

## Strategic Alliance Partnership Program

## OUR PARTNERS



Mount The Tisch Cancer Institute



COLUMBIA UNIVERSITY MEDICAL CENTER Herbert Irving Comprehensive Cancer Center



Comprehensive Cancer Center



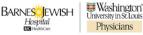


Fred Hutchinson Cancer Research Center UW Medicine Seattle Children's



Memorial Sloan-Kettering Cancer Center







Every month, our editors collaborate with renowned cancer centers across the country to bring you reports on cutting-edge developments in oncology research and treatment. Our unique Strategic Alliance Partnership program now includes 11 members (see column at left). If you are part of a cancer center that you think might want to participate in our program, please reach out to Jason Broderick at <u>jbroderick@onclive.com</u>.

## Neurosurgical Innovations Advance Safe Resection of Difficult Brain Tumors



By Arnold B. Etame, MD, PhD Moffitt Cancer Center, Neuro-Oncology Program Tampa, FL

G liomas as a group represent the most common primary brain tumor in adults. Surgery plays a critical role in the multimodal management of gliomas with respect to tissue diagnosis as well as symptomatic relief from mass effect. Moreover, the combination of surgery, chemotherapy, and radiation therapy has been shown to confer a survival benefit for patients with malignant glioblastoma multiforme, a very aggressive glioma.<sup>1</sup> In addition, a series of studies has demonstrated a correlation between extent of surgical resection and clinical outcome benefits in patients with gliomas.<sup>2-9</sup> Accordingly, there is a drive toward neurosurgical innovations that promote the safe maximal resection paradigm.

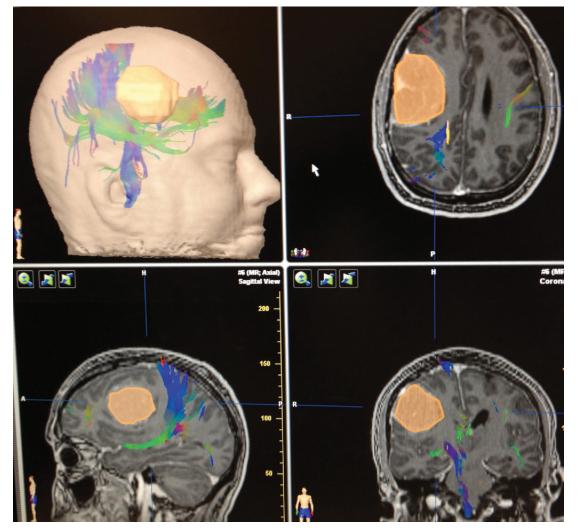
Rapid technological advances and refinements in intraoperative neurosurgical strategies have facilitated the goal of maximum and safe resections. The impetus toward minimally invasive neurosurgical intracranial techniques with respect to minimizing morbidity has been a driving force as well. In particular, image-guided stereotactic techniques have been extremely valuable in this endeavor by providing intraoperative neuronavigational capabilities for the neurosurgeon. Furthermore, recent advances in MRI diffusion tensor tractography have facilitated the acquisition and incorporation of critical white matter pathways onto neuronavigational plans, thereby providing the anatomical correlate and localization for critical pathways such as the corticospinal fibers for motor and optic radiations for vision. As a consequence, minimally invasive brain tumor resections are now feasible for tumors in eloquent or even deep cortical locations that were previously deemed high risk, and hence nonresectable.



Modern stereotactic systems incorporate specialized optical detection systems for neuronavigation, and reflect a marked improvement from older systems that mainly generated coordinates within the brain based on the three cardinal planes (ie, sagittal, coronal, and axial). The patient undergoes acquisition of a thin-cut, high-resolution MRI of the brain, which could also include functional MRI data for motor and language areas, if applicable. The imaging data are then processed through an algorithm to generate a three-dimensional (3D), patient-specific model for that particular patient (Figure). Three-dimensional navigation within the brain is then accomplished by integrating surface landmarks on the patient's head with similar landmarks on the 3D-model generated from stored, highresolution CT or MRI scans. The combination of optical detectors and a navigational probe permits pinpoint







**FIGURE.** This navigation screen picture shows a model, top left, generated from a high-resolution MRI. The tumor and associated pathway fibers and other MRI images are depicted in the accompanying three key projections. When the surgeon navigates with a probe on the patient, it is possible to see that location in real-time on all four images on the navigation screen.

localization of any point in space within millimeter precision in the brain relative to the patient and the model. Incorporation of intraoperative MRI data taken during surgery can correct for any discrepancies or brain shift that typically occurs as a result of surgery.<sup>10-14</sup>

For resection of tumors in noneloquent areas of the brain, neuronavigation without incorporation of functional MRI or diffusion tensor imaging (DTI) data is usually sufficient. However, in patients whose tumors are within speech, motor, or visual areas, incorporation of functional MRI and white matter pathway data is very feasible, with the potential to minimize surgical morbidity.<sup>15,16</sup>

One technique of immense interest has been DTI tractography. The technique examines the differential movement of water molecules within the brain between gray and white matter. Since white matter fiber tracts are directional, there is a direction movement of water molecules within white matter. Algorithmic processing of such directionality generates the fiber profile within the region of interest. Hence, during neuronavigation, the relationship of critical fibers and pathways is available (Figure). DTI is especially valuable for deeper lesions where a transcortical trajectory is required. For instance, a trajectory that spares the corticospinal motor fibers is therefore desirable. Moreover, DTI navigation data for deeper lesions have been shown to correlate nicely with intraoperative electrical stimulation data for corticospinal motor fibers, suggesting its role as a localization surrogate for white matter fibers.<sup>17-19</sup> In addition, other functional MRI data for speech or motor can be incorporated and visualized in real-time. Lastly, a select group of patients might benefit from awake-craniotomy where patientdependent function can be assessed in real-time.

As we experience rapids advancement in MRI and optics, stereotactic neuronavigation will offer more surgical visualization capabilities for the neurosurgeon. The ability to navigate around critical white matter fibers for resection of tumors will be markedly enhanced. These advanced stereotactic techniques have already been incorporated at our comprehensive cancer center, where we encounter a significant number of tumors in critical areas of the brain. •

## REFERENCES

**OncLive**®

- Stupp R, Mason WP, Van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med. 2005;352(10):987-996.
- Hardesty DA, Sanai N. The value of glioma extent of resection in the modern neurosurgical era. *Front Neurol.* 2012;3:140. doi:org/10.3 389%2Ffneur.2012.00140.
- Sanai N, Polley MY, McDermott MW, et al. An extent of resection threshold for newly diagnosed glioblastomas [published online ahead of print March 18, 2011]. J Neurosurg. 2011; 115(1):3-8.
- Sanai N, Berger MS. Operative techniques for gliomas and the value of extent of resection. *Neurotherapeutics*. 2009;6(3):478-486.
- Smith JS, Chang EF, Lamborn KR, et al. Role of extent of resection in the long-term outcome of low-grade hemispheric gliomas. *J Clin* Oncol. 2008;26(8):1338-1345.
- Sanai N, Berger MS. Glioma extent of resection and its impact on patient outcome. *Neurosurgery*. 2008;62(4):753-764; discussion, 264-756.
- Lacroix M, Abi-Said D, Fourney DR, et al. A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. J Neurosurg. 2001;95(2):190-198.
- Keles GE, Anderson B, Berger MS. The effect of extent of resection on time to tumor progression and survival in patients with glioblastoma multiforme of the cerebral hemisphere. *Surg Neurol.* 1999;52(4): 371-379.
- Simpson JR, Horton J, Scott C, et al. Influence of location and extent of surgical resection on survival of patients with glioblastoma multiforme: results of three consecutive Radiation Therapy Oncology Group (RTOG) clinical trials. *Int J Radiat Oncol Biol Phys.* 1993;26(2):239-244.
- Black PM, Moriarty, Alexander E 3rd, et al. Development and implementation of intraoperative magnetic resonance imaging and its neurosurgical applications. *Neurosurgery*. 1997;41(4):831-842; discussion, 842-845.
- Ganslandt O, Behari S, Gralla J, et al. Neuronavigation: concept, techniques and applications. *Neurol India*. 2002;50(3): 244-255.
- Nimsky C, Ganslandt O, Cerny S, et al. Quantification of, visualization of, and compensation for brain shift using intraoperative magnetic resonance imaging. *Neurosurgery*. 2000;47(5):1070-1079; discussion, 1079-1080.
- Buchfelder M, Ganslandt O, Fahlbusch R, Nimsky C. Intraoperative magnetic resonance imaging in epilepsy surgery. J Magn Reson Imaging. 2000;12(4): 547-555.
- Nimsky C, Fujita A, Ganslandt O. et al. Volumetric assessment of glioma removal by intraoperative high-field magnetic resonance imaging. *Neurosurgery*. 2004;55(2): 358-370; discussion, 370-371.
- Nossek E, Korn A, Shahar T, et al. Intraoperative mapping and monitoring of the corticospinal tracts with neurophysiological assessment and 3-dimensional ultrasonography-based navigation [published online ahead of print August 27, 2010]. *J Neurosurg.* 2011;114(3):738-746.
- Kamada K, Todo T, Masutani Y, et al. Combined use of tractography-integrated functional neuronavigation and direct fiber stimulation. J Neurosurg. 2005;102(4):664-672.
- Ohue S, Kohno S, Inoue A, et al. Accuracy of diffusion tensor magnetic resonance imaging-based tractography for surgery of gliomas near the pyramidal tract: a significant correlation between subcortical electrical stimulation and postoperative tractography. *Neurosurgery*. 2012;70(2):283-293; discussion, 294.
- Kamada K, Todo T, Ota T, et al. The motor-evoked potential threshold evaluated by tractography and electrical stimulation. *J Neurosurg*. 2009;111(4):785-795.
- Berman JI, Berger MS, Chung SW, et al. Accuracy of diffusion tensor magnetic resonance imaging tractography assessed using intraoperative subcortical stimulation mapping and magnetic source imaging. *J Neurosurg.* 2007;107(3):488-494.