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1.5 T: spectroscopy-supported brain biopsy

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Since the 1970s, the technique for performing brain biopsy has changed significantly as the ability of the neurosurgeon to visualize the target site has improved [1–9]. Initially, CT allowed clinicians to obtain images of the brain in the axial plane using x-rays. The first brain biopsies were performed in the CT scanner in a freehand manner [1]. Stereotactic head frames were introduced in the early 1980s and were first combined with CT guidance until MRI became available by the end of the decade. MRI represents one of the most important technologic advances for neurosurgeons developed over the last 20 years. This radiologic tool can demonstrate the brain in axial, coronal, and sagittal projections with excellent soft tissue discrimination.

After stereotaxis and MRI, the next significant advancement in neurosurgery was frameless neuronavigation systems. These systems rely on acquiring preoperative images immediately or several days before a planned surgical procedure. With neuronavigation, the imaging is oriented to a constant set of fiducial markers that are fastened to the head of the patient. Optical, ultrasound, or radiofrequency sensors are used to detect the movement of surgical instruments, such as a brain biopsy needle during surgery, with respect to these reference points. Neuronavigation, however, is limited by two distinct disadvantages: the potential for movement of the fiducial markers during the procedure, resulting in registration inaccuracy, and the ability of the brain to shift once the cranium is opened and cerebrospinal fluid is drained.

In the mid-1990s, MRI was adapted for use in a surgical environment in which intraoperative imaging could provide near–real-time updates of the operative site without concern for brain shift [10–16]. Lesions within the brain could now be accessed or resected without fear of displacement, and neurosurgeons would have the ability to alter their surgical approach dynamically to compensate for brain shift [5,7]. The capability to alter the surgical approach during surgery is not possible with framed or frameless stereotaxy unless it is combined with intraoperative CT or MRI. The ability to visualize the biopsy needle directly within the target tissue during surgery has resulted in an increase in the diagnostic yield for brain biopsy when it is performed with intraoperative MRI guidance compared with conventional stereotaxis [2,5].

The first intraoperative MRI-guided brain biopsies were performed in a freehand fashion as was initially done with the advent of CT, largely because there was no way to direct the passage of the needle through the brain or to stabilize the needle once it had reached the intended target [3].

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Such concerns led to the development of various trajectory guides that facilitated tissue sampling [4,17]. To further enhance the diagnostic yield of intraoperative MRI-guided brain biopsy, particularly for patients thought to harbor a neoplastic process, magnetic resonance spectroscopy (MRS) was performed during the procedure to identify areas in the brain having increased levels of certain metabolites believed to represent tumor, which were then sampled in near–real time [6,8,18,19].

MRI-guided brain biopsy technique

MRI-guided brain biopsy can be performed under local or general anesthesia. We have tended to use general anesthesia more commonly, because it is difficult for a patient to remain calm for extended periods. The noise associated with MRI scanning could startle the patient during the procedure, which may lead to displacement of the head and the biopsy needle while it is within the brain. Many of the lesions that are biopsied are in locations where it would be difficult for the patient to maintain the proper position for the entire duration of the procedure.

Patients are placed under general anesthesia before or after transport to the intraoperative MRI suite. An MRI-visible marker is placed on the scalp at the location where the skull will undergo perforation. By defining a safe and accurate trajectory for the brain biopsy, the neurosurgeon can ensure that critical structures are avoided and that a diagnostic sample is obtained. At the University of Minnesota, two flexible radiofrequency coils are placed around the surgical site to perform high-resolution scanning. The scalp is shaved and then prepared in a sterile manner. The skin is incised, and a twist drill craniostomy or a burr hole is made through the skull. The dura mater is incised, and the base of the trajectory guide (Navigus; Image-Guided Neurologics, Melbourne, Florida) is secured in place with three self-tapping titanium screws (Fig. 1). A variable-diameter guide tube is then snapped into the base and secured in place with a plastic locking nut. The alignment stem is inserted into the guide tube to determine an appropriate trajectory in multiple MRI planes for the biopsy using prospective stereotaxy [5,20]. To visualize the alignment stem, it is filled with saline or contrast, depending on which MRI sequences best demonstrate the target lesion. After a trajectory has been chosen that encounters the target in at least two projections, the guide tube is locked in place and the alignment stem is removed. In a stepwise fashion with periodic "snap-shot" MRI updates, the titanium brain biopsy needle is gradually advanced toward the target in near–real time.

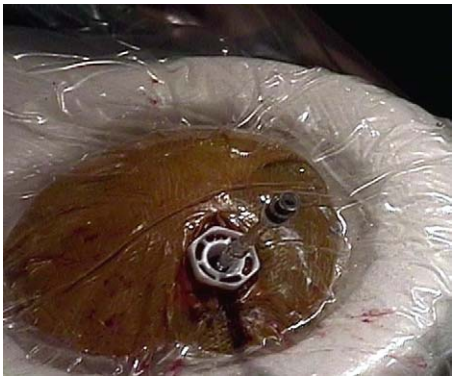

Fig. 1. Navigus trajectory guide (Image-Guided Neurologics, Melbourne, Florida) enables the neurosurgeon to choose a safe and accurate surgical pathway for brain biopsy while securing the needle in place at the time when the tissue samples are obtained. The biopsy is being performed through a radiofrequency coil, and the alignment stem has been inserted into the guide tube.

For most lesions, T2-weighted, orthogonal, half-Fourier acquisition single-shot turbo spin echo (HASTE) imaging is used to determine the surgical trajectory to the target because of its rapid scan acquisition time. Once the biopsy needle reaches the target, imaging is performed in two orthogonal planes along the entire length of the biopsy needle to document the location of the biopsy and to confirm the accuracy of the procedure (Fig. 2). Multiple samples are usually obtained from the target tissue at different depths and in different directions for frozen section and permanent pathologic analysis. At present, we still confirm the presence of pathologic tissue before leaving the operating room; however, in the future, we will probably forego this practice because of the accuracy of the sampling technique. While the pathologist is analyzing the tissue samples, the biopsy needle is removed and the sample site is evaluated for intraoperative hemorrhage. Because the presence of hyperacute blood (before conversion of intracellular oxyhemoglobin to deoxyhemoglobin) can be difficult to detect on MRI, a combination of HASTE, gradient echo (GE)-T2*, and turbo fluid-attenuated inversion recovery sequences has proved

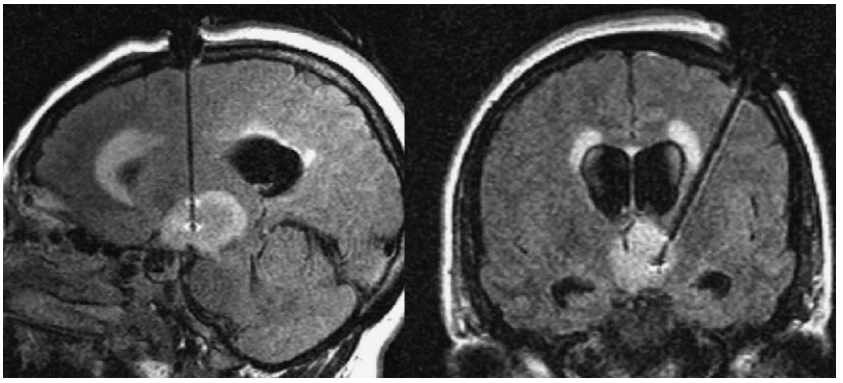

Fig. 2. Orthogonal sagittal (left) and coronal (right) turbo fluid-attenuated inversion recovery MRI along the entire length of the titanium brain biopsy needle once it has reached the target in the left thalamus found to be an astrocytoma.

sensitive to detect intraoperative hemorrhage accurately (Fig. 3). After the presence of diagnostic tissue has been confirmed, the trajectory guide is removed and the scalp is sutured closed. The patient is then transported to the recovery room for extubation. Usually, the patient is discharged home the following morning, although some patients have been discharged home the same day at their own request after several hours of observation. Performing outpatient brain biopsies should clearly help to curtail rising medical costs.

Prospective stereotaxy

Prospective stereotaxy represents a novel way to determine the surgical path for the brain biopsy needle using the trajectory guide that starts at the target and moves from the target to the distal end of the alignment stem. After the neurosurgeon has chosen the biopsy location (target point), it is necessary to determine two additional points in space to align the trajectory guide with the target. The second point is the pivot point, which is located at the tip of the alignment stem. The third point is a point in space that represents the desired location of the alignment stem, which can be oriented until all three points are collinear, thereby ensuring that the passage of the biopsy needle through the trajectory guide will encounter the target.

The alignment stem is filled with an appropriate fluid for visualization on MRI and then inserted into the guide tube before performing prospective stereotaxy. The alignment stem can be

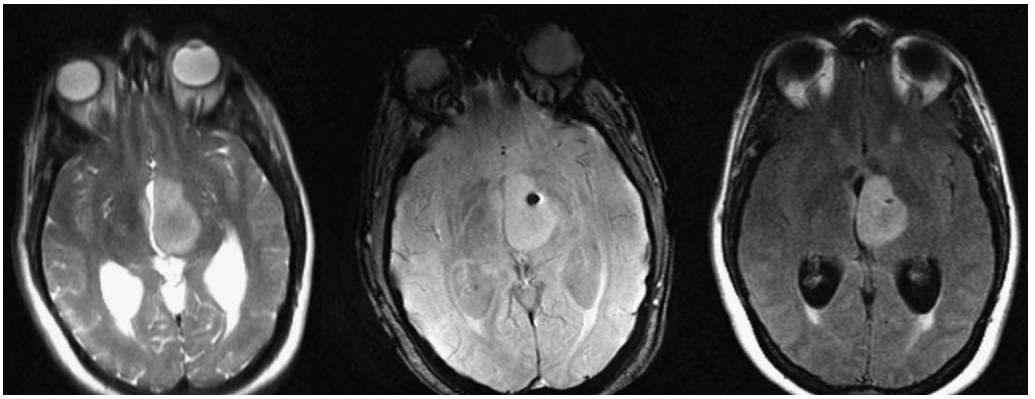

Fig. 3. A combination of half-Fourier acquisition single-shot turbo spin echo (left), gradient echo (GE)-T2* (middle), and turbo fluid-attenuated inversion recovery (right) sequences has proved sensitive to detect accurately the presence or absence of intraoperative hemorrhage after brain biopsy. The prominent signal void seen within the left thalamus on the GE-T2* image is thought to represent air because of its sharp border.

rotated freely in space because of a ball joint until all three points are aligned, which can be completed in less than 5 minutes. After the points are aligned, scanning along the entire length of the alignment stem is performed to confirm that the trajectory guide is pointed toward the target and that the biopsy needle will access the tissue of interest once it is passed through the brain. If the surgical path is considered satisfactory, the locking nut is tightened to prevent redirection or displacement of the trajectory guide while the biopsy is being performed.

Magnetic resonance spectroscopy–guided brain biopsy

Since April 1998, we have used MRS to guide brain biopsy in the intraoperative MRI unit [6,18,19]. Successfully combining the trajectory guide with MRS to guide brain biopsy was first accomplished in January 1999 [6]. The MRS techniques that we have used during brain biopsy include single-voxel spectroscopy (SVS) or turbo spectroscopic imaging (TSI) obtained under general anesthesia individually or in combination. General anesthesia is used to prevent movement of the head during the examination, which would invalidate the MRS data. A phased-array head coil was used to acquire the MRS data initially in the ACS-NT 1.5-T, high-field, short-bore, interventional MRI system (Philips Medical Systems; Best, The Netherlands) and, more recently, using the 1.5-T Intera I/T system (Philips Medical Systems) (Fig. 4). SVS (1.5-cm^3 × 1.5-cm^3 × 1/5-cm^3 voxel, 1-Hz spectral resolution, echo time (TE)/repetition time (TR) = 136/2000 milliseconds, 4.5-minute acquisition) was obtained on a region of interest in the brain to be biopsied and on a control area in a comparable location in the contralateral hemisphere [7]. TSI (32-mm × 32-mm grid of spectra in a single plane, 0.66-cm^3 × 0.66-cm^3 × 2.0-cm^3 spatial resolution, 4.4-Hz spectral resolution, TE/TR = 272/2000 milliseconds, turbo factor = 3, 11-minute acquisition) was performed on a single axial slice to measure brain metabolites [7]. Intravenous contrast was not used during MRS to prevent alteration of the spectral data by those agents. Regions of elevated phosphocholine on SVS and TSI, which are believed to represent areas of rapid membrane turnover and increased cellular density suspicious for tumor tissue, were selected for biopsy during the procedure (Fig. 5). If elevated phosphocholine was not identified on MRS, areas of contrast enhancement were chosen for biopsy.

MRI- and magnetic resonance spectroscopy–guided brain biopsy results

The first 35 MRI-guided brain biopsies performed between January 1997 and June 1998 were freehand, because the trajectory guide had not yet been developed for clinical use [3]. At that time, the brain biopsy needle was stabilized in the burr hole using bone wax after it had reached the target. All 35 brain biopsies yielded diagnostic tissue, and the

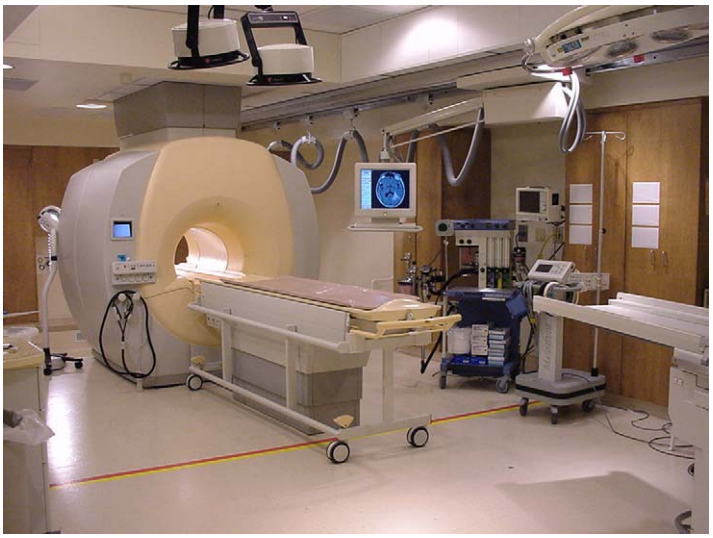

Fig. 4. Intera I/T intraoperative MRI system (Philips Medical Systems, Best, The Netherlands).

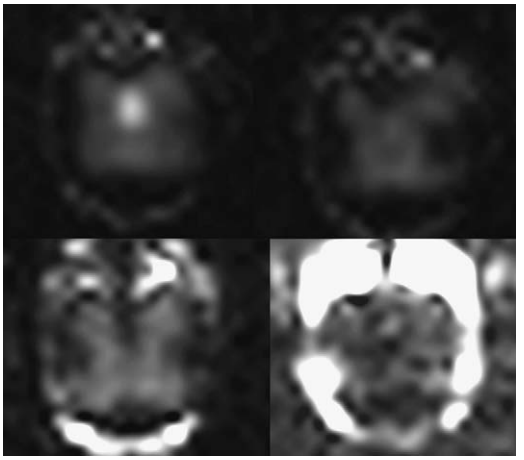

Fig. 5. Turbo spectroscopic imaging (TSI) metabolite map of the left thalamic astrocytoma. The upper left panel represents the TSI phosphocholine map, and the creatine map is in the upper right panel. The *N*-acetylaspartate map is in the lower left panel, and the lactate/lipid map is in the lower right panel. The tumor clearly demonstrates an elevated phosphocholine level representative of rapid membrane turnover and increased cellular density.

diagnoses obtained included 28 primary brain tumors, 1 metastatic tumor, one meningioma, one cerebral infarct, one demyelinating process, and three cases of radiation necrosis. One patient with a pontine glioma had a temporary hemiparesis after the biopsy that improved with physical therapy, and another patient who experienced scalp cellulitis was successfully treated with antibiotics. No patient sustained a clinically or radiographically significant hemorrhage during the procedure. Six of these patients had SVS at the time of their biopsies. The results of the SVS in five of the patients demonstrated elevated phosphocholine levels in comparison to the creatine levels, with a decrease in the *N*-acetylaspartate levels. The diagnoses found in these five patients were astrocytoma, anaplastic astrocytoma, and three glioblastomas multiforme. In the single patient in whom the phosphocholine level was not elevated, radiation necrosis was found. The results of the SVS correlated well with the pathologic findings in each case.

After the advent of the trajectory guide, the results of the first 40 brain biopsies that were performed in 38 patients between January 1999 and March 2000 were reviewed for safety and accuracy [5]. All biopsies were diagnostic, and there were no clinically or radiographically significant hemorrhages detected. Thirty-three (83%) lesions were primary brain tumors, 5 were radiation necrosis, 1 was vasculitis, and 1 was a demyelinating process. One patient with a lesion adjacent to the motor cortex sustained a temporary hemiparesis related to edema that occurred with the passage of the biopsy needle, and another elderly patient experienced a fatal myocardial infarction after the biopsy despite preoperative cardiac clearance. The accuracy of the device was measured to be 2 mm at a depth of 70 mm within the brain [5].

Over a concurrent 12-month period, we coupled MRS with the use of the trajectory guide in an attempt to improve the diagnostic yield in 17 patients [6]. Before the procedure, 10 patients had TSI and 7 patients had TSI and SVS. All tissue samples were diagnostic, and the diagnoses obtained included six glioblastomas multiforme, three anaplastic astrocytomas, three anaplastic oligodendrogliomas, germinoma, ganglioglioma, astrocytoma, and two cases of radiation necrosis. No clinically or radiographically significant hemorrhage was visible on postbiopsy imaging. In all 7 patients who had SVS, there was a 100% spectral correlation with the pathologic results. In the 17 patients who had TSI, the correlation was similar in only 13 (76%), however. In those patients who had SVS and TSI, the results correlated in 6 (86%) of 7 patients. Overall, it was thought that the MRS data enhanced the diagnostic yield of brain biopsy [6].

To determine the utility of TSI, a group of 26 patients underwent brain biopsy using this imaging technique [19]. An area of elevated phosphocholine was seen on TSI in 17 of 21 patients who had a confirmed neoplasm on pathologic examination of the biopsy sample. Radiation necrosis was found in 5 patients in whom the phosphocholine level was low and consistent with that diagnosis. Four patients with tumors had low phosphocholine levels that were indistinguishable from the levels present in radiation necrosis. Of the 10 patients who had SVS in addition to TSI, the results were qualitatively similar for both techniques, although more spectral contamination was seen with TSI than with SVS. Quantitative analysis of TSI was limited by the low spatial resolution for that technique. The diagnostic yield for TSI-guided brain biopsy was 100%.

In our first 140 brain biopsies performed under MRI guidance, we sought to determine what influence the imaging had on surgical decision making [21]. In 42 (30%) brain biopsies, we used

MRS to guide the brain biopsy. Twenty-nine (71%) patients had TSI and 21 (48%) patients had SVS. Twenty-one (48%) patients had TSI alone, 13 (31%) patients had SVS alone, and 8 (19%) patients had TSI and SVS. In the patients who were thought to have tumor, the areas of elevated phosphocholine on SVS, TSI, or both were targeted during the biopsy. In those 8 patients who had SVS and TSI, there was excellent correlation between the phosphocholine levels. Radiation necrosis was diagnosed in 10 (20%) patients, glioblastoma multiforme in 12 (24%), anaplastic oligodendroglioma in 6 (12%), anaplastic astrocytoma in 6 (12%), astrocytoma in 2 (4%), oligodendroglioma in 4 (8%), germinoma in 1 (2%), and lymphoma in 1 (2%). SVS was performed in 5 patients with radiation necrosis, 1 with anaplastic oligodendroglioma, 3 with glioblastoma multiforme, 2 with anaplastic astrocytoma, and 2 with astrocytoma. TSI was obtained in 6 patients with glioblastoma multiforme, 4 with radiation necrosis, 4 with oligodendroglioma, 3 with anaplastic astrocytoma, 2 with anaplastic oligodendroglioma, 1 with lymphoma, and 1 with germinoma. The diagnoses that were found in those patients who had TSI and SVS were three glioblastomas multiforme, three anaplastic oligodendrogliomas, one anaplastic astrocytoma, and one case of radiation necrosis.

Review of brain biopsy results

The first CT-guided brain biopsies were performed freehand [1]. The diagnostic yield was 90% and ranged from 79% to 97% in 344 patients having this type of biopsy [1]. The morbidity rate was 7.8% and ranged from 2% to 14%, and the mortality rate was 2.5% and ranged from 0.5% to 4.7%. Stereotactic head frames were used shortly after the development of CT to guide the performance of brain biopsy. A review of 17 stereotactic brain biopsy series that included nearly 7500 patients demonstrated that the diagnostic rate was 91% and ranged from 80% to 99%, the morbidity rate was 3.5% and ranged from 0% to 13%, and the mortality rate was 0.7% and ranged from 0.5% to 2.6%. Diagnostic failure in stereotactic brain biopsy patients was attributed to small sample size, small target size, displacement of the lesion away from the biopsy needle, inability to penetrate the lesion with the biopsy needle, inaccurate tissue targeting resulting in sampling error, poor target choice in areas of high T2-weighted signal on MRI, and lesion proximity adjacent to the ventricular system resulting in the aspiration of cerebrospinal fluid [2].

Intraoperative MRI-guided brain biopsy results

The presence of MRI in the operating room allows for intracranial tissue to be sampled in near–real time [3]. Compared with conventional frame-based brain biopsy, intraoperative MRI-guided brain biopsy has a diagnostic yield of 100% in some reports and allows for the confirmation that a clinically or radiographically detected hemorrhage has not been sustained during the procedure [5]. Of the first 140 cases that were performed using 0.5-T midfield intraoperative MRI at the Brigham and Women's Hospital, 63 were brain biopsies [12]. The lesions were located in various areas throughout the brain, including the thalamus, basal ganglia, brain stem, cerebellum, deep white matter, and cerebral hemispheres. One patient sustained an intraoperative hemorrhage that was detected on intraoperative scanning and was emergently evacuated. The authors concluded that the intraoperative MRI enabled them to evaluate the surgical site rapidly and to intervene dynamically if necessary [12].

Using a low-field 0.2-T MRI scanner, 10 brain biopsies were performed in a series of 27 patients [14]. All brain biopsies yielded diagnostic tissue, and the authors concluded that they could adjust for brain shift during the operative procedure by obtaining updated image sets. Another group performed 16 brain biopsies in the magnetic fringe fields using the same low-field intraoperative MRI system [15]. Fifteen (94%) of the 16 brain biopsies were diagnostic, and the single nondiagnostic biopsy attempt was aborted because the brain stem tumor could not be safely accessed through the cerebellum. No hemorrhages were detected that required surgical evacuation, and the only morbidity that was experienced was a temporary hemiparesis that resulted after a lesion near the motor cortex was biopsied. Using a low-field 0.2-T vertical gap system, 36 neurosurgical procedures were performed over a 1-year period, of which 12 cases were brain biopsies [16]. One patient had postoperative hand weakness after a brain biopsy that demonstrated a lymphoma, and all biopsies yielded diagnostic tissue. There were several technical issues raised by the authors concerning brain biopsy using their intraoperative MRI system, including poor image quality in five cases, instrumentation concerns in

two cases, and the probe not being visualized in three cases. The two most useful features of intraoperative MRI-guided surgery that were noted by the authors were the ability to visualize the brain biopsy needle within the region of interest and to confirm the absence of intraoperative hemorrhage.

Technical advances in intraoperative MRI-guided brain biopsy

Neurosurgeons operating in the intraoperative MRI environment realized rapidly the need to guide biopsy needles through the brain and then to secure the needle in place once it had reached the target tissue. Frameless stereotaxy has been combined with an optical triangulation system to localize the burr hole, to plan the surgical pathway, and to guide the needle to the target at some intraoperative MRI sites [17]. In the first 20 procedures that were performed in this manner, there were 15 brain biopsies, three abscess drainages, one cyst aspiration, and one fenestration for multiloculated hydrocephalus. The positional accuracy of this system was believed to be comparable to that of conventional stereotaxy, with a mean error of 1.5 mm [17].

Prospective stereotaxy represents another advancement in the evolution of intraoperative MRI-guided brain biopsy [5,20]. Although framed or frameless stereotaxy and prospective stereotaxy require preoperative images to locate the target and to plan the surgical approach, the two techniques are quite different during the performance of the biopsy. Frameless stereotaxy requires that fiducial markers be placed on the scalp before the preoperative imaging is obtained to register or localize the markers with respect to the position of the target. An external probe is used to register the fiducial markers, which will generate an image on a computer monitor, which is then viewed by the neurosurgeon. Once the fiducial markers have been registered, the target can then be displayed on the monitor by changing the position of the probe in space. The most concerning issue that is associated with frameless stereotaxy is the potential for brain shift with subsequent displacement of the target once the dura mater is opened and cerebrospinal fluid is lost. Prospective stereotaxy does not require fiducial markers, because the imaging will demonstrate the target and the trajectory that the biopsy needle will traverse to reach the target. After aligning the trajectory guide, the biopsy needle can be passed in a stepwise fashion in near–real time until the target is encountered. The techniques are diametrically opposed. Frameless stereotaxy demonstrates the target lesion on a computer screen as it is related to an external probe in contrast to prospective stereotaxy, which displays the desired trajectory on a computer monitor as it is determined. By rotating the alignment stem that is within the guide tube like a joy stick, the surgical channel can be directed toward the target. Concerns about brain shift are minimized with prospective stereotaxy.

The trajectory guide can be used with frameless and prospective stereotaxy, and two other MRI-compatible needle stabilization devices are also currently available (MRI Devices Corporation, Waukesha, Wisconsin; Snapper-Stereo-Guide, MagneticVision, Zurich, Switzerland) [17]. Since the introduction of the trajectory guide at our institution, our diagnostic rate for brain biopsy has been 100%. Biopsies have been safe and accurate, with the alignment of the device being rapid and efficient without extending the length of the operative procedure. MRS measures specific metabolites noninvasively within the brain, which may help to distinguish tumor recurrence from radiation necrosis in patients with brain tumors who have received radiation therapy, much like positron emission tomography. By combining the use of the trajectory guide with MRS, we hope to enhance our diagnostic yield for patients who have intraoperative MRI-guided brain biopsies.

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