Neuronavigation by Intraoperative Three-dimensional Ultrasound: Initial Experience during Brain Tumor Resection

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OBJECTIVE: Three-dimensional (3-D) ultrasound is an intraoperative imaging modality used in neuronavigation as an alternative to magnetic resonance imaging (MRI). This article summarizes 4 years of clinical experience in the use of intraoperative 3-D ultrasound integrated into neuronavigation for guidance in brain tumor resection.

METHODS: Patients were selected for inclusion in the study on the basis of the size and location of their lesion. Preoperative 3-D MRI data were registered and used for planning as in other conventional neuronavigation systems. Intraoperative 3-D ultrasound images were acquired three to six times, and tumor resection was guided on the basis of these updated 3-D images.

RESULTS: Intraoperative 3-D ultrasound represents a good solution to the problem of brain shift in neuronavigation because it easily provides an updated, and hence more accurate, map of the patient’s true anatomy in all phases of the operation. Ultrasound makes it possible to follow the progression of the operation, and it improves the radicality of tumor resection by detecting tumor tissue that would remain if the imaging technology had not been used (in 53% of the cases). Integration of 3-D ultrasound with navigation technology solves the orientation problem experienced previously with two-dimensional ultrasound in neurosurgery. The technology makes it possible to directly compare intraoperative ultrasound and MRI data regarding visualization of the lesion. Ultrasound image quality is useful for guiding surgical procedures.

CONCLUSION: Intraoperative 3-D ultrasound seems to provide a time- and cost-effective way to update high-quality 3-D maps used in neuronavigation. (Neurosurgery 50:804–812, 2002)

Key words: Brain shift, Brain tumor surgery, Intraoperative imaging, Minimally invasive surgery, Neuronavigation, Sonography, Three-dimensional ultrasound

Neuronavigation systems have been demonstrated to convey several advantages in improved planning and performance of image-guided surgery (16, 40, 41). However, the conventional systems still have practical limitations owing to the lack of an intraoperative imaging modality to provide the surgeon with information regarding dynamic changes that occur during surgery. Intraoperative imaging technologies such as magnetic resonance imaging (MRI) and ultrasound have been demonstrated to be beneficial for monitoring the progression of the operation and for resection control (17, 24, 31, 38), as well as in coping with the brain shift that occurs during surgery (19, 22, 30). The optimal solution for the neurosurgeon would be a navigation system with high-quality, real-time, three-dimensional (3-D) imaging capabilities. Although this is not yet a reality, different approaches toward this ultimate goal have been presented by various companies and research groups in recent years.

Intraoperative MRI and intraoperative computed tomography (CT) give the surgeon an opportunity to obtain scans of the patient one or more times during surgery by transporting the patient in and out of the scanner. The advantage is an updated, high-quality, 3-D map that may be used for further guidance and resection control (23, 28, 34, 39). An important drawback is the relatively long image acquisition procedure (typically, a total of 20–60 min), which limits the practical number of acquired 3-D scans allowed during surgery. A registration technique is also required to calibrate these intraoperative 3-D scans to the patient.
Three-dimensional Ultrasound in Neuronavigation

Intraoperative MRI, in which the surgeon stands inside the magnet during surgery, provides the surgeon access to nearly-real-time two-dimensional (2-D) images as well as the opportunity to update the 3-D map in minutes without moving the patient (5, 6, 35). Drawbacks of this technique include high investment and running costs, limited working space, and special surgical equipment and system requirements. These systems do not, however, require a patient registration algorithm, because the images as well as the surgical instruments can be handled from the same reference system.

Preoperative MRI has been combined with intraoperative ultrasound in an attempt to provide the surgeon with an updated 3-D map (7, 18, 22, 33, 37). The preoperative MRI scans are modified during surgery according to landmark movements that are registered through ultrasound imaging. The ultrasound images are used in an indirect manner, i.e., only to provide information so that the MRI data set can undergo an elastic warping procedure.

Ultrasound has been used directly for guidance. In these studies, ultrasound seems to provide valuable information in terms of updated 2-D images several times per second, but image quality varies (3, 9, 11, 13, 15, 25, 43). However, efforts have been made to improve the image quality in terms of technical adjustments of parameters (13) and optimal clinical setup (G Unsgaard, A Gronningsaeter, S Ommedal, TAN Hernes, submitted for publication). To enable guidance of surgical instruments by means of real-time 2-D images, the scan plane must be aligned so that the instrument is observed properly at all times. This is challenging and time consuming even for an experienced user. This orientation problem has been solved by combining 3-D ultrasound and navigation technology (13, 38). The surgeon may update the 3-D map in seconds during surgery and navigate directly on a map that reflects the patient’s true anatomy without a requirement for patient registration and probe adjustment procedures. All of these improvements, including the future capabilities of real-time 3-D imaging and the relatively lower costs of the equipment, as compared with present alternatives, may establish ultrasound in future neuronavigation. This article describes the initial clinical results and experiences from 1997 to 2001 in Table 1.

Ultrasound equipment

Different solutions and equipment were used in the present study because of the continuous development of the technology. From 1997 to 2000, we used a two-rack prototype consisting of a high-end System FiVe ultrasound scanner (GE Vingmed Ultrasound, Horten, Norway) and navigation software (developed in our group) integrated to an optical tracking system. Beginning in 2000, a high-end ultrasound scanner and a Polaris optical tracking system (Northern Digital, Waterloo, ON, Canada) were integrated with the navigation software into one single-rack navigation system, a prerelease version of the final product, SonoWand (MISON AS, Trondheim, Norway) (13) (Fig. 1). Since the study began in 1997, the system-user interface and the speed of data transfer have been improved considerably. The most recent prototype requires approximately 30 seconds for 3-D data transfer and reconstruction.

This combined system may be used as an ultrasound scanner, a conventional neuronavigation system, or an integrated, ultrasound-based neuronavigation system that uses features of both technologies. This makes it possible to present updated 3-D image volumes. The camera reads the position of the patient reference frame, the ultrasound probe, and surgical instruments such as a Caviron ultrasonic surgical aspirator (CUSA) (Valleylab, Boulder, CO) and biopsy forceps (Fig. 2). A 4- to 8-MHz flat phased-array probe (Fig. 2C) with optimal focusing properties at 3 to 6 cm was used in all cases. The ultrasound probe was covered with a sterile condom containing sterile gel. The scanner factory and clinical setups were optimized for brain surgery applications as described previously (13; G Unsgaard, A Gronningsaeter, S Ommedal, TAN Hernes, submitted for publication).

**TABLE 1. Patient Data**

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Total No. of Image-guided Procedures</th>
<th>Second Minicraniotomy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glioblastoma</td>
<td>19</td>
<td>52%</td>
</tr>
<tr>
<td>Anaplastic astrocytoma</td>
<td>11</td>
<td>54%</td>
</tr>
<tr>
<td>Low-grade astrocytoma</td>
<td>17</td>
<td>47%</td>
</tr>
<tr>
<td>Metastasis</td>
<td>17</td>
<td>65%</td>
</tr>
<tr>
<td>Meningioma</td>
<td>6</td>
<td>0%</td>
</tr>
<tr>
<td>Other tumors</td>
<td>21</td>
<td>24%</td>
</tr>
<tr>
<td>Total</td>
<td>91</td>
<td>45%</td>
</tr>
</tbody>
</table>
Preoperative preparation and planning

Five fiducial markers were placed at the following positions on the patient’s head: behind right ear, behind left ear, right forehead, left forehead, and parietal region. The patients were scanned using Picker (Picker International, Inc., Cleveland, OH) or Siemens (Siemens Medical Systems, Inc., Erlangen, Germany) 1.5-T MRI technology, and a high-resolution 3-D MRI volume with a slice thickness of 1.5 mm was acquired (Fig. 3A). The 3-D MRI volume was registered to the patient (Fig. 3B), and the surgical procedure then was planned in the operating room. The position of the craniotomy, and in some cases an additional minicraniotomy for the ultrasound probe, was planned on the basis of the preoperative images. In 45% of the cases (Table 1), a second minicraniotomy was used to obtain optimal image quality and surgical setup, as described previously (G Unsgaard, A Gronningsaeter, S Ommedal, TAN Hernes, submitted for publication).

3-D ultrasound acquisition and neuronavigational guidance

Immediately after exposure of the dura, sterile ultrasound gel was applied and the first 3-D ultrasound volume was acquired (Fig. 3C). The probe was tilted at angles of approximately 80 degrees over the anatomic area of interest by free-hand movement for 15 seconds. The pyramid-shaped 3-D data sets (Fig. 4A) were transferred to the navigation computer and reconstructed to a 3-D volume as described (13). However, no patient registration was needed for the 3-D ultrasound volume. When necessary, the maximum depth of the ultrasound image and the focus positions of the ultrasound beams were adjusted to obtain optimal image quality at the tumor location. In some of the more superficial lesions, a gelatin stand-off pad with a thickness of 1 to 2 cm was used to increase the distance between the probe and the lesion. This improved focusing conditions and ensured that a larger part of the tumor and surrounding anatomy was covered by the ultrasound sector. After 3-D acquisition, the ultrasound probe could be removed from the working area and image guidance could be performed on the basis of the acquired 3-D volume.

Tumor resection was performed using a CUSA (Fig. 3D) or biopsy forceps with positioning devices attached. Hence, the position of the surgical tool determined the images to be displayed on the navigation monitor. This made it possible to steer the tools down to the lesion as guided by the 3-D images. Preoperative MRI and intraoperative ultrasound images were displayed simultaneously. Slices from the 3-D volumes were displayed as ordinary orthogonal slices (Fig. 4B) or as single slices (any plane) from the 3-D volumes (Fig. 4C). The any-plane slice from the ultrasound 3-D volume was displayed according to the orientation of the surgical tool and not limited by the scan plane of the real-time 2-D ultrasound probe. Image slices that were lying parallel to the brain surface in a slice perpendicular to the ultrasound image scan plane then could be displayed easily and used for surgery guidance as needed (Fig. 4D). As in any other navigation system, the position of the pointer or surgical tool tip was displayed as lines and crosshairs in the corresponding images. Another 3-D update was acquired whenever tissue changes made it unsafe to proceed; typically, updates were obtained three to six times during a surgical procedure. At the end of each operation, the surgeon evaluated whether ultrasound had been essential to detect tumor tissue that would not have been found without this technology.
RESULTS

Interpretation of ultrasound imaging modality

Most neurosurgeons are more familiar with MRI and CT than with ultrasound images. In the present study, we found that it was important to be familiar with ultrasound imaging of the lesion early in the operation. After exposure of the dura, but before the resection was started, an initial 3-D ultrasound image was acquired. Corresponding slices from MRI and ultrasound 3-D volumes (similarly scaled and oriented) were then displayed simultaneously (Fig. 5). Preoperative MRI scans were useful, both for presenting an overview of the anatomy in areas where ultrasound images were not acquired and for learning to interpret information in the corresponding ultrasound images. In many cases, however, our experience was that ultrasound image quality was comparable to or even better than the corresponding MRI scans when tumor and landmark visualization were considered.
Faster and more precise image-guided resection

A sterile pointer is one of the most frequently used instruments in neuronavigation. We found, however, that a biopsy forceps or CUSA with an attached tracking device represented a safer and more effective way to perform image-guided surgery and navigation (Fig. 3D). The CUSA was calibrated in the operating room, and the images to be displayed on the monitor were determined. However, the conventional orthogonal patient-oriented slicing of the 3-D volume, as shown in Figure 6, made it quite challenging and time consuming to guide the procedure directly and follow the progression of the operation. Therefore, a more intuitive and user-friendly display technique frequently was used, i.e., the any-plane display technique, in which the slices displayed on the screen were selected by the surgical tool position and orientation (Fig. 4C). This made it possible to navigate the surgical tool more easily down to the lesion on the basis of a single slice from each 3-D volume without concentrating on the orientation of the patient on the operating table. This novel display technique also made it possible to interpret information from two or three image volumes simultaneously and thus easily follow the progression of the operation (Fig. 7). This user-friendly display technique also made it possible to effectively remove the central part of the tumor with no other visualization than 3-D images, thus reducing the pressure on surrounding brain tissue. This blinded procedure was performed initially only during the portion of the operation when the surgical tool could be navigated easily by safe margins to the normal brain. A cavity for direct sight was then established.

After some resection, when the resection cavity came closer to the tumor border, updates of the 3-D volumes were acquired and the resection was continued on the basis of updated image information. The microscope was used for work that demanded more precision closer to the tumor border. Resection proceeded on the basis of visual control until no tumor tissue was detected by the naked eye or through the microscope.

Removal of remaining tumor tissue

Toward the conclusion of the operation, another 3-D ultrasound volume was acquired. In our experience, ultrasound was important for detecting remaining tumor tissue that was not discovered through the microscope or by the naked eye (Fig. 7). Tumor tissue that was present behind the normal tissue, which therefore could not be observed with the microscope, often was detected on ultrasound images. The process of localizing residual tumor tissue required some experience, but the progression information, which was available in the preceding 3-D ultrasound volumes, simplified this task considerably. Position of anatomic landmarks and tumor border in relation to the resection cavity could be followed via images throughout the operation. Our subjective experience was that residual tumor tissue was discovered through the last 3-D ultrasound scan in 53% of the cases in which the resection otherwise was considered complete. Therefore, a more radical resection was achieved in these cases because of ultrasound imaging.

Practical considerations in the operating room

The SonoWand prototype is simple to place in the operating room, and it has adjustable cameras and a monitor arm, which makes it easy to optimize the ergonomic situation for

FIGURE 5. Correct scaling and orientation of the ultrasound images to corresponding 3-D MRI scans makes it easier to compare MRI and ultrasound imaging modalities and to interpret important information from both imaging modalities simultaneously. In many cases, the image quality of ultrasound was even better than that of MRI for locating tumor and landmarks. Examples of some of the tumor types included in the study, as visualized by corresponding any-plane slices of MRI scans (T1-weighted images, top row) and ultrasound (bottom row), include a metastasis (A), a glioblastoma (B), an anaplastic astrocytoma (C), and a low-grade astrocytoma (D).
In our experience, adjustments were occasionally necessary, however, to obtain visual contact between the camera and the surgical instruments. The system is easily transported in and out of the operating room (Fig. 1) and represents a compact and powerful system for surgical planning and intraoperative navigation. In our experience, the tight integration of ultrasound and neuronavigation represents an improvement as compared with conventional neuronavigation systems presently available.

**DISCUSSION**

The use of computer-assisted systems in neurosurgery has evolved since the 1980s. Most of these systems have been demonstrated to be useful, especially for planning the surgical procedure. The patient outcome of surgery, however, seems to be based on several factors; the extent of tumor resection is important, especially for a variety of gliomas as well as for pediatric tumors (1, 2, 4, 8–10, 12, 20, 21, 26, 29, 32, 36). Although conventional navigation systems seem to enhance the extent of tumor resection (41), these systems may have even more value when used in combination with an intraoperative imaging modality. This makes it possible to follow surgery progression via images as well as to control resection radicality toward the conclusion of surgery (38, 39, 42, 43). This also was demonstrated in the present study.

Intraoperative imaging technologies are now emerging in clinics and are being tested by research groups around the world. The attempts of research groups to explore alternative intraoperative imaging solutions demonstrates the need for an imaging modality that potentially can monitor tumor tissue at the conclusion of surgery, which may increase the extent of tumor resection and patient outcome, including survival time.

Intraoperative images from open MRI systems are easily integrated into navigation systems and have been demonstrated to increase the extent of tumor resection and prolong patient survival (42). These systems are, however, time-consuming and costly alternatives. CT usually is not the in-

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**FIGURE 6.** As the operation progresses, orthogonal slicing of a metastasis may be visualized with preoperative MRI (top row), intraoperative ultrasound before opening of the dura (middle row), and 3-D ultrasound close to the end of the operation (bottom row). The MRI scans provide an overview of the anatomic area and help inexperienced ultrasound users to interpret ultrasound image information. Ultrasound provides updated image information in the important area where resection is performed. Axial, sagittal, and coronal slices from the 3-D ultrasound volume all show an image quality useful for interpreting tumor border and for detecting remaining tumor tissue toward the conclusion of surgery.

**FIGURE 7.** Because the corresponding slices from all 3-D scans are displayed on the screen simultaneously, the progression of the resection may be followed easily. Corresponding single slices from a preoperative MRI volume (A), initial 3-D ultrasound volume (B), a 3-D ultrasound volume in the middle of the operation (C), and a 3-D ultrasound volume close to the completion of the resection (D) in a patient with a glioblastoma. Arrows indicate remaining tumor tissue. In this operation, some tumor tissue was purposely left behind because of its location in eloquent areas. In other operations, we found that tumor tissue not detected by the microscope or by the naked eye could be detected by use of 3-D ultrasound and removed, thus increasing the radicality of the tumor resection.
traoperative imaging modality of choice because of ionizing radiation and limited tumor definition. The most discussed issues and objections regarding the use of ultrasound to guide surgical procedures so far have involved the variable image quality achieved by different users. In addition, most surgeons are more familiar with MRI or CT and may need some time to become familiar with the nature and interpretation of information in the ultrasound images. Several research groups have demonstrated that the image quality of ultrasound has improved considerably and is good enough to visualize and guide tumor resections (3, 13, 43).

We have described various clinical and technical adjustments and arrangements for improving ultrasound image quality in practical neurosurgery (13; G Unsgaard, A Gronningsaeter, S Ommedal, TAN Hernes, submitted for publication). One of the clinical arrangements we have developed is to perform a second minicraniotomy for the ultrasound probe, which ensures optimal imaging conditions. We have not detected complications because of this special clinical setup, the image quality seems improved, and the flexibility of use of additional real-time imaging is available. However, the orientation, scaling, and interpretation of information from real-time 2-D ultrasound images also have made it difficult for experienced users to benefit from this imaging modality in guided neurosurgery procedures (G Unsgaard, A Gronningsaeter, S Ommedal, TAN Hernes, submitted for publication). This situation is soon to change, because new developments that result in tighter integration of 3-D ultrasound imaging technology with navigation technology will solve the orientation problems experienced with 2-D ultrasound (13). Ultrasound may now be used like any other 3-D imaging modality in neuronavigation.

Access to high-quality intraoperative 3-D ultrasound has enabled us to perform open tumor surgery through a slightly narrower channel than would be possible without image guidance. Tumor structures can be easily identified and located by use of the navigation system, and the surgeon can remove the structures with less visual control of the resection cavity. In our patients, this minimally invasive approach was required to scientifically explore the potential future value of ultrasound in neuronavigation. Future real-time 3-D capabilities of ultrasound make this imaging modality especially attractive. However, the unsolved issue common to all of the alternative intraoperative imaging technologies is their sensitivity and specificity in detecting remaining tumor tissue at the conclusion of surgery, which will affect patient survival time. Therefore, studies initiated by Tronnier et al. (38) to compare the intraoperative imaging modalities, as well investigations to compare intraoperative imaging modalities with histopathological evaluation (3, 43), must continue. These studies should also include an evaluation of the time and cost effectiveness of the systems in practical, daily hospital function to fully compare and evaluate the usefulness of the alternative navigation technologies for guiding neurosurgical procedures.

CONCLUSION

The introduction of 3-D ultrasound has increased the value of neuronavigation substantially in our clinic, making it possible to update 3-D maps several times during surgery and thereby minimize the problem of brain shift. The surgical tool may be navigated down to the lesion with a high level of precision. Novel and user-friendly display techniques make it possible to perform faster and more intuitive image-guided surgery as compared with conventional neuronavigation systems and real-time 2-D ultrasound. These features allow the neurosurgeon to follow the progression of the resection and identify, localize, and remove residual tumor tissue. Although our initial experience is promising, more research will be required to scientifically explore the potential future value of ultrasound in neuronavigation.

ACKNOWLEDGMENTS

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DISCLOSURE

At the time this study was initiated, all authors were research scientists and had no financial interest in the outcome of the study. AG currently is employed by MISON AS and may benefit from future success of the company resulting from the use of ultrasound in neurosurgery. However, AG

Neurosurgery, Vol. 50, No. 4, April 2002
Three-dimensional Ultrasound in Neuronavigation

was not involved in the study after he became Chief Executive Officer of MISON AS in 1998.

REFERENCES


COMMENTS

In 1985, our group performed a few imaging-based volumetric stereotactic tumor resections using a two-dimensional ultrasonic transducer mounted on the arc-quadrant of an arc-quadrant stereotactic frame. The technique, as presented in this article and in the hands of a moderately experienced team, clearly is useful. It certainly provides a more convenient and less expensive alternative for intraoperative imaging.

Patrick J. Kelly
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The authors have achieved an important integration of a navigation system driven by preoperative imaging with real-time, three-dimensional, intraoperative ultrasound imaging. Modern ultrasound imaging of the brain has become extremely detailed, and in many instances it provides more useful information regarding a lesion than the preoperative MRI scan. The authors have integrated the ultrasound imaging device into the navigation system by allowing the navigation system camera to recognize the exact location and position of the ultrasound probe. This allows the constructed three-dimensional MRI scan of the lesion to be corrected in space when brain shifts occur during surgery.

The authors also have integrated surgical tools, such as the ultrasonic aspirator, into the navigation system. This allows precise localization of the instrument relative to the preoperative MRI scan and the intraoperative ultrasound imaging of the lesion.

The authors conclude that in 53% of cases, residual tumor was identified by intraoperative ultrasound after it was thought by the surgeon that the tumor had been maximally resected. This marriage of ultrasound and frameless stereotaxy is an important step forward and will lead to more precise lesion localization.

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