Gerald J. Glasser
Brain Tumor Center

Atlantic
Health System
Neuroscience

The Science of Medicine.

Inside Look

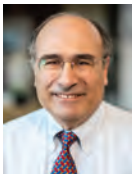
SPRING 2022 | INSIDE THIS ISSUE:

Every day, the Gerald J. Glasser Brain Tumor Center team – along with medical professionals, researchers and clinicians worldwide – search for new ways to treat brain cancer.

From next-generation sequencing – treatments that zero in on specific genes in cancer cells – to novel therapies that prevent cancer from metastasizing to the brain, immunotherapy and personalized medications that bring renewed hope to patients, and more, we are making a difference.

In this issue, read about the latest advancements in brain tumor prevention and care from our brain cancer experts. Hear an inspiring story from one of our patients, and learn about the resources available to our brain tumor patients.

We – in collaboration with our partners at Atlantic NeuroSurgical Specialists – are committed to leading the way in delivering best-in-class, multidisciplinary care for brain tumors of all types.



Co-Directors

Yaron A. Moshel, MD, PhD
Neurosurgery

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Neuro-oncology

Living with Brain Cancer:

Attitude is everything

Lindsay Vieira is living her best life with her hus

At 43, Lindsay Vieira is no stranger to dealing with cancer. Her father passed away from the disease in 2015 at the age of 65, and one of the things she has carried with her since then is his insistence that attitude is everything – especially when it comes to cancer. Little did she know that saying would hit home again when she was diagnosed with brain cancer in 2018.

"My life was completely normal – until it wasn't," says Lindsay, who has been a principal in Morris Plains School District since 2007. "On a day like any other, I was getting ready for work and suddenly had a massive seizure on my bathroom floor. My daughter, who was just shy of three years old at the time, brought me my phone so I could call my husband. I told him I thought I was having a stroke and asked him to call 911."

Emergency responders took Lindsay to Hackettstown Medical Center, where an MRI showed a large mass in her brain. She was immediately transferred to the Gerald J. Glasser Brain Tumor Center at Overlook Medical Center and had brain surgery the next day.

"At the time, Lindsay's tumor was compressing her motor cortex, the part of the brain responsible for controlling body movements. While we needed to preserve the motor cortex, we wanted to push to remove as much of the tumor as possible to have a better long-term outcome. Adding to the challenge, the tumor did not have clear boundaries separating it from healthy brain matter, making a gross total resection even more difficult to achieve," explains Yaron A. Moshel, MD, PhD, co-director of the Gerald J. Glasser Brain Tumor Center and a neurosurgeon with Atlantic NeuroSurgical Specialists, who led Lindsay's surgical team.

To define the tumor boundaries during surgery, the team used three-dimensional stereotactic imaging, which combines multiple types of MRIs and 3-D images of the tumor, as well as GPS-like technology. They also performed

band Fabio and daughter Renata.

"The most positive part of my journey is using my story to help other people. I have a daughter. I have a husband. I have a great life. And thanks to the Glasser Brain Tumor Center, I also happen to be living with brain cancer."

electrical stimulation brain mapping to detect the precise locations of Lindsay's brain functions. With this high-tech approach, Dr. Moshel was able to remove all of Lindsay's tumor and kept all of her neurological functions intact.

Pathology confirmed Lindsay's tumor was an anaplastic oligodendroglioma, a cancerous and rare type of glioma with a high likelihood of recurrence. She went through chemotherapy and radiation therapy. However, one and a half years later, the tumor returned.

"Lindsay's treatment course highlights the importance of treating patients individually and tailoring their care to their specific needs," says Nicholas Metrus, MD, one of only four neuro-oncologists in New Jersey who are board-certified by the United Council for Neurologic Subspecialties.

Lindsay's previous chemotherapy had a side effect of reducing her number of platelets, a vital blood component that prevents bleeding. She needed a second surgery, but having low platelets made this far too dangerous. Dr. Metrus gave her a medication that helped boost her platelet level so she could have surgery. The team then analyzed the tumor tissue from both surgeries to determine which mutations her tumor may or may not have.

"In the past, it was routine to analyze tumor tissue under a microscope and classify it based on its appearance. With our ever-growing knowledge of brain tumors, we now understand this is only a piece of the puzzle," Dr. Metrus continues. "Molecular information – coming from the presence or absence of different mutations at the DNA level – can tell us so much more about how a tumor may behave and respond to different treatments."

Genetic testing revealed Lindsay's tumor had an IDH1 mutation. Using that knowledge to determine the best course of maintenance treatment, Dr. Metrus narrowed his focus on medications that have shown promise in targeting this specific mutation. He selected a drug called Olaparib based on preclinical and clinical trial data that shows IDH-mutant tumors could be vulnerable to this type of medication.

"Lindsay has done incredibly well on this medication," he adds. "The collaborative effort between neurosurgery, neuropathology and neuro-oncology, backed by cutting-edge technology, played a huge role in controlling Lindsay's disease for the long term."

Lindsay says having this expertise at her disposal has been extremely valuable. She has been stable for two years since her second surgery and hasn't let cancer hold her back. She has been back at school working with students and colleagues she adores. She recently got back from a three-week vacation with her family to her husband's homeland in Brazil and has several trips planned for the future. Lindsay also serves as a mentor for families who are dealing with the same type of cancer through the Cancer Hope Network.

Next-Generation Sequencing: The Key to Next-Level Brain Tumor Treatment

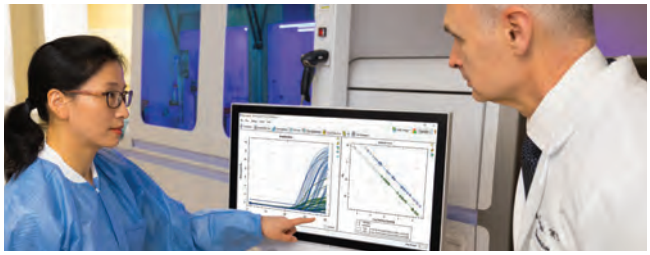
Targeted therapies – treatments that zero in on specific genes present in an individual's cancer cells – are changing the world of oncology. This personalized approach is revolutionizing cancer care, improving drug efficacy and extending life expectancy, and it all starts with next-generation sequencing (NGS).

NGS in a Nutshell

According to John Paul Bouffard, MD, a neuropathologist at the Gerald J. Glasser Brain Tumor Center, the easiest way to understand next-generation sequencing is to think about your DNA like a library.

"All the different genes in your DNA are like individual books. Of the thousands of books – or genes – in your library, only one or two may be responsible for a cancer," he explains. "Next-generation sequencing is like a search engine that can comb through thousands of books on hundreds of shelves and find abnormalities in the single book – the single gene – linked to a patient's cancer."

These abnormalities are called gene mutations. Many people have heard of HER2-positive breast cancer, which refers to a protein found in the cells of some types of breast cancer caused by a mutation in the ERBB2 gene. Similarly, the IDH1 gene mutation is a common driver mutation associated with brain cancer, as are MGMT and BRAF mutations.



Diagnoses Driven by Genetic Science

This genetic knowledge is transforming the way brain tumors are classified and treated. Traditionally, pathologists evaluate tumors using light microscopy, which is essentially examining tumor samples under the microscope and classifying them based on how they look. Now, with NGS and other advanced technology, neuropathology is being driven by genetic science.

"When we identify a tumor as a glioblastoma, for example, we don't stop there. We classify it as an IDH wild-type glioblastoma or an IDH-mutant glioblastoma," Dr. Bouffard notes. "Though they are the same type of tumor when viewed through a microscope, they are genetically very

different, carry different prognoses and lend themselves to different treatments and clinical trials. This is precisely why molecular diagnostics is so critical."

Targeted Brain Tumor Treatments

Television and movies lead us to believe that any type of mutation is inherently bad. However, according to neuro-oncologist Nicholas Metrus, MD, when it comes to brain tumors, it is these mutations that open up a number of possibilities for meaningful treatments.

"A tumor's mutations, or lack thereof, tell us more information about how they behave and which medications they may or may not respond to," he says. "An intimate understanding of the details can make all the difference. If molecular testing reveals a mutation in a tumor and we have a known medication that targets that mutation, we can create an even more personalized and effective treatment plan."

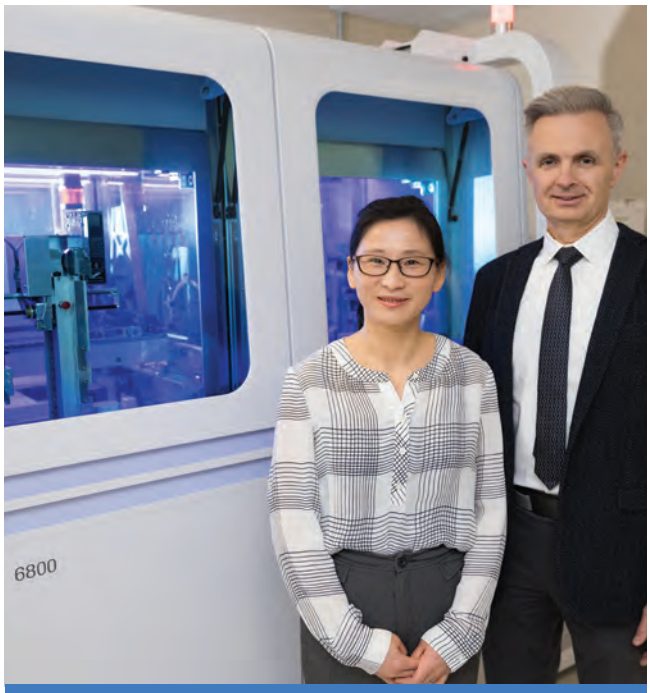
"Knowing every detail possible about a specific brain tumor can ensure the most targeted, effective approach to treatment."

INVESTING IN THE **FUTURE OF CANCER CARE**

Recognizing that molecular diagnostics like next-generation sequencing will continue to drive the future of cancer care, Atlantic Health System recently unveiled a best-in-class molecular laboratory at the Atlantic Consolidated Laboratory.

A major investment for Atlantic Health, the lab is home to the experts and equipment needed to perform comprehensive molecular testing in house. This enables physicians to get the genetic intelligence they need to guide advanced patient care – faster than ever before – from experts directly within the health system.

With an increasing number of clinical trials focused on tumors with specific mutations, having this genetic knowledge as quickly as possible is also key to getting patients enrolled in investigational studies that may be their most promising course of treatment.



Molecular supervisor Min You, PhD, and neuropathologist John Paul Bouffard, MD, showcase the cobas® 6800 System, a new molecular diagnostics system that expands access to testing and improves patient care.

Preventive Chemotherapy Slashes the Risk of CENTRAL NERVOUS SYSTEM LYMPHOMA

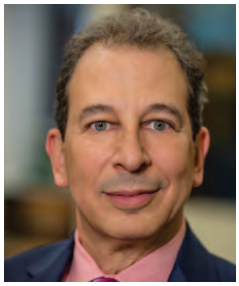
Certain types of lymphoma and certain patients with lymphoma are predisposed to the disease metastasizing in the brain. However, preventive chemotherapy can reduce that risk from about 25% to 2 or 3%. Oncologist Charles M. Farber, PhD, MD, explains.

Why is it important to talk about systemic lymphoma in regard to the central nervous system?

Approximately 75,000 to 80,000 individuals are diagnosed with non-Hodgkin's lymphoma – cancer of the lymphatic system including the lymph nodes – every year. We know certain lymphomas tend to enter the central nervous system and reach the brain. This includes aggressive lymphomas, high-grade lymphomas and individual subtypes such as Waldeyer's ring lymphoma and mantle cell lymphoma. Patients whose disease is not confined to the lymph nodes and who are immunosuppressed are also predisposed to central nervous system lymphoma.

What does treatment for central nervous system lymphoma entail?

The central nervous system is like a sanctuary for cancer cells because most traditional chemotherapies cannot penetrate the blood-brain barrier (hence our saying in oncology, "Chemotherapy in the vein does not penetrate the brain"). While the blood-brain barrier naturally protects the central nervous system from bacteria and viruses, it doesn't keep all pathogens out … or necessarily allow cancer-fighting drugs in. This requires us to take a more direct approach in administering chemotherapy to the central nervous system. Beyond chemotherapy, treatment can also entail surgical removal of the tumor(s) and/or targeted radiation therapy.



Charles M. Farber, PhD, MD

Is preventive therapy available?

Yes, preventive therapy is critical for individuals who are at high risk for central nervous system lymphoma. We start by proactively identifying those who are most likely to be affected and then administer a low dose of chemotherapy directly into the cerebrospinal fluid through a series of lumbar punctures. This enables the chemotherapy to penetrate the blood-brain barrier and enter the central nervous system. This preventive measure can reduce the likelihood of a patient developing brain metastases by approximately 90%.

How do you instill hope in patients facing a difficult prognosis despite these advancements?

I focus on sharing stories from other patients who have rallied and done much better than anticipated, even when they were in statistically tough situations. I also encourage them to believe in the power of positivity. Of course we don't have statistics to measure that, but I will tell you people who have a positive outlook seem to do much better overall. I encourage them to fight on and be optimistic as we use every resource available – including new advances in medicine happening all the time – to provide the best possible outcome.

BREAST CANCER AND THE BRAIN:

Staying on Top of Neurologic Symptoms Is Key

With new advances in breast cancer care, Stage IV breast cancer patients are living longer than ever before. However, even when the disease is controlled systemically, patients and survivors are at risk of the cancer metastasizing in the brain. Medical oncologist May Abdo-Matkiwsky, DO, explains why monitoring neurologic symptoms is critical and how new treatments are preserving patients' quality of life.

Is the prevalence of metastatic breast cancer in the brain increasing?

Thanks to the development of more therapeutic options for women and men with metastatic breast cancer, patients are living longer. With longer survival and systemic control of the disease, we are seeing a slight increase in incidence. The overall incidence of brain metastases in metastatic breast cancer is approximately 10 to 30%.

How does the type of breast cancer a patient has impact the spread to the brain?

The subtype of breast cancer does play a role in its likelihood to metastasize to the brain. Triple-negative breast cancers are typically aggressive and most likely to metastasize to the brain, followed by HER2-positive breast cancers and hormone-positive breast cancers.

Can brain metastases develop after patients are cured?

Patients and caregivers always need to keep in mind the possibility that the disease will progress. An individual's tumor type, stage and receptor status play a role in how likely, or unlikely, it is that the cancer will metastasize to the brain. For example, earlier stage breast cancers are typically less likely to metastasize to the brain. Post-diagnosis surgery and completion of the recommended therapy can help reduce this risk.

What are some of the warning signs of brain metastases?

Some of the warning signs include visual changes, difficulty with balance, severe headaches, personality changes or unexplained nausea or vomiting. It is important that patients be diligent about their follow-ups as well as comfortable talking with their oncologist about potential symptoms they are experiencing. I tell my patients to inform me of any new sign or symptom, even if they do not believe it is related to the underlying breast cancer diagnosis.

What are some of the latest advances in treating breast cancer that has metastasized to the brain?

We feel more confident about treating patients with metastatic breast cancer to the brain in the setting of targeted therapies. These are intravenous therapies that have been proven to improve brain metastases by crossing the blood-brain barrier.

Radiation has been a standard of care to treat brain metastases. In addition to whole-brain radiation, which is used to treat multiple brain metastases, CyberKnife® radiation can be used if only a few lesions are detected. This highly targeted form of radiation can preserve healthy brain tissue and reduce toxicities while maximizing performance status and quality of life.

May Abdo-Matkiwsky, DO

Prevention of Brain Metastases from Small Cell Lung Cancer Is IMPOSSIBLE

In 2021, 230,000 adults in the U.S. will be diagnosed with lung cancer. Of those, 13% will have small cell lung cancer – an aggressive form of cancer known for spreading quickly throughout the body and to the brain. The good news is, preventing brain metastases from this type of cancer is possible. Maithili V. Rao, MD, who is board-certified in hematology and medical oncology by the American Board of Internal Medicine, explains.

What is small cell lung cancer, and how is it different than other types of lung cancer?

Lung cancer is the second most common cancer in both men and women. Small cell lung cancer accounts for approximately 13% of lung cancer cases and is almost always seen in people who have a history of heavy smoking. What's most notable about small cell lung cancer is the rapid onset of symptoms, such as a worsening cough, shortness of breath or coughing up blood, and how quickly it spreads throughout the body. By the time it is diagnosed, 90% of cases are locally advanced or in an advanced metastatic stage. Given the extraordinarily fast pace of disease progression, I cannot stress how important it is for individuals who qualify to get their annual lung cancer screening. This primarily includes people between the ages of 50 and 80 who are, or were, heavy smokers.

Does small cell lung cancer often metastasize to the brain?

It absolutely does. As many as 40 to 50% of patients with small cell lung cancer will develop brain metastases at some point during the course of their disease. In fact, 45% of patients who respond well to treatment for small cell lung cancer at other sites in their body will go on to relapse in the brain within the first two years. This means that even if the systemic disease is controlled, there is a high probability of patients developing brain metastases over the next year or two.

How can you prevent metastatic disease from small cell lung cancer in the brain?

Prophylactic cranial irradiation (PCI) is a preventive radiotherapy treatment of the entire brain designed to prevent small cell lung cancer cells from developing in the brain. Knowing there is a high percentage of patients who have subclinical brain metastases – growths that are so small they are virtually invisible on MRI scans – this preventive modality is key to stemming the growth of malignant cells. Clinical trials have proven that PCI reduces the incidence of future brain metastases by about half and improves long-term survival.

As with any treatment, a trusted oncologist – or even better, a multidisciplinary team of medical experts – can help you weigh the benefits and the risks of PCI. While the data are limited, neurocognitive toxicity is a potential concern. However, there are measures that can be taken to minimize cognitive risks, such as shielding the hippocampus and modifying the dosage or therapy schedule. People with lung cancer are living longer than ever before – and we want to ensure they have the best quality of life possible.

Maithili V. Rao, MD

Clinical Trials:

The Key to Advancing Brain Tumor Treatment

We are very excited – and encouraged – about our participation in a potentially game-changing brain cancer vaccine. The "SURVIVE" Phase 2B trial enables our team to treat newly diagnosed glioblastoma patients with SurVaxM. This first-of-its-kind vaccine targets survivin, a cell-survival protein found in 95% of glioblastomas and many other cancers. Overlook Medical Center is the only site in New Jersey and one of the first in the nation to participate in this trial.

We are also involved in a study of Berubicin in adults with recurrent glioblastoma multiforme. Berubicin is part of a class of chemotherapy agents that leverages natural processes to damage an enzyme that allows cancer cells to spread. This agent is one of the first to cross the blood-brain barrier and overcome drug resistance.

We are also involved in developing novel treatments such as immunotherapies, CAR-T strategies, oncolytic tumor viruses and other targeted therapies for:

- Low-grade gliomas
- Other high-grade primary brain tumors
- Metastatic brain tumors
- Tumors that cause malignant cells to spread to the fluid surrounding the brain and spinal cord (leptomeningeal cancer)

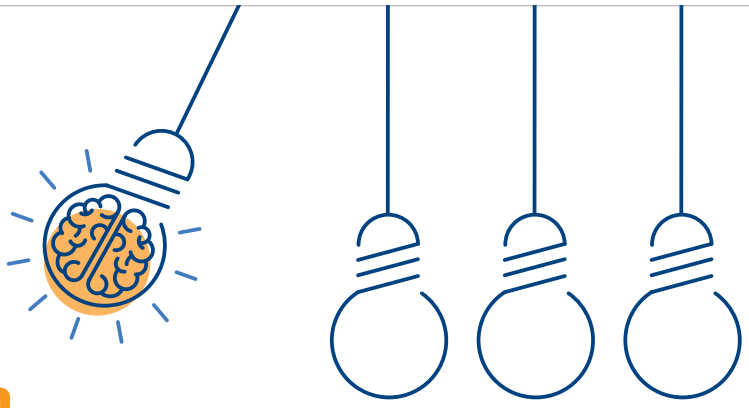
Please consult our clinical trial website at atlantichealth.org/braintumortrials or email NeuroscienceResearch@atlantichealth.org to get more information about our clinical trials.

Brain Tumor Support Groups

Patients, family members and caregivers are invited to participate in the Glasser Brain Tumor Center's support group. During our hour-long, monthly, virtual meetings hosted by our clinical staff members, attendees share, learn and grow together.

To learn more about our support group and how you or a loved one can benefit, please contact Janet LeMonnier at janet.lemonnier@atlantichealth.org or call 908-522-5159.

Changing the Paradigm for the Treatment of Metastatic Lung Cancer in the Brain



Survival for people who had brain metastases associated with lung cancer used to be about two to three months. Now, with advancements in immunotherapy and personalized medications that target specific gene mutations, many people are alive and well three or four years later. Oncologist Neil Morganstein, MD, explains.

What are the latest advancements in the treatment of lung cancer?

In the last three to five years, treatment for lung cancer has undergone the greatest evolution of any cancer that we have seen. This has taken shape through two different pathways: the utilization of immunotherapies (therapies that use your own immune system to fight cancer) starting three to four years ago, and the ongoing utilization of targeted or personalized medications that allow a small, but significant, portion of people to get a very specific medication for their individual cancer. Advancements in these two areas have essentially changed everything.

How do genetic mutations factor into lung cancer treatment?

Since the EGFR (epidermal growth factor receptor) mutation in lung cancer was first discovered about 15 years ago, we have been learning about and targeting many more driver mutations, which are the specific genes that went awry and are replicating again and again. We have also been focused on making medications that target these mutations better tolerated and better at penetrating the blood-brain barrier as lung cancer often spreads to the brain.

If we find a driver mutation in a patient's metastatic disease, we target that specific mutation first. Often, there are multiple targeted agents for a specific mutation. These types of targeted therapies have rapidly moved up to the front line of treatment, with chemotherapy now generally being reserved for later lines of therapy.

How has the paradigm for treating brain metastases from lung cancer shifted in recent years?

The paradigm has dramatically shifted for the treatment of brain metastases from lung cancer. When I started my practice, most people who had brain metastases associated with lung cancer had whole-brain radiation therapy. Today, it is an exceedingly uncommon person who gets whole-brain radiation therapy. That's due to significant progress in the ability to take out brain tumors safely with surgery, stereotactic radiation therapy – which allows us to target numerous lesions – and, even more importantly, medications targeted to specific driver mutations that can penetrate into the brain and have a high likelihood of success.

How are immunotherapies and targeted therapies changing the outlook for people who have brain metastases associated with lung cancer?

If you told me 20 years ago you could cure people with potentially Stage IV lung cancer, I would have said you are out of your mind. Today, Stage IV lung cancer is a curable cancer largely due to immunotherapies and targeted therapies. While that only holds true for a minority of people right now, the fact that we can say that is truly mind-boggling.

Neil Morganstein, MD

OUR INTEGRATED CARE TEAM


Yaron A. Moshel, MD, PhD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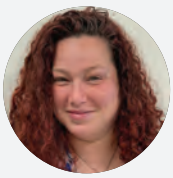
Fabio Frisoli, MD

NEUROSURGERY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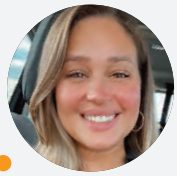
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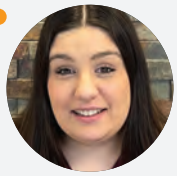
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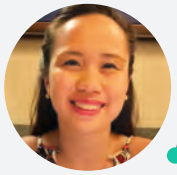
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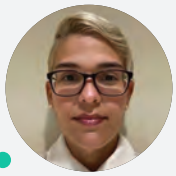
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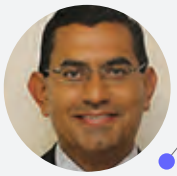
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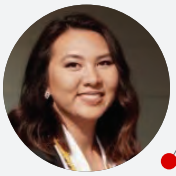
PALLIATIVE CARE

RESEARCH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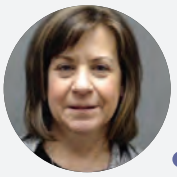
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John Paul Bouffard, MD

FAMILY ADVOCACY


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NEUROPATHOLOGY

The Power of Hope.

Atlantic Health System, home to the Gerald J. Glasser Brain Tumor Center, is partnering with the New Jersey Hospital Association, the Ukrainian National Women's League of America and the Afya Foundation to provide critical resources to medical teams and personal items to those impacted by the situation in Ukraine. Visit afyafoundation.org/campaign/ukraine to learn how you can participate.

About the Gerald J. Glasser Brain Tumor Center

The Gerald J. Glasser Brain Tumor Center brings the most comprehensive and innovative treatments to benign and malignant tumors of the brain, skull base, spine and spinal cord.

Our team of experts – including neurosurgeons from Atlantic NeuroSurgical Specialists – help patients and their loved ones navigate the journey from diagnosis through treatment. Every patient who visits the center has access to a panel of experts. The group meets regularly during a dedicated Tumor Board Review meeting to create a personalized treatment plan for all patients based on their clinical evaluation.

All this is possible thanks to the generous donation of the Glasser family's founding gift and support.

Atlantic Health System
Neuroscience

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