main approaches to performing intraoperative MR imaging. As a first option a system like the Signa SP “double doughnut” scanner (GE, Milwaukee, WI) can be used. Because the patient is lying in the scanner during the whole procedure it is possible to use the scanner as a navigational device directly [1,2]. Sequences with scanning times of only a few seconds allow a nearly online orientation in the surgical field. However, this has the drawback of low image quality. Nearly all other MR systems used in a neurosurgical operating theater, like the low-field systems Magnetom Open (Siemens AG, Erlangen, Germany) [30,32] and Airis II (Hitachi Medical Corporation, Tokyo, Japan) [3], as well as the high-field systems from Philips Medical Corp. (Gyroscan ACS-NT) [11] and IMRIS Corp. (Neuro II) [31] necessitate some kind of intraoperative transport, either of the patient or of the system itself, when craniotomy procedures are performed. In these setups an online orientation is not possible. In consequence, the described update procedure is the most suitable method to provide orientation in the surgical field, compensating for the effects of brain shift. The integration of a navigation system into the GE scanner, as recently proposed [28], also allows online orientation in this system with high-quality 3-D intraoperative MR data, which needs some minutes scanning time.

An alternative to intraoperative MR imaging is intraoperative ultrasound, especially intraoperative 3-D ultrasound [4,5,13,16]. Whether image quality to evaluate the extent of a glioma resection is equivalent among the different imaging modalities is still controversial. However, intraoperative ultrasound has the advantage of being a real-time modality. Ultrasound data may provide information on how to modify high-quality preoperative MR image data to represent the real intraoperative situation, thus compensating for the effects of brain shift. This approach relies on the non-linear registration of intraoperative ultrasound data with preoperative MR volume data. The MR data are modified by using a mathematical model describing the movement of the brain during surgery [10,18,27].

Instead of using ultrasound images to adapt preoperative image data, so-called sparse data (i.e., measured movements of some known landmarks) are used in mathematical models that try to predict the deformation of the brain [22,27]. Based on the known movement of the scanned brain surface, it might be possible to compute the movement of subsurface structures. The mathematical models mostly rely on finite element methods [7,20]. However, it is too early to predict whether these approaches will be successful in the individual patient, since intraoperative MR examinations for quantification of brain shift have shown a great inter-individual variability [23]. Furthermore, it is also influenced by a variety of internal and external factors during the surgical procedure.

Up to now, updating the neuronavigation system with intraoperative MR image data seems to be the most reliable way to compensate for the effects of brain shift. Nevertheless, this update is an anatomic update only. Functional information (for example from MEG and fMRI) integrated into the preoperative dataset for functional neuronavigation, is lost in the update procedure. Nonlinear registration techniques including sophisticated techniques from pattern recognition analysis may allow a matching of preoperative MR data sets containing functional information with intraoperative MR image volumes. This will result in a compensation for the effects of the displacement of functional markers [12,34]. These techniques may not be necessary for the preservation of functional markers used for the identification of eloquent brain areas at the cortical surface. However, they will be indispensable when further information, such as the displaced course of brain pathways imaged by diffusion weighted imaging or vascular structures, is integrated in the navigational setup. Reliable neuronavigation should also be available during the critical steps of a tumor resection; for example, when the deep tumor margin is accessed, normally at a late stage of surgery. In this situation the negative effects of brain shift have already significantly decreased the accuracy of the neuronavigation system. To use neuronavigation for subsurface structures the information should be displayed reliably, including not only the tumor border but also the surrounding anatomy with pathways and the localization of function. To reach this goal, brain shift has to be compensated for.

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COMMENTARY

Nimsky et al present 16 patients who had surgery in the intraoperative MR unit and during surgery required re-registration of their imaging data in the neuronavigation system because of brain shift. These 16 patients were out of entire cohort of 145 patients. This re-registration allowed a complete radiographic tumor resection in 14 of the 16 patients. The other 2 patients had tumor infiltration into eloquent cortex, preventing complete resection. The registration error was 1.1 mm and the time added to the operative procedure was only 15 minutes.

The importance of the paper is that the authors clearly define how frequently brain shift is an issue with tumor resections (11%). They also document how long the additional imaging and re-registration take. This information is of great use to neurosurgeons who use intraoperative MRI guidance during tumor resections. As intraoperative MR units increase in number, this article will provide neurosurgeons who are unfamiliar with the MRI environment with important information on the issues described herein. This work has much clinical applicability, particularly as the interest in intraoperative MR imaging continues to escalate around the world. This group is one of the leaders in the development of this technology. The feasibility of updating imaging information during surgery with the intraoperative MR is convincingly demonstrated in their work.

Because of neurosurgeons' reliance on imaging either before or during surgery, this work will be increasingly important to practicing neurosurgeons. This group convincingly demonstrates how to compensate for brain shift, which is the primary concern of neurosurgeons using neuronavigational systems.

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The problem of using preoperatively acquired images for intraoperative navigation is central to all navigation systems presently available. In this article, Nimsky et al. point out the difficulties with using preoperative images throughout a resection procedures. The Surgical Planning Laboratory at Brigham and Women's Hospital has also demonstrated the importance of this problem by showing two kinds of shift, one of which is surface and can be modeled, the other subsurface and difficult to model [1]. This problem may be responsible for the difficulty in using preoperative images to guide resection, as noted by Dr Nimsky et al.

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The incorporation of co-registered image guidance systems and of intraoperative MRI units into routine neurosurgical practice has progressed rapidly. This paper by Nimsky and colleagues contributes to our understanding of how this technology may advance the field by presenting a credible clinical experience, a focus on the practical problem of brain shift, and perhaps most importantly, a very balanced perspective. Not every case requires every technology, and no one technology is the optimal solution to the complexity of problems confronting operative neurosurgery.

At the present time, intraoperative MR imaging is providing the most reliable and data-intense updated information for the surgeon. The authors' methodology for using that resource is reasonable and appropriate. There remain areas of difficulty, of course, and these include inefficiencies with respect to operative procedure and time, changes in the surgical field between imaging and resumed operating that may result from such steps as retractor repositioning and irrigation, and incorporation of preoperatively obtained data, such as physiological mapping, into the intraoperatively acquired images (a problem the authors and others are working on).

Where along the spectrum of imaging technologies we eventually settle for intraoperative imaging needs is, at this time, not at all clear. It is unlikely that the operating room will have to replicate all the functionality of our extra-operative facilities. The incorporation of stereotactic (i.e., co-registration) principles and increasingly more sophisticated registration and deformation algorithms will undoubtedly enable worthwhile efficiencies of time and