by Juan C. Fernandez-Miranda, MD; Sudhir Pathak, MS; Walter Schneider, Ph.D.

early two decades ago, Sir Francis Crick, neuroscientist, discoverer of the DNA molecule and 1962 Nobel Prize for Medicine, wrote: “to interpret the activity of living human brains, their neuroanatomy must be known in detail. New techniques to do this are urgently needed, since most of the methods now used on monkeys cannot be used on humans.”

The introduction of Diffusion Tensor Imaging (DTI) a decade ago represented a major step toward this goal. DTI is a Magnetic Resonance Imaging (MRI) technique that measures the diffusion of water within the axons (“wires”) of the brain. The information obtained with DTI-MRI is then processed mathematically to obtain a graphic representation of the water channels or tracks within the brain, a method called fiber tractography. The ability to non-invasively map fiber tracts in the living human brain will facilitate numerous applications in the diagnosis and treatment of brain disorders, and for this reason, the National Institute of Health (NIH) stated that the Human Connectome Project (the complete description of the “wiring” of the human brain) is one of the great scientific challenges for the upcoming decade.

We initiated our studies of the brain fiber tracts using DTI almost a decade ago, and we demonstrated that DTI provides accurate reconstruction of the major stem of fiber tracts, in agreement with classical and contemporary neuroanatomical studies. DTI, however, has several limitations since it is unable to solve the crossing of fibers and determine with accuracy the origin and destination of fibers, producing multiple artifacts and false tracts. These limitations significantly decrease the accuracy of the technique in the clinical setting.

For the last four years, our group at University of Pittsburgh has focused on optimizing brain fiber mapping techniques to obtain what we refer to as High Definition Fiber Tracking (HDFT). HDFT is a novel combination of processing, reconstruction, and tractography methods that can track several hundred thousand fibers from cortex, through complex fiber crossings, to cortical and subcortical targets with at least millimeter resolution. This disruptive technique has been applied in dozens of normal subjects and more than a hundred neurosurgery patients.

In this newsletter, we aim to introduce to the community our results with the application of HDFT for the study of structural connectivity in normal subjects, and we present our experience with the clinical application of HDFT for neurosurgery patients. This remarkable innovation has been possible at University of Pittsburgh thanks to a unique collaboration between clinicians and researchers with expertise in diverse disciplines such as neurosurgery, neuroanatomy, psychology, computer science, mathematics, and physics.

(continued on back cover)
The history of the Department of Neurological Surgery at the University of Pittsburgh has been highlighted by the development and implementation of important advances in neurosurgery that have altered the manner in which neurosurgical care is delivered. Initially, these changes were viewed with skepticism and, at times, have taken decades to be widely accepted into neurosurgical practice.

Innovations in this novel approaches have ultimately resulted in paradigm shifts for mainstream neurosurgery.

The most notable examples of such transforming technical advances include microvascular decompression for trigeminal neuralgia, hemispheric speech and other neurovascular compressive pathologies, skull base surgery for complex skull base pathologies; radiosurgery for vascular malformations, tumors and functional disorders; and, finally, endoscopic endonasal surgery for anterior skull base lesions.

These advances, in their own way, revolutionized the care of neurosurgical patients. These approaches provided options to patients who, either had no options, or significantly reduced the overall morbidity and mortality for the treatment of their specific diseases. We are extremely proud of the remarkable impact these advances that we previously only could have imagined. The potential of HDFT is boundless and is now changing the practice of neurosurgery as Pittsburgh. I look forward to its broad implementation in the years to come.

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HDF T latest game-changer in neurosurgical field

Chairman’s Message

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Using high resolution white matter mapping to detect traumatic brain injury

Jo-Samuel Shin, David Onokwo, MD, PhD; Walter Schneider, PhD; Timothy Westenberg

These text findings suggest that HDF T may provide a diagnostic advantage in evaluating modality for TBI. This will also become important in the future as various therapeutic options for TBI will become available, and optimal management of TBI will need to take into account the individual characteristics of each case.

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Lateral view of the corona radiata of TBI subject (a) shows fiber tract loss on the right side (outlined in red). Oblique (b) and magnified view of the tracts at the level of midbrain (c) reveals the details of fiber loss.
A 47-year-old woman presented with headache and right visual field disturbance. Her Karnofsky performance score was 90, with preserved motor function. An MRI scan detected a corticobasal glioblastoma near the motor region. The HDFT reconstruction confirmed the spatial relationship of the tumor with adjacent fiber tracts. Figure 2: The cortico-spinal (motor) tract was segmented from PET images, which were used to guide the surgical resection. The anterior portion of the resection approach was performed using HDFT within the operating room to visualize and preserve the motor fibers during tumor resection.

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Deep brain tumors are often not considered for surgical removal because of concern over morbidity related to tumor access and visualization. However, it is known that surgical resection can improve both neurological and oncological outcomes for patients with brain tumors. The Neuroendoscopy is a minimally invasive access tool for deep tumor resection that has been implemented in the removal of deep brain tumors using a technique called endoscopic port surgery (EPS). It is a transparent cylindrical retractor, 11.5 mm in diameter and of varying length, which facilitates deep brain access with minimal brain trauma while still allowing for bimanual microsurgery to remove the tumor. At UPMC, a significant experience has been developed using the Neuroendoscopy to remove deep tumors.

Prior experience with endoscopic port surgery has demonstrated that high definition fiber tracking (HDFT), a MRI-based technique for identifying critical fiber tracts, such as the corticospinal tract (CST), the optic radiations, or the central and anterior genuae of the corpus callosum, can be used to guide cannulation of a tumor using an endoscopic port, minimizing damage to functional surrounding nerve fascicles. This technique helps to ensure that critical fiber tracts, such as the corticospinal tract (CST), the optic radiations, or the anterior genuae of the corpus callosum are not damaged by the port during deep brain surgery.

Illustrative Case

A 60-year-old physician presented with complaints of headache, left-sided incoordination and mild motor weakness. Magnetic resonance imaging (MRI) scans demonstrated a heterogeneously enhancing mass surrounded by substantial peri-tumoral T2 signal change. The presumptive diagnosis of a high-grade glioma, surgical resection was recommended. The key concern was the presence of the tumor abutting and possibly involving the corticospinal tract (A8 motor tract) at the anterior portion of the tumor. Injury to these fibers would result in a significant risk for motor deficit. In order to better visualize peri-tumoral motor fibers, the patient underwent HDFT prior to surgical resection. We found that the motor fibers appeared to be displaced anteriorly by the tumor, which infiltrated much of the parietal lobe. We elected to resect the tumor via an awake craniotomy with cortical mapping, which facilitates real-time monitoring for any neurologic deficit. The HDFT images were transferred into our image-guidance navigation software by an image uplink interface to allow them to be tracked during surgery. The fiber tract imaging was cross-referenced to the anatomical images of the T1 MRI. As expected, intra-operative cortical mapping identified that the motor cortex was anterior to the tumor. A corticotomy was made immediately posterior to the motor cortex, and tumor was identified and the resection started using an ultrasonic aspirator. The navigation workstation showed the motor fibers either projected to the skin surface of the patient or overlaid on the structural MRI of the patient at the tumor resection proceeded. The anterior portion of the resection approached the motor fibers as visualized on HDFT on the image guidance system, but these fibers were all left intact. Post-operatively, the patient was neurologically limited using standard MRI imaging techniques, even with diffusion tensor imaging (DTI). In contrast, we found that high definition fiber tracking (HDFT) provides fiber tracking imaging that is more robust in the setting of variegated edema and has the ability to deal with fiber crossings. Here, we present a case where we utilized HDFT within the operating room to visualize and preserve the motor fibers during tumor resection.

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Intra-operative use of HDFT with image-guidance valuable in awake craniotomy for tumor resection

Current strategies for the surgical treatment of malignant brain tumors are directed towards maximal tumor resection while preserving neurological function. Injury to adjacent critical brain tissue can occur during the approach through the cortex and also via injury to eloquent fiber tracts that surround the tumor. However, fiber tract visualization surrounding the tumor is significantly limited using standard MRI imaging techniques, even with diffusion tensor imaging (DTI). In contrast, we found that high definition fiber tracking (HDFT) provides fiber tracking imaging that is more robust in the setting of variegated edema and has the ability to deal with fiber crossings. Here, we present a case where we utilized HDFT within the operating room to visualize and preserve the motor fibers during tumor resection.

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HDFT provides key edge in presurgical planning of brainstem cavernomas

Robert M. Friedlander, MD; Juan C. Fernandez-Miranda, MD; Amir Faraji

Brainstem cavernomas are one of the most challenging congenital lesions the neurosurgeon can face. The natural history of such lesions must be weighed against the risk of surgical resection. Surgical access to the brainstem is extremely delicate given the intricacy and eloquence of the fiber tracts and nuclei that form its structure. Historically resection has been fraught with significant rates of complications. One of the complexities in accessing the brainstem is that it is not predictable in which direction has the cavernoma displaced functional fibers. Here we report the innovative application of HDFT to map the fiber tracts within the brainstem and around a cavernoma to safely access and remove the lesion. HDFT provides information on the remaining normal fibers in relation to the cavernomas.

Understanding this relationship provides the surgeon the ability to plan a trajectory through the brainstem which maximizes the safety of resection of such lesions. Tipping the balance towards increased safety and efficacy allows for the ability to offer a therapy that is overall safer than the natural history of the untreated malformation. We have used HDFT to test a number of different types of lesions in eloquent areas of the brain and brainstem. Here we describe a case of the first cavernous malformation removed from the brainstem, using the information provided by HDFT to plan the trajectory and execute the resection

A 24-year-old female patient experienced a hemorrhage from a previously undiagnosed left pontomesencephalic cavernous malformation, and was subsequently admitted to an outside center. She suffered from a dense right upper and lower extremity hemiparesis, right gaze preference, and moderate dysarthria. Brain MRI demonstrated a left cavernous malformation within the brainstem. Given the location of the lesion the neurosurgeons recommended conservative management. After approximately one week, she was transferred to a rehabilitation facility where her speech progressively improved and the hemiparesis persisted. While at the rehabilitation facility, she became lethargic and developed a new left arm and leg weakness. She had right facial droop and dysarthria. Upon arrival the patient was awake, alert and oriented to person, place, and time. She had a right facial droop and dysarthria. Her speech was slow and her tongue deviated towards the right. Brain MRI demonstrated the cavernous malformation had bled one more time, and had more swelling around it. Given the aggressive nature of this malformation we recommended that the lesion be resected. The challenges of such a procedure are access as well as deciding the specific location to enter into the brainstem. Once inside the brainstem, understanding the location of the remaining normal structures provides the ability to remove the lesion with the greatest degree of safety.

To gather information as to the location of the normal fibers, the patient underwent on MRI study with HDFT imaging analysis. HDFT indicated severe deformation of the ipsilateral motor tract, with apparent disruption of some of its fibers with significant posterior displacement of a large number of motor fibers. Based on this tractography data and image guidance correlation, the surgical approach was carefully considered and a trajectory was selected to provide more immediate access to the intra-parenchymal hematoma and cavernous malformation. In accordance with this pre-operative planning, the patient underwent a left-sided frontotemporal, temporal transtemporal approach to access the pontomesencephalic cavernous malformation under image guidance. The lateral surface of the midbrain was visualized with a surgical microscope and a subtle yellow stain was observed, suggesting that this may be the most superficial location of the malformation. A small opening was made into the brainstem where the cavernous malformation was readily encountered. The hematoma and cavernous malformation were completely resected.

Her immediate post-operative examination revealed improvement in her double vision, her facial droop, as well as her right sided weakness. Her sensation remained intact throughout. Post-operative HDFT study was completed to evaluate the impact of surgical resection on the motor fibers, demonstrating preservation of the posteriorly displaced motor fibers and transaction of the previously disrupted fibers, as expected.

Over the course of the next six months, the physical displacement of white matter fibers continued to resolve, as revealed by a third HDFT scan. Moreover, her neurological examination continued to progressively improve. She is able to perform her activities of daily living with minimal to no assistance.

HDFT provided an edge in order to be able to offer a procedure in this specific young patient. Knowing the exact location of critical fibers within the brainstem provides the ability to approach and remove these lesions with much higher degree of safety. The surgeon can not see these fibers when operating under the microscope. However, knowing where they are located allowed us to provide the excellent result to our patient.
Solving Enigmas: the Anatomy of Language

HDFT provides a unique opportunity to study the connectivity of certain brain areas and functions that are largely unknown. Our studies on the arcuate tract, which is a major fiber system that interconnects different speech centers, have revealed an intriguing arrangement of the language circuitry: an inner semicircular tract that interconnects both primary speech centers (expressive or Broca’s and receptive or Wernicke’s), and a pair of outer parallel semicircular tracts that interconnect secondary or supplementary speech areas (figure at right). There is no doubt that a better delineation of the intricate structure of the human brain will improve our understanding of its complex functions, such as language, and the treatment of disorders of the human brain.

HDFT reconstruction (right) and anatomical fiber microdissection (left) of the left arcuate tract. With HDFT we can investigate the structural connectivity between multiple areas of the human brain. The arcuate tract is considered the “language” tract because interconnects distant language centers. Our investigations have revealed a complex network formed by several cortical centers interconnected by multidirectional pathways, organized in a concentric and parallel fashion. The inner or primary circuit (purple) is thought to be mostly related to the phonological aspect of language, while the outer circuits (red, yellow) are in charge of the semantic aspect of language. Further investigation is needed to ascertain the complete structure of the language system in the human brain.