Strategic and Multipronged Approaches to Spinal Tumors

NewYork-Presbyterian is among the most advanced centers in the nation for the diagnosis and treatment of both primary and metastatic tumors of the spine. The brain and spine tumor programs at NewYork-Presbyterian/Weill Cornell Medical Center and NewYork-Presbyterian/Columbia University Irving Medical Center integrate multiple disciplines to provide comprehensive treatment strategies that include minimally invasive surgery, radiation therapies, and intra-arterial chemotherapy. While surgery remains the cornerstone of treatment for pain, instability, and improved neurological function, today a number of options and alternatives have emerged from the medical, interventional radiology, and radiation oncology fields that are offering patients better outcomes and prolonged quality of life.

Detecting Tumors Sooner and Smaller

Neurosurgeon Paul C. McCormick, MD, MPH, Director of The Spine Hospital at the Neurological Institute of New York at NewYork-Presbyterian/Columbia, is a world-renowned expert in the microsurgical management of spinal tumors and vascular malformations. In his more than 25-year career at Columbia, Dr. McCormick has performed nearly 7,000 spinal procedures for patients from around the world.

Dr. McCormick has a particular interest in benign tumors located both inside and outside of the spinal cord. In the 1990s, he served as lead author in the development of a classification system for the clinical evaluation and correlation of risk with respect to surgery of spinal cord tumors. The McCormick Classification System, which remains in use today, grades the clinical severity of spinal cord tumors. “We developed the classification for intramedullary spinal cord tumors that has allowed us to define and determine appropriate treatment modalities for patients,” says Dr. McCormick. “Part of the point of establishing the system was that in years past, patients’ diagnosis would be delayed because we didn’t have the precision of imaging. Tumors were larger, and patients were not in good neurologic condition. The larger the tumor, the more impaired the patient would be.”

“The improved sensitivity, specificity, and availability of imaging have allowed us to diagnose tumors at a much earlier stage now and have also lessened the risk of surgery,” continues Dr. McCormick. “We’ve also moved forward in terms of our techniques, procedures, and technology.”

Dr. McCormick notes that with the advent of more precise imaging, including MRI, physicians are also seeing very small tumors that are clearly incidental in nature in patients who are not symptomatic. “This has created a dilemma as to what to do for these patients,” says Dr. McCormick. “It’s a burden (continued on page 2)
Strategic and Multipronged Approaches to Spinal Tumors (continued from page 1)

Dr. Ali A. Baaj, MD, of the Department of Neurological Surgery at NewYork-Presbyterian/Weill Cornell, specializes in spinal surgery with advanced training and expertise in spinal oncology and complex reconstructive surgery for spinal deformity and scoliosis for both adults and children. Accomplished in both minimally invasive and open complex spine surgery, one of Dr. Baaj’s interests focuses on spinal cord and spinal column pathologies.

“In some cases, these are benign conditions, and in other instances, they are malignant and require a multidisciplinary team in order to evaluate, treat, and manage the patient both surgically and non-surgically,” says Dr. Baaj. “The mainstay of treatment for many of these metastatic diseases involves chemotherapy and radiation therapy and not necessarily surgery. Surgery is not used to cure the disease; it’s used to remove the focal pressure off the spinal cord.”

Dr. Baaj maintains a close relationship with providers in medical oncology, radiation oncology, neuroradiology, and specialists in pain management and rehabilitation medicine. “It is truly a multidisciplinary process when it comes to metastatic disease, the most common condition in the spine oncology world,” says Dr. Baaj, who serves on a tumor board that meets each week to discuss treatment plans for complex cases.

During surgery, Dr. Baaj utilizes neuronavigation tools and intraoperative neuromonitoring. “A technician present in the operating room monitors the function of the nerves and the spinal cord in real time,” he says. “At the same time, that data is being reviewed remotely by a neurologist to ensure that what we’re doing is safe and that we’re not crossing the boundary into normal tissue, remaining focused only on the abnormal tissue.”

“In terms of imaging,” continues Dr. Baaj, “we have close and important interactions with Weill Cornell neuroradiologists, frequently reviewing films together. The type of tumor dictates how much of it we need to resect. We don’t always need to remove entire metastatic tumors, especially where there is extensive tumor infiltration of the spinal column. Many times, we need only to remove the part that’s compressing on the spinal cord and causing neurological dysfunction. This approach minimizes complications.”

As Dr. Baaj explains, pain control and palliation are of utmost importance with spinal oncology specifically related to metastatic disease. “Because many of these conditions are not curable, our goal is to provide the best quality of life for patients with excellent pain control. We do that with surgery and non-surgical interventions, such as systemic therapy and radiation oncology with the assistance of the palliative pain service, to make sure that the patient isn’t suffering.”

Benign spinal cord tumors represent a small percentage of the overall spinal oncology program at Columbia, says Dr. McCormick. “Treatment for malignant metastatic tumors that affect the spinal column itself requires a team effort,” says Dr. McCormick, who frequently collaborates with Andrew B. Lassman, MD, Chief of Neuro-Oncology, and Simon Cheng, MD, a radiation oncologist. “It is critically important – especially from a patient’s standpoint – to have leaders in these fields evaluating and recommending appropriate treatment plans. We work closely together to achieve the best outcomes for our patients.”

Navigating the Complexities of Spine Oncology

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Although most of Dr. Baaj’s work in spinal oncology involves metastatic spine disease, he also treats a significant portion of benign spine tumors as well. “These intramedullary tumors, which involve the spinal cord itself or the area just outside of the spinal cord, are very challenging to treat,” he says. “They’re difficult to resect technically,
requiring microsurgical skills. However, in some instances, patients can receive a total cure after surgical resection. Those types of tumors provide for some successful outcomes and very happy patients.”

Targeting Tumors with Stereotactic Radiosurgery
Susan C. Pannullo, MD, Director of Neuro-Oncology and Neurosurgical Radiosurgery in the Department of Neurological Surgery at NewYork-Presbyterian/Weill Cornell, is one of the few physicians in the world who is board certified in both neurology and neurological surgery, and perhaps the only one also fellowship trained in neuro-oncology.

“My role on this team is to provide patients with stereotactic radiosurgery procedures, which can be useful not only by shrinking tumors, but also by helping patients with symptoms from spine tumors, such as pain or weakness,” says Dr. Pannullo. “Patients often will have surgery first and then we’ll do radiosurgery, targeting remaining visible tumor or microscopic tumor cells that may be left behind after the surgery.”

“If we consider cancer more like diabetes or high blood pressure where we don’t have a cure, but we have management options that can help patients live with excellent quantity and quality of life, we can more effectively create optimal customized treatment plans to approach effects of cancer such as brain and spine metastases.”

— Dr. Susan C. Pannullo

Occasionally, when tumors are found early and are not encroaching upon the spinal cord or the spinal nerves, Dr. Pannullo uses stereotactic radiosurgery to manage definitively the tumor and inhibit its further growth, as well as to manage the pain that can come from tumors replacing the normal elements of the spine.

“Stereotactic radiosurgery, unlike the older forms of radiation for spinal tumors, is very focused,” explains Dr. Pannullo. “Years ago, and still now in some situations, a larger blanket of radiation was provided to the area involved with the tumor and the area surrounding it. Now, we prefer to limit radiation to just the area involved with the tumor in order to minimize the dose of radiation that goes to normal surrounding tissues, such as the spinal cord, spinal nerves, and nearby organs. In addition, patients who are receiving chemotherapy may have a need to preserve the normal bone marrow in the surrounding spinal bones. So, we limit the amount of radiation delivered to adjacent, normal spinal segments so as to lessen the impact upon the bone marrow, which is needed to create the normal blood cells that are reduced in number by the chemotherapy. Advances in the field have enabled us to refine this technique over the past few years to the point where we can be extremely precise and perform the treatment with little or no discomfort to the patient.”

Dr. Pannullo stresses the importance of modern communication that enables the care team to rapidly coordinate care for patients. “With a single email, I can pull in multiple specialists in order to coordinate a treatment plan and patient appointments, often within minutes,” she says. “For a patient who has a compelling and complicated problem like a spinal metastasis, this type of rapid deployment of expertise and resources is particularly crucial.”

“Patients who have spine metastases should be approached in a strategic and thoughtful way with a long-term view of quality of life and long-term side effects of treatments,” adds Dr. Pannullo. “If we consider cancer more like diabetes or high blood pressure where we don’t have a cure, but we have management options that can help patients live with excellent quantity and quality of life, we can more effectively create optimal customized treatment plans to approach effects of cancer such as brain and spine metastases.”

Managing Symptoms with Less Invasive Interventions
Athos Patsalides, MD, MPH, an interventional neuroradiologist in the Department of Neurological Surgery at NewYork-Presbyterian/Weill Cornell, practices in a rapidly evolving subspecialty that offers minimally invasive image-guided procedures for spinal tumors. “My role is to provide percutaneous treatments that specifically target the spinal tumor or spinal metastasis in terms of pain or tumor control,” says Dr. Patsalides. “When a patient has a tumor anywhere in the spine that is causing significant pain and/or pathologic vertebral compression fractures, we can offer vertebral augmentation. In vertebroplasty, we inject a cement mixture into the fractured bone to restore bone integrity. We can also perform kyphoplasty by inserting a balloon into the fractured bone to create a space and then fill it with cement.”

Dr. Athos Patsalides

Dr. Patsalides also performs fluoroscopic-guided thermal radio-frequency ablation for nonresectable spinal tumors. “The purpose of ablation, which also includes cryoablation and microwave ablation, is to treat at least part of the tumor and offer tumor control. It is a minimally invasive percutaneous procedure that involves the placement of a needle through a very small incision in the back and into the tumor in the spine with little trauma to the patient,” says Dr. Patsalides. “Often we do kyphoplasty and ablation together in a single session when the patient has a very painful metastasis that is causing a fracture in the spine. The patient goes home on the same day and the recovery process is minimal.”

When standard treatments, such as radiation and systemic chemotherapy, have failed, Dr. Patsalides can deliver chemotherapy

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Randomized participants will return to the clinic for follow-up have an alternative cause for neuropathy are potentially eligible. Adults, ages 18 to 75, diagnosed with CSPN who also have therapy for cryptogenic sensory peripheral neuropathy (CSPN). 100 mg daily (50 mg twice daily) as a potentially disease altering placebo-controlled trial of oral topiramate at a target dose of The TopCSPN trial is a 96-week, double blind, randomized, NN108 TopCSPN: A Study of Oral Topiramate as a Therapy for Cryptogenic Sensory Peripheral Neuropathy

The TopCSPN trial is a 96-week, double blind, randomized, placebo-controlled trial of oral topiramate at a target dose of 100 mg daily (50 mg twice daily) as a potentially disease altering therapy for cryptogenic sensory peripheral neuropathy (CSPN). Adults, ages 18 to 75, diagnosed with CSPN who also have metabolic syndrome (defined by the ATPIII criteria) and do not have an alternative cause for neuropathy are potentially eligible. Randomized participants will return to the clinic for follow-up visits every 16 weeks. The treatment phase will last 24 months.

NN107 FX-LEARN: A Study of AFQ056 in Fragile X Syndrome

Fragile X syndrome is a single-gene disorder and the most commonly inherited cause of intellectual disability. Effects range from learning disabilities to severe intellectual impairment. This study will examine if drug therapy with AFQ056 can improve communication and learning in children with Fragile X syndrome. The study will also determine the most effective dosing to improve neural plasticity, which is the core deficiency in Fragile X, as well as the safety of the therapy.

Participants between the ages of 32 months and six years of age will be randomized to either receive the drug therapy or a placebo for the initial period of about one year. All participants will be evaluated by speech language therapists, who will analyze and measure change in language skills in response to the intervention and deliver language therapy sessions to the family. In the study’s extension phase, all participants will be treated with the active drug for a period of about 8 months. The study is the first of its kind to evaluate whether a treatment aimed at improving a core deficit of brain connectivity can change the ability to learn in young children with Fragile X syndrome.

For More Information
NewYork-Presbyterian/ Columbia University Irving Medical Center
Principal Investigator: Jeremy Veenstra-VanderWeele, MD
(646) 774-5251
jv2511@columbia.edu
Study Location
Center for Autism and the Developing Brain
NewYork-Presbyterian Westchester Division
21 Bloomingdale Road
White Plains, NY 10605

Study Clarifies ApoE4’s Role in Dementia

ApoE4, a protein linked to both Alzheimer’s disease and a form of dementia caused by damage of blood vessels in the brain, increases the risk of cognitive impairment by reducing the number and responsiveness of blood vessels in the organ, a study by Weill Cornell Medicine researchers suggests. Published September 19, 2018, in Nature Communications, the study helps explain the connection between ApoE4 and vascular dementia, as well as vascular lesions that occur frequently in Alzheimer’s disease patients. “We found that the brains of mice with ApoE4 have less blood flow in the resting state and are also less able to increase blood flow when brain activity demands it, which leaves them much more vulnerable to brain damage,” says senior author Costantino Iadecola, MD, Director and Chair of the Feil Family Brain and Mind Research Institute at Weill Cornell Medicine.

How ApoE4 promotes damage in the nerve fiber tracts has been a challenge to determine because of the technical difficulty of studying blood vessels deep in the substance of the brain. Dr. Iadecola’s team overcame this hurdle with the help of 3-photon microscopy, which enabled the investigators to image at high resolution blood vessels and nerve fiber tracts deep within the brains of living mice.

The scientists examined mice whose ApoE4 gene had been replaced with the gene for ApoE4, which normally occurs only in humans. Comparing these ApoE4 mice to normal mice, they found that the former, while at rest, had 14 and 19 percent less blood flow, respectively, in two brain regions, the caudate nucleus and the somatosensory cortex – representing areas affected in humans with vascular dementia. By contrast, mice engineered with ApoE3 had the same level of cerebral blood flow as normal mice. Close inspection of the ApoE4 mice’s cerebral vessels revealed the reason for the reduced blood flow: The density of vessels was lower.

Further experiments showed that the cerebral vessels of the ApoE4 mice were also less able to dilate themselves to increase their flow, as they normally do in response to increased brain activity. When the major arteries supplying blood to the brain were narrowed artificially, modeling the age-related thickening of arterial walls that happens in humans, the lower baseline flow and reduced responsiveness of the ApoE4 mice’s cerebral vessels led to much greater brain damage. The pattern of brain damage resembled that seen in human vascular dementia and in a large number of Alzheimer’s disease patients.

Initial tests suggested that ApoE4 exerts these deleterious effects by causing certain immune cells in the brain to release superoxide and other highly reactive oxygen-containing molecules. These potentially damaging molecules inhibit vessel development and interfere with vessels’ abilities to increase local blood flow as needed. “We suspect that this ‘oxidative stress’ is the driver of the vascular impairment in ApoE4-positive individuals,” says Laibaik Park, PhD, co-senior author of the study.

Dr. Iadecola and his laboratory are continuing to investigate how ApoE4 harms normal cerebral vessel function. The research could lead to future therapies that block ApoE4-induced oxidative stress to ameliorate vascular dementia and potentially other ApoE4-linked conditions such as Alzheimer’s disease.
Dr. Cigdem Akman Leads Child Neurology at Columbia

Cigdem Akman, MD, has been named Chief of Child Neurology at NewYork-Presbyterian Morgan Stanley Children’s Hospital. An expert in child and adolescent epilepsy, Dr. Akman has served as Director of the Pediatric Epilepsy Program since 2010 and was named Interim Chief of the Division of Child Neurology in 2017. With this formal appointment, Dr. Akman continues the exceptional leadership she has demonstrated over the past year in driving the overall expansion of the division’s clinical, research, and education programs.

“I am truly honored to lead the Division of Child Neurology,” says Dr. Akman, an Associate Professor of Neurology and Pediatrics in the Department of Neurology at Columbia University Vagelos College of Physicians and Surgeons. “My goal is to ensure that we provide the most advanced treatments available to address the full spectrum of both common and complex pediatric neurological disorders. Through our recent and ongoing recruitment of talented physician-scientists in key areas of need, including autism and learning disabilities, pediatric neuromuscular disease and multiple sclerosis, sleep disorders, and transcranial electrostimulation, we are well-poised to take child neurology services at NewYork-Presbyterian Morgan Stanley Children’s Hospital to the next level.”

Under Dr. Akman’s leadership, the division has already expanded its outpatient practice to include two new locations, at 21 West 86th Street in Manhattan and 155 White Plains Road in Tarrytown, New York. In addition, plans are underway to expand pediatric epilepsy and child neurology inpatient services at NewYork-Presbyterian Lawrence Hospital in Bronxville, New York.

“Currently, there are only a few centers providing pediatric epilepsy surgery in New York City, and we are one of them,” explains Dr. Akman. “What makes our program unique is the level of engagement and expertise offered by our multi-disciplinary team of pediatric specialists, all of whom are committed to a highly personalized, compassionate approach to care. With our expansion into Westchester County, we hope to offer families in the tri-state area more treatment options, including access to less invasive, cutting-edge techniques for hard-to-treat epilepsy and other neurological disorders.”

About Dr. Akman

Dr. Akman, who was born in Ankara, Turkey, graduated from Ankara University School of Medicine. “It was my father who first encouraged me to consider becoming a doctor. I always trusted his judgment and listened to his advice. I still do,” says Dr. Akman. “Going to medical school turned out to be the best decision I could have made. In medicine, every day brings a different challenge but also different opportunities to help others.”

Starting out in internal medicine, Dr. Akman quickly realized she was drawn to pediatrics. “When you are treating a child, it’s very much a team approach with the family,” she says.

“Understanding their needs, gaining their trust, and collaborating on the decision-making all require much more in-depth connections.”

Dr. Akman came to the United States to continue her medical education, completing her residency in pediatrics and neurology with special qualifications in child neurology at State University of New York. She subsequently completed a fellowship in clinical neurophysiology and epilepsy at Boston Children’s Hospital, Harvard Medical School. “What’s rewarding about pediatric epilepsy is the impact you can have,” says Dr. Akman. “By making timely diagnoses and choosing the right medications, treatment methods, and surgical options, you truly have the ability to change the course of someone’s life.”

Dr. Akman joined the Division of Child Neurology at NewYork-Presbyterian Morgan Stanley Children’s Hospital in 2003, where she participated in clinical education and patient care until 2008. Between 2008 and 2010, Dr. Akman served as the Director of Clinical Epilepsy Research at Texas Children’s Hospital-Baylor College of Medicine. Dr. Akman returned to NewYork-Presbyterian Morgan Stanley Children’s Hospital in 2010.

Dr. Akman is a member of multiple national organizations, including the Child Neurology Society and the American Epilepsy Society, and her work on the diagnosis and treatment of childhood-onset epilepsy has been widely published in peer-reviewed journals.

“Over the years, I have learned that success in medicine requires not only hard work, but also empathy and patience,” adds Dr. Akman. “Listening to the concerns of our patients and their caregivers, understanding their needs, and observing their progress are essential to accomplish our goals in medicine.”

For More Information

Dr. Cigdem Akman • cia11@cumc.columbia.edu
Strategic and Multipronged Approaches to Spinal Tumors

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directly to the tumor through a catheter inserted into the femoral artery that supplies blood to the tumor. "Spinal intra-arterial chemotherapy is a unique, therapeutic treatment developed here at Weill Cornell — the only hospital where this procedure is performed. The treatment is used with carefully selected patients who are at risk for paralysis from spinal cord compression," he explains. "We don't do this very often, thankfully, because most patients respond to the standard treatments."

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— Dr. Athos Patsalides

Dr. Patsalides and his colleagues tested this novel treatment in a Phase 1 clinical trial of nine patients with progressive spinal metastatic disease and cord compression. All of the patients had metastatic disease from solid organs and were not candidates for further radiation therapy or surgery. A total of 19 spinal intra-arterial chemotherapy (SIAC) procedures were performed, and the follow-up period ranged from one to seven months. Local tumor control was seen in eight of the nine patients. The preliminary results of this study, which were published in the *Journal of Neurosurgery: Spine* in 2016, support the hypothesis that SIAC is feasible and safe. The clinical trial is ongoing with completion slated for early 2021.

"We showed that this minimally invasive approach can stop the tumor progression by directing chemotherapy into the arteries that supply the tumor," says Dr. Patsalides, noting that some 20 patients have been successfully treated with this approach to date. "This is also a nontraumatic outpatient procedure without any significant or adverse effects to the patient."

Dr. Patsalides is optimistic that the future will bring more minimally invasive approaches that will target spinal tumors, and at the same time will not compromise other treatments that patients are receiving. "We've made a lot of progress in the last two years, and I believe there are going to be many more options soon."

Reference Article

For More Information
Dr. Ali A. Baaj • alb9140@med.cornell.edu
Dr. Paul C. McCormick • pcm6@cumc.columbia.edu
Dr. Susan C. Pannullo • scp2002@med.cornell.edu
Dr. Athos Patsalides • atp9002@med.cornell.edu