

ADVANCES IN NEUROLOGY AND NEUROSURGERY



Comprehensive Programs Address Brain and CNS Metastases

Secondary, or metastatic brain tumors, are among the most common mass lesions in the brain. NewYork-Presbyterian/Columbia University Medical Center and NewYork-Presbyterian/Weill Cornell Medical Center have each developed brain metastases programs that provide patients with the latest diagnostic and treatment modalities and access to resources to help address the consequences of metastases and side effects of therapy. Multidisciplinary “brain mets” teams offer patients and their caregivers compassionate care and support aimed at improving quality of life and allowing patients to live months and sometimes years after diagnosis.

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Multidisciplinary Central Nervous System Metastases Clinic

Andrew B. Lassman, MD, is Chief of the Division of Neuro-Oncology and Co-Director of the Brain Tumor Center at NewYork-Presbyterian/Columbia. **Guy M. McKhann II, MD**, is Director of Awake Brain Mapping for Tumors and Epilepsy in Columbia’s Department of Neurological Surgery. **Adrian G. Sacher, MD**, is a medical oncologist who specializes in lung and thoracic cancers.

Under the auspices of Columbia’s Division of Neuro-Oncology, CNSMets grew out of the need to organize and focus the complex array of specialist expertise – neurosurgery, neurology, radiation oncology, medical oncology, palliative care, social work, neuroradiology, neuropathology, molecular pathology, and complementary and alternative medicine among others – to address the many and varied challenges that can accompany a diagnosis of brain metastases.

These physicians are key members in the development of the Multidisciplinary Central Nervous System Metastases Clinic (CNSMets), recently established to coordinate and advance the treatment of brain, leptomeningeal, skull base, spinal cord, and spine

metastases. “Patients who have central nervous system – brain or leptomeningeal – metastases often need to see several different specialists on different days in

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NewYork-Presbyterian Neurology and Neurosurgery ranks #4 in the nation.

Brain Metastases Clinic

“Today, therapeutic advances are making it possible for patients with cancer to live longer and with better quality of life,” says **David M. Nanus, MD**, Chief of the Division of Hematology and Medical Oncology at NewYork-Presbyterian/Weill Cornell. “At the same time, however, higher survival rates have also been accompanied by a higher incidence of cancer spreading to the brain. Cancer cells are basically smart. Their goal is to grow, so they’ll find a new environment in which to grow. The brain acts like a sanctuary site for many treatments.”

“The Brain Metastases Clinic at the Weill Cornell Brain and Spine Center is a much-needed program for these patients,” adds Dr. Nanus. “They are provided with access to comprehensive care that promotes their physical and psychological well-being, while at the same time addressing the myriad

clinical issues, including the toxic side effects of therapy, that accompany this diagnosis.”

“A brain metastasis is clearly a critical point in a patient’s cancer care,” says neurosurgeon **Rohan Ramakrishna, MD**, Director of the Brain Metastases Clinic. “I’ve seen the consequences of brain metastases on patients. It’s not the immediate aftermath; it’s what happens months and years following treatment and the kinds of problems they can encounter.”

The newly launched Brain Metastases Clinic provides comprehensive care to patients diagnosed with metastatic brain tumors and leptomeningeal disease. “The treatments can be surgery, chemotherapy, and radiation,” says Dr. Ramakrishna. “However, the consequences of combinations of those therapies often get lost or are not managed in a proactive way.

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Multidisciplinary Central Nervous System Metastases Clinic *(continued from page 1)*

different locations,” says Dr. Lassman. “Many of our patients are frequently dealing with physical disabilities and concurrent cognitive limitations making it difficult to navigate the numerous and varied appointments. Our new program makes it logistically easier for patients to obtain care, including rapid access to appointments.”

“I think the key factor in this day and age is finding ways to optimize communication among physicians and with the patient,” says Dr. McKhann. “It is so important for patients with metastatic brain disease to have coordinated, multidisciplinary care where teams of experts are reviewing not just what’s going on in the brain, but what is happening in the body as a whole. Then you can integrate their treatment in the best possible way.”

The CNSMets Clinic takes place every Wednesday afternoon. Patients are first seen by a neuro-oncologist. Cases are then discussed at a multidisciplinary tumor board specifically for brain and spine metastases led by neuro-oncologist **Teri N. Kreisl, MD**. Dr. Kreisl and representatives from relevant specialties develop a consensus of opinion for a comprehensive treatment plan. Depending on the plan of care, patients may then meet with consultative specialists from neurosurgery, radiation oncology, medical oncology, palliative care, social work, and complementary and alternative medicine that same afternoon.

The CNSMets Clinic utilizes a multidisciplinary and multi-tumor site approach that allows for high level discussion of unique cases and rapid planning of individualized, cutting-edge therapy for each patient.

Among the immediate benefits of the tumor board, Dr. Lassman cites the team’s extensive knowledge of Columbia’s many ongoing trials to identify the one that is most appropriate for an individual patient. “This approach, where we are co-located together, can yield additional therapeutic options for the patient,” says Dr. Lassman. “For example, we are currently running a trial through the NRG Oncology research group – part of the NCI-funded National Clinical Trials Network – that involves radiotherapy, a standard treatment for brain metastases that’s been in existence for decades. But whole brain radiotherapy can cause memory problems. So this is a clinical trial that tries to bend the radiation beam around the areas of the brain that are thought to be important for memory and therefore reduce the potentially deleterious effects on the parts of the brain that are memory forming. Our goal is to apply new treatments that may lengthen life or improve quality of life. Sometimes that involves using standard technology in a new way, such as this. Through the tumor board, clinical trials and other research efforts that, without the tumor board mechanism, may not otherwise have been brought to light, are able to be shared and quickly determined for their appropriateness for the patient.”

For Dr. McKhann and his surgical colleagues, the tumor board optimizes the process of coming to key surgical decisions. “The coordination of therapies with sensitivity in timing helps in the decision-making regarding employing open surgery, the



Dr. Andrew B. Lassman



Dr. Guy M. McKhann II



Dr. Adrian G. Sacher

Gamma Knife, often a combination of both, or no surgery at all,” notes Dr. McKhann. “For example, when timed with Gamma Knife procedures, the efficacy of some chemotherapy protocols is enhanced by increasing the permeability of the brain-blood barrier. Sometimes immunotherapy has proven more effective than chemotherapy and can be a factor in delaying or avoiding surgery. It’s also how symptomatic the patient is. If they’re particularly symptomatic, it will push them more towards surgery and away from the Gamma Knife. However, if it’s a single seizure and the patient is otherwise asymptomatic, and we already know this is clearly metastatic disease, then the Gamma Knife is going to make sense. These myriad complex choices become research informed, deeply explored, and clearly communicated group decisions.”

“This program is unique in that it brings together experts from multiple clinical fields with experts in different scientific fields, creating an ideal environment for the management of patients who are grappling with an incredibly complex medical problem,” adds Dr. Sacher, whose research explores why some patients will have fantastic responses to immunotherapy, or a more targeted therapy, whereas other patients might not achieve that same benefit. In the CNSMets program, Dr. Sacher serves as a representative of the medical oncology program and the Phase 1 Drug Development Program.

“The CNSMets group is interested in opening specific clinical trials where the focus is just on the treatment of brain metastases,” continues Dr. Sacher. “We are trying to develop new techniques that are aimed at providing optimal treatment while attempting to minimize neurocognitive side effects. These include CNS penetrant-targeted therapies, immunotherapy trials, and trials focused on novel devices or approaches to radiation therapy. So, we are connecting clinical trials to translational research by those who are primarily foundational scientists. We work seamlessly together to make sure that we’re able to advance the science of clinical care for cancer, but also to make sure that we’re bringing the best possible care and the most forward-thinking care to our patients with respect to standard treatment. That’s something I’m very proud to be part of.”

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Brain Metastases Clinic *(continued from page 1)*

For example, patients can suffer chronic pain issues, depression, dementia, neurocognitive issues, and rehabilitation issues, and spiritual concerns related to their own mortality.”

“Our multidisciplinary group includes not only neurosurgery, radiation oncology and medical oncology, but also psycho-oncology, a burgeoning field in this area, as well as palliative care,” continues Dr. Ramakrishna. “We have also incorporated an integrated health program that offers acupuncture, yoga, mindfulness, and meditation. We believe that integrative therapies that address the whole patient should be as important as any of the traditional therapies offered to control the patient’s brain cancer.”

Navigating a large healthcare system is particularly difficult for a patient with brain cancer. “Figuring out which doctor to go to and which appointments to schedule can be overwhelming,” says Dr. Ramakrishna. To that end, the program offers a program coordinator who answers 646-NYP-METS. The goal here is to spare the patient from having to call so many different physicians. The navigator will go through a questionnaire with the patient, determine their availability, and then put together a day of scheduled appointments. It’s concierge medicine that caters to the patient’s needs.”

Support groups run by patients or caregivers and groups specifically for caregivers are also in development. “Taking care of someone with a chronic illness who is near or at the end of their life can be extraordinarily stressful from both an emotional and financial aspect,” says Dr. Ramakrishna.

The reality of brain metastases, adds Dr. Ramakrishna, is that patients must often face their own mortality. “Spirituality means different things to people. I think that when most people see that the end of their life is coming, they want to engage in some aspect of spirituality in order to have inner peace. To that extent, we tell our patients that whatever they are feeling is not only okay, but we encourage them to explore their feelings with people who are trained and interested in helping them.”

Research is another component of the program. “Our goal is to study the impact of a comprehensive program like this on the well-being of our patients,” says Dr. Ramakrishna. “We do quality-of-life questionnaires with patients, each of whom is unique with different cancers and different systemic disease. We also plan to study how we can make radiation therapy less toxic on the brain. Neurocognitive decline happens after radiation, but it also happens in patients who have brain mets, period. Learning how to minimize the complications of neurocognitive decline, as a result of not only the disease, but also the therapy, is integral to our research strategy.”

The increasing incidence of brain metastases is likely the result of better treatments for systemic cancer as well as improved monitoring. “Unfortunately, the brain is a place where metastases can potentially be shielded from systemic treatment,” says neuro-oncologist **Rajiv S. Magge, MD**. “The blood-brain barrier blocks many drugs from reaching the brain and creates a major challenge in treating brain tumors. We’re trying to focus on better treatments that may target metastases in the brain.”

Dr. Magge believes that the depth of expertise at the Brain Metastases Clinic allows physicians to tackle it from several



Dr. Rajiv S. Magge



Dr. David M. Nanus



Dr. Rohan Ramakrishna

directions. “Newer systemic treatments may get past the blood-brain barrier. These include immunotherapy, which has shown efficacy in treating brain metastases from specific cancers, especially lung cancer and melanoma.”

“With the advent of 3-D cross-sectional imaging and a better understanding of the natural history of cancer, we can focus our treatments more on the tumor deposits themselves,” says **Jonathan P.S. Knisely, MD**, Medical Director of Stich Radiation Oncology at NewYork-Presbyterian/Weill Cornell, Director of Neuro-Oncology in the Department of Radiation Oncology, and Associate Director of the Brain Tumor Center. “This enables us to minimize the dose of radiation delivered to normal tissue, while greatly increasing the dose of radiation to the tumor deposits.”

“With an MRI scan we can see precisely where a spot or spots are within the brain,” continues Dr. Knisely. “This allows us to map out exactly where the tumor is and where any normal tissues are that you don’t want to have irradiated. We can then treat that very small volume with very high doses of radiation that will often achieve a 95 percent control rate at one year’s time.”

“Managing disease that spreads to the brain is an area of study that is needed more and more today,” says Dr. Nanus. “It used to be that if you wanted to get a new drug for metastatic cancer, nothing was available in clinical trials. But now we have a number of trials that we are opening where there is a cohort specifically for patients with brain metastases.”

Drawing on his neuro-oncology and neurology background, Dr. Magge says, “I would like to be considered a resource – especially for the medical oncologist – to help manage and follow patients with brain metastases. We work with oncologists in coordinating management and helping decide which treatments – systemic therapy, surgery, and/or radiation – may be most effective. With our experience in neurology and oncology, we are able to help manage both brain metastases and other neurologic complications unique to the cancer patient population.”

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Expanding Expertise in Neurology and Neurosurgery



Dr. Babacar Cissé

Brain and Spinal Tumors

Neurosurgeon Babacar Cissé, MD, PhD, has joined the Weill Cornell Brain and Spine Center at NewYork-Presbyterian/Weill Cornell. Dr. Cissé's particular expertise is in primary and metastatic brain and spinal tumors, incorporating multiple modern and advanced techniques that include neuro-navigation, ultrasound, advanced imaging, motor and speech mapping, and endoscopic and minimally invasive surgical techniques.

Dr. Cissé also serves as the principal investigator of a basic research laboratory that studies the interactions between the immune system and brain tumors using human brain tumor samples and mouse brain tumor models. "Our goal is to develop a thorough and basic understanding of how immune cells inhibit the development and/or progression of brain tumors. This understanding will eventually lead to identifying therapeutic targets against which agents can be developed," says Dr. Cissé, whose work has been published in journals that include *Clinical Cancer Research*, *Cell*, and *Immunity*.

Born and raised in Senegal, Dr. Cissé received his BA in chemistry from Bard College and then joined the Medical Scientist Training Program at Columbia University College of Physicians and Surgeons where he earned his medical degree and PhD with Distinction. He then went on to complete his residency and chief residency in neurological surgery at NewYork-Presbyterian/Weill Cornell and Memorial Sloan Kettering Cancer Center. "My neurosurgical training at Weill Cornell was superb in every respect," notes Dr. Cissé. "The diversity of the patient population and the commitment of every staff member to the highest standards of patient care are everything that I was looking for in a training environment."

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Dr. Jonathan P.S. Knisely

Radiation Oncology

In June 2017, Jonathan P.S. Knisely, MD, was appointed Medical Director of Stich Radiation Oncology at NewYork-Presbyterian/Weill Cornell, Director of Neuro-Oncology in the Department of Radiation Oncology, and Associate Director of the Brain Tumor Center. Dr. Knisely brings significant expertise and experience in the treatment of brain and spinal tumors with image-guided radiotherapy, intensity modulated radiation therapy, and stereotactic radiosurgery. Prior to joining Weill Cornell, he served as Chief of the Radiosurgery and Stereotactic Program and Co-Director for Radiosurgery and Stereotactic Radiation Therapy in the Northwell Health System and the Hofstra Northwell School of Medicine where he was principal investigator for the Radiation Therapy Oncology Group.

"As a radiation oncologist with a subspecialty practice in managing tumors arising in or metastatic to the brain, I look forward to participating in the exciting translational work that's being done at the interface of immunology and radiation therapy here at Weill Cornell," says Dr. Knisely.

Dr. Knisely has conducted bench and clinical brain tumor research throughout his career, publishing numerous journal articles and book chapters. He is a Fellow of the American Society for Radiation Oncology and holds memberships in additional medical societies, including the International Stereotactic Radiosurgery Society, the Society for Neuro-Oncology, the Leksell Gamma Knife Society, and the NCI-sponsored NRG oncology clinical trials network. He is the current CNS Scientific Program Committee Chairman for the American Society for Radiation Oncology's annual scientific meeting.

Dr. Knisely's clinical focus will be to strengthen the stereotactic body radiation therapy and stereotactic radiosurgery programs at Weill Cornell Medicine through close interactions with colleagues in neurosurgery, neuro-oncology, neuroradiology, neuropathology, and medical oncology, while conducting clinical research in the optimization of care for central nervous system tumors. "What is very attractive about this institution is the multidisciplinary approach to the management of neuro-oncologic issues," adds Dr. Knisely. "We have a team that is focused on patient care and, at the same time, is trying to figure out how to better treat patients in the future."

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Expanding Expertise in Neurology and Neurosurgery *(continued from page 4)*



Dr. Philip L. De Jager

Neuro-Immunology

Committed to transforming the management of multiple sclerosis and other neurodegenerative diseases, **Philip L. De Jager, MD, PhD**, has joined the Department of Neurology at NewYork-Presbyterian/Columbia as the Director of the Center for Translational and Computational Neuro-Immunology and the Director of the Multiple Sclerosis Center. “The goal of my work as a clinician-scientist is to apply modern methods of human immunology, statistical genetics, epigenomics, and systems biology to the understanding of common neurodegenerative diseases,” says Dr. De Jager, who also serves as Chief of the Division of Neuro-Immunology, which focuses on characterizing and targeting the neuro-immunologic component of neurodegenerative diseases.

“Our new division seeks to provide innovative, compassionate care to patients with immune dysfunction that targets the brain and spinal cord,” says Dr. De Jager. “We also hope to lead transformative, rigorous human research studies to first understand and then to target the role of the immune system in neurodegenerative diseases such as ALS, Alzheimer’s, Parkinson’s, and multiple sclerosis.”

Dr. De Jager, who is also the Weil-Granat Professor of Neurology in the Taub Institute for Research on Alzheimer’s Disease and the Aging Brain and the Columbia Precision Medicine Initiative, has a rich educational background. After graduating from Yale University with a degree in French literature and molecular biophysics and biochemistry, he received a PhD in neurogenetics from The Rockefeller University and his medical degree from Weill Cornell Medicine, followed by an MMSc in clinical investigation at Harvard Medical School and MIT. He then pursued a residency in neurology and additional training in clinical neuro-immunology at Massachusetts General Hospital and Brigham and Women’s Hospital.

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NeuroNEXT

CYTO-C (Cytochrome c Oxidase Activity in Newly Diagnosed GBM)

Glioblastoma multiforme (GBM), a malignant form of astrocytoma, is the most common and most aggressive glioma. Subjects with newly diagnosed GBM who undergo standard of care treatments (maximal surgical resection, 60 Gy radiotherapy together with Temozolomide, followed by maintenance Temozolomide for 6 months) have been found to have a median survival time of 14.6 months. It is postulated that overall survival in patients with newly diagnosed GBM treated with standard of care measures is correlated with Cytochrome c Oxidase (CcO). The greater the CcO activity, the shorter the overall survival time. Thus, CcO activity as a biomarker could have valuable clinical implications in guiding patient therapy.

This research study is being conducted to determine the relationship between CcO activity in GBM tumors and overall survival time (time from diagnosis to death) and to

compare the usefulness of CcO as a biomarker to an already well-known biomarker, MGMT.

The study seeks to recruit 200 male and female subjects, aged 21 or older, with newly diagnosed GBM who are undergoing standard of care treatment as defined above and have a KPS score >60. Tumor tissue samples will be sent to assess CcO activity and brain imaging, and medical records will be utilized to assess disease progression.

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NewYork-Presbyterian Establishes the William Rhodes and Louise Tilzer-Rhodes Center for Glioblastoma

NewYork-Presbyterian has established the William Rhodes and Louise Tilzer-Rhodes Center for Glioblastoma led by renowned experts in neuro-oncology from Columbia University Medical Center and Weill Cornell Medicine. The Center is focused on pursuing groundbreaking research and providing advanced treatments for glioblastoma and other deadly brain cancers. Made possible by a major gift from Mr. Rhodes, a Life Trustee of NewYork-Presbyterian since 1992, the program was created to honor Louise Tilzer-Rhodes, who passed away from glioblastoma in 2016.

“Thanks to the generosity of Mr. Rhodes, we have an opportunity to make tremendous strides in our understanding and treatment of glioblastomas,” says Steven J. Corwin, MD, President and CEO of NewYork-Presbyterian. “NewYork-Presbyterian is committed to becoming the world’s leader in the fight against this deadly disease.”

“Glioblastoma has had a profound impact on my family and countless others,” says Mr. Rhodes. “It’s so important that we bring together and empower the brightest minds to bring new therapies – and one day, a cure – to patients.”

The William Rhodes and Louise Tilzer-Rhodes Center for Glioblastoma at NewYork-Presbyterian aims to advance care for glioblastoma and other brain cancers via a three-pronged approach: providing multidisciplinary, research-driven patient care, with a focus on genomic and precision medicine; emphasizing translational research

to rapidly bring promising new therapies from the bench to the bedside; and educating the next generation of clinicians and scientists with new fellowships created to expose young physicians to the most cutting-edge work being done in the field.

William Rhodes and Louise Tilzer-Rhodes Center for Glioblastoma – Leadership

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