MOFFITT MODMENTUM®

IMMUNE CELLS ON A MISSION

One patient's journey in search of a cure

BATTLING BRAIN TUMORS

Surgical outcomes benefit from iMRI

TRACKING A SILENT KILLER

Improving surveillance for pancreatic cancer



Leadership Message



Patrick Hwu, MD President and CEO

Dear Friends,

Throughout history, cancer has been one of the most profound and complicated mysteries in medicine. The earliest known identification of the disease dates back to 1600 BC when ancient Egyptians described cases of tumors in the breast, stating "the disease has no treatment." More than three millenniums later, scientists are still unraveling the complexities of cancer. That pursuit has been marked by relentless perseverance and the continual asking and answering of questions: what causes it, how to prevent it, how best to treat it and how to stop it from returning. With each new answer comes more understanding, sometimes completely transforming how we confront cancer. We call this transformative knowledge a breakthrough.

In 1882, William Halstead, MD, performed the first radical mastectomy, a procedure that would be the standard treatment for breast cancer for more than 90 years. In 1969, the invention of the modern mammogram allowed for earlier detection of breast cancer, compelling doctors to explore options for less extensive surgical treatment. This "less is more" step may have seemed counterintuitive but represents an evolution in care balancing patient outcomes with quality of life. Because of scientific discovery, patients like Angela Stout, featured in this issue, have options for their treatment and the extent and type of reconstruction that will make them feel whole again.

As physicians and scientists have uncovered more about various cancer types, their work stems far beyond just understanding disease mechanisms and treatment. In 1886, Brazilian ophthalmologist Hilário de Gouvêa documented for the first time that cancer risk could be inherited. Over 100 years later, we are exploring all avenues of the genetics of cancer, including surveillance of those at high risk. In March 2023, Moffitt launched the Pancreatic Interception Center to give predisposed patients the best chance at prevention and early detection of one of the deadliest cancers.

Much of my own research has centered around the body's immune response to cancer. The exploration of the immune system and cancer dates back to the 18th century, but it took until the 1980s for momentum to build around immunotherapy, with the first agent FDA approved in 1986. This year, a breakthrough called tumor-infiltrating lymphocyte (TIL) therapy crossed the finish line after more than 30 years of research, gaining FDA approval for advanced melanoma. Even with one line of TIL approved, Moffitt doctors continue to push forward. Patient Michelle Shannon is a participant in a new TIL trial at Moffitt, which aims to build on the work that's been done. Research is ongoing, but we hope that future iterations of TIL will treat many other cancer types.

Woven through each story in this issue of Momentum is a common theme: breakthroughs. Backing those breakthroughs is a global web of physicians and scientists who share a common trait: determination. Determination to never stop asking questions. Determination to always seek the best outcomes. Determination to continue contributing to the prevention and cure of cancer.

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Jasmine Cherry, a cell therapy technologist, holds a block of frozen tumor-infiltrating lymphocytes that have been harvested from a patient and expanded in the lab. Once thawed, the immune cells are infused back into the patient



'I Feel More Hopeful' One TIL therapy patient's journey



Intraoperative Imaging Improving brain surgery outcomes



A Race for Research Funding future breakthroughs

With one TIL therapy approved by the FDA, doctors push to optimize the treatment. Michelle Shannon is living for the next breakthrough.

Michelle Shannon lies in a hospital bed, her husband, Russell, sitting in a chair by her side. A cooking show is on the TV, and they laugh about never wanting to eat squid ink

pasta. They're trying to pass the time, patiently waiting for Michelle's treatment.

It's not the first time they've found themselves waiting. For three years, they've waited for the good news that has never come. For the past four months, they've waited for this next chance for a cure.

Down the hall, a flat metal box containing a frozen bag of immune cells is taken out of a giant tank of liquid nitrogen. Vapor fills the air, the lab technician wearing giant gloves that look like



oven mitts so he doesn't get burned. A lukewarm bath is waiting. The cells are placed inside, and in just a few minutes they are transformed from a solid frozen mass into a clear, slightly pinkish liquid.

The bag is filled with only 55 milliliters of liquid, but that liquid contains hundreds of millions of tiny cells. This lifesaving material has been on an extraordinary journey over the past four months. Harvested from inside Michelle's body and transported across the street from Moffitt McKinley Hospital to the lab on Moffitt's McKinley Campus. Prepared, frozen, combined with antigens gathered from Michelle's blood and bathed in a mixture of proteins to encourage the immune cells to grow. Then transported 2 miles to Moffitt's main campus for infusion.

On Jan. 12, 2024, the journey comes to the most important end. After their final thaw, the cells are carefully carried about 200 meters from the holding lab area to Michelle's room on the cellular therapy patient floor.

"It's showtime," Michelle's nurse says as he hangs the bag of cells and connects it to her central line.

The Long Journey in Search of a Cure

By Sara Bondell

Photos by Nicholas J. Gould and Kevin Kirby

A chaplain walks into the room, and Russell bows his head. They pray these cells will be the cure the 61-year-old needs. The nurse opens the line and liquid begins to slowly drip,

Michelle Shannon, with husband Russell by her side, prepares for her TIL infusion that has been months in the making.

traveling down into Michelle. Russell grabs her hand. They both shed tears – happy and scared tears, they say - and wait for the bag to empty. When the bag finishes, the nurse swishes anything that may be remaining with some water to make sure Michelle gets every last drop. Then another bag is brought in.

There are three bags of immune cells, and it takes about an hour for all of them to be infused into Michelle. Surgically removed from her lung months before, the cells have made their way back home. They now are on a

mission to seek and destroy the cancer that has evaded so many other treatments over the past three years.

'THE FEAR OF THE UNKNOWN'

In December 2020, Michelle started having trouble with her vision. A visit to the optometrist led to a referral to a specialist, who confirmed a mass protruding into the iris of Michelle's left eye. She had uveal melanoma, a rare type of cancer that occurs in eye tissue. The American Cancer Society predicts only around 3,320 people in the United States will be diagnosed with eye cancer in 2024.

"I was totally surprised," Michelle said of her diagnosis. "There is always the fear of the unknown because you don't know what to expect because you have never been in that position before and you haven't heard of that type of cancer before."

She immediately started a type of radiation treatment called plaque therapy at a hospital in Miami, more than 200 miles from her home in Lake Wales, Florida. In this approach, a small carrier the size of a bottle cap containing radioactive "seeds" is surgically placed over the eye where the tumor is. It helps more precisely deliver radiation to the affected area,

THE TIL THERAPY PROCESS



1 The creation of TIL therapy starts with a surgical team removing the patient's tumor to extract T cells.







3 The cells are initially frozen for preservation. They are periodically thawed and mixed with antigens and proteins to promote growth.

Amod Sarnaik, MD, a trial for patients whose advanced melanoma failed to respond to other treatments reported a 38% response rate to TIL, promising results for patients who have run out of treatment options.

That data helped lead to the FDA approval of TIL therapy, now called lifileucel, for advanced melanoma in February 2024. Trials have shown the treatment can be successful in multiple types of melanoma, including the more difficultto-treat mucosal melanoma, acral melanoma – which is commonly found on the palms of hands and soles of feet -

and uveal melanoma.

"It's mind-blowing because you get your hopes up and then you get dashed ..."

The goal of the treatment is to harness the power of the body's immune cells called lymphocytes, which include T cells. It begins with surgery

to remove some of the patient's tumor. Once in the lab, the tumor tissue is divided into smaller bits and the samples are bathed in a protein mixture that encourages the cells to grow. Surviving T cells are tested to see which react most strongly to the tumor. Those are then multiplied by the billions to be infused back into the patient to attack the cancer.

During the clinical trial period for lifileucel, Moffitt was one of only five cancer centers nationwide that could manufacture a patient's TIL cells, thanks to its multimilliondollar Cell Therapies Core on Moffitt's McKinley Campus. Since the treatment's approval, all lifileucel cell products are manufactured at an offsite facility to ensure standardization and safety.

Now that the first TIL product is approved, it's time to find ways to optimize the treatment. More trials are being conducted to find ways to cut down on manufacture time and create a better product with a higher success rate.

"We are not going to stop here. We aren't going to be satisfied with what we have now. We are greedy in terms of wanting to get better responses for patients," Sarnaik said.





4 The goal is to grow billions of the strongest T cells. During the monthslong process, the team monitors the cells for quality and safety.

Michelle Shannon's trial is one of the newer TIL trials that aims to create an even more responsive treatment. In addition to harvesting T cells from the tumor in her lung, antigenpresenting cells were collected from her blood during a process called apheresis. Those cells are used to stimulate TILs that have been grown to help hand select the most responsive TILs. The nonreactive TILs are discarded, and the responsive TILs are then expanded before being infused back into the patient.

"You always hope you're on the breakthrough, the one that will work," Michelle's husband, Russell, said. "But even if it doesn't work for her, it will help others."

'I FEEL MORE HOPEFUL THIS TIME'

Five days before her surgery in September 2023 to remove the T cells from her lung tumor, Michelle drove the hour and 15 minutes from her Lake Wales home to Moffitt. She had an entire day of appointments ahead of her. She met with the anesthesiologist and cellular immunotherapy doctor. She needed blood work, a brain MRI, heart echo, full body scan and a pulmonary function test.

She was nervous about what's to come but tried to focus on the positives in her life. She had just returned from her happy place, a hunting cabin in Varnville, South Carolina, where she took in the sunrise alongside the chirping birds. She had the support of her family – Russell, her husband of 42 years; son Christopher and daughter Amber; and four grandkids under 10.

> "We are not going to stop here.... We are greedy in terms of wanting to get better responses for patients."

my faith, but it's intimidating with all the information. You have to try this and try that and figure out this step and that step. Sometimes it's overwhelming, but we will get through it. We will wade our way through the waters."

shielding nearby healthy tissue. The treatment left Michelle

with intense headaches, eye pain and light sensitivity. She

works in payroll for a golf course in Lake Wales and had to

work with all the lights off in her office. In 2022, she decided

Shortly after the surgery, Michelle learned the cancer

had spread to her liver and lungs. She transferred her

care to Moffitt Cancer Center and joined two different

immunotherapy clinical trials over the next year. Neither

was successful at keeping her cancer at bay.

"It's mind-blowing because

you get your hopes up

and then you get dashed

whenever the results come

back that aren't so favorable,"

Michelle said. "I try to keep

to have her eye removed and replaced with a prosthetic.

In the summer of 2023, Michelle's team presented her with another clinical trial involving tumor-infiltrating lymphocyte, or TIL, therapy. This approach harvests naturally occurring T cells that have already infiltrated a patient's tumor, activates and expands them in a lab, then reinfuses those cells into the patient to seek out and destroy cancer.

Willing to do whatever it takes, Michelle enrolled.

'WE ARE NOT GOING TO STOP HERE'

Although TIL was a novel treatment option for Michelle, the National Cancer Institute began studying the therapy in the 1980s. In 2009, Moffitt researchers visited the institute to learn the protocol, and Moffitt became the first cancer center outside of the institute to offer TIL to melanoma patients. Since then, Moffitt has opened eight TIL trials, treating about 100 patients. Led by Moffitt cutaneous surgical oncologist



5 Once the cells have been sufficiently expanded, they are carefully thawed and transported to the patient's bedside.





6 The bag of cells is connected to the patient's central line for infusion. The expanded cells go back to work destroying the cancer.

"I feel more hopeful this time," Michelle said. "The first treatment you are scared to death, and then it's heartbreaking when it doesn't work. But the doctors gave us hope, and there are other things we can do if this doesn't work."

She brought that same attitude to Moffitt McKinley Hospital the following week. She and Russell were calm, ready to get the process started. In the operating room, the thoracic surgeon removed about a 5-inch piece of Michelle's lung tumor. Sarnaik, the principal investigator for her trial, joined them in the operating room and dissected the tumor into three pieces with a scalpel and tweezers. One piece was put into a specimen cup filled with red liquid to be transported to the Cell Therapies Core to begin the TIL process. Another piece was saved for further research. The rest went to pathology for evaluation.

Michelle was wheeled into the recovery room, and the waiting game began. Because her trial involved additional steps and her manufacturing process had some setbacks, it took longer to manufacture her TIL. The newly FDA-approved TIL product takes on average eight to 12 weeks. She waited four months for hers.

'YOU CAN'T STOP LIVING YOUR LIFE'

After Christmas, Michelle got the call she had been waiting for: Her cells were ready. She had squeezed in another trip to the hunting cabin for Thanksgiving and spent Christmas surrounded by her grandchildren. She would start 2024 off with a new "birthday," the day she is reborn from a cellular level.

- Amod Sarnaik, MD



First, Michelle underwent five days of induction chemotherapy. The treatment reduces the number of circulating lymphocytes in the body to create a more favorable environment for the TIL. After two days off, she returned for her TIL infusion. Her cancer had grown while she waited for her cells to be ready, but she had held onto hope that this new army of cells would do its job.

After the TIL infusion, Michelle got a drug called interleukin-2 every eight hours for up to six rounds. It helps encourage immune cells to grow but comes with intense side effects such as fevers, rigors and nausea. A patient only takes as many doses as they can tolerate. Michelle pushed through all six.

"It was actually better than I expected," she said. "Now keeping my fingers crossed that it worked."

She was ready to go home after five days. Although she had to travel back to Moffitt for daily checkups and injections to help boost her immune system, she said it was worth it to be sleeping in her own bed and getting back to her routine. Because the treatment depleted her white blood cell count, she left the hospital with a giant bag of medications antibiotics, antibacterials and antifungals to protect her against infection.

The waiting game began again, this time six weeks until a scan to find out if the TIL was showing early success.

When the time came in mid-February, Michelle had lost her hair from the chemotherapy and her stomach was covered in bruises from the immune-boosting injections. But on the inside, she was the same strong and determined woman who enrolled in the trial almost six months before.

She was overjoyed when the doctor told her the scan showed no new tumor growth. It's too soon to tell if the treatment will be her cure, but it's a great start. She will continue to wait and continue to hope.

"You always have the thought how is it going, how is it going to turn out, but you can't stop living your life," Michelle said. "I am glad I went through this. We are really hopeful."

"I am glad I went through this. We are really hopeful."



Six weeks after her TIL infusion, Michelle and her husband, Russell, were relieved to find out her scan showed no new tumor growth.

Jasmine Cherry, a cell therapy technologist, holds a block of frozen tumor-infiltrating lymphocytes that are being $transformed\ into$ a personalized treatment.

EXPANDING THE REACH OF TIL Therapy

Based on the success in treating melanoma, doctors see promise in using the immunotherapy to treat sarcoma and other cancers

By Sara Bondell | Photos by Kevin Kirby and Nicholas J. Gould

While tumor-infiltrating lymphocyte (TIL) therapy was FDA approved first for cutaneous melanoma, Moffitt Cancer Center researchers are investigating the treatment for several other solid tumor types. So far, novel trials led by Moffitt physicians have found promising results in non-small cell lung cancer and most recently sarcoma.

"The problem with TIL therapy in many solid tumors is that you must expand TIL from the tumor itself after surgical removal. Cutaneous melanoma is the gold standard for TIL therapy since 95% of patients grow TIL," said John Mullinax, MD, a surgeon in Moffitt's Sarcoma Department. "But as you start investigating other tumor types such as lung cancer, cervical cancer, bladder cancer and sarcoma, the rate of success in terms of expanding TIL from individual tumors is much less."

Traditionally, sarcoma has a low sensitivity to immunotherapy treatments like TIL therapy. Sarcoma $patients\,also\,have\,the\,disadvantage\,that\,almost\,all\,have$

been heavily treated prior to undergoing experimental therapy such as TIL on clinical trials, so it is unclear if prior therapy hinders the treatment's success.

To determine if TIL is a safe and feasible option for sarcoma patients, Mullinax opened a first-of-its-kind $phase 1\,TIL\,trial\,for\,adolescent\,and\,young\,adult\,sarcoma$ patients ages 18 to 39. It's a patient population that is historically underrepresented in clinical trials.

The trial was a last-chance opportunity for Oscar Hernandez.

The Puerto Rico native was celebrating graduation with a vacation to Florida when Hurricane Maria devastated the island in 2017. He decided to stay with family in Orlando and got a job working at a hotel.

In 2018, the then 24-year-old started having ankle pain. He noticed a lump but thought it was from being on his feet all day at work. When the swelling didn't go down, he

went to the doctor. He was shocked when an MRI showed it was a cancerous mass.

Hernandez returned to Puerto Rico for a biopsy that confirmed myxoid liposarcoma, a cancer that grows in the cells that store fat in the body. It has a high recurrence rate and, unlike other sarcomas, can recur almost anywhere in the body. His doctors recommended treatment at a specialized cancer center. He began treatment at Moffitt, undergoing intense inpatient chemotherapy, surgery and radiation.

"It was very difficult workwise because I had just graduated and was in between jobs finding out what I wanted to do with my business degree," Hernandez said. "But I wasn't scared because I felt confident in what the doctors were saying. I knew the alternative to doing this treatment was losing my leg."

Although Hernandez was confident, his family was extremely worried. His aunt accompanied him to appointments and his mom attended via video chat from Puerto Rico.

"When you are treating a 50-year-old or a 60-year-old patient, you are often treating them individually. But when you are treating a 25-year-

old or 30-year-old, you are more often treating the entire family since they aren't yet as independent," Mullinax said.

A year after his initial treatment, Hernandez's cancer returned in his chest. He did more chemotherapy, and surgeons had to cut open his chest to remove the tumor.

He was in remission for a year, but the cancer came back again, this time around his colon and above his pectoral muscle.

"It's really frustrating," Hernandez said. "I knew my type of cancer tends to move around the body and recur, so I just had the mindset where I accepted that if it happens,



Oscar Hernandez was one of seven adolescent and young adult sarcoma patients on a first-of-its-kind phase 1 TIL trial.

I know what the game plan will be."

After the second recurrence, his care team decided it was time to change the game plan. Surgery wasn't working, and chemotherapy was no longer the best option. Mullinax told him about the TIL clinical trial.

"At first I wasn't too sure what it would entail because it's experimental. There were no guarantees," Hernandez said. "He told me I would be one of the first few people with this type of cancer doing TIL, but I figured the last treatment didn't work and this was proven to work in other cancer types."



"When you are treating a 25-year-old or 30-year-old, you are more often treating the entire family since they aren't yet as independent."

- John Mullinax. MD

"If I hadn't done the trial - I try not to think about that scenario – but realistically I probably wouldn't be here right now."

Hernandez was one of seven patients with metastatic disease treated on the trial. Mullinax started by removing the tumor on his pectoral muscle to extract the T cells that would be used to create the TIL therapy. Hernandez underwent his TIL infusion in the summer of 2022. While the treatment was not easy, it stopped the progression of the tumor in his colon. After a year of no disease progression, the colon tumor was surgically removed as well, and Hernandez was declared cancer free.

"If I hadn't done the trial – I try not to think about that scenario — but realistically I probably wouldn't be here right now," Hernandez said. "It's worked so far, and I am happy about that, but if it didn't work at least I know they can learn more from me. It's good to know being on a trial is a way to help others."

Hernandez is still being scanned for cancer every few months and is back to work. He can't run or put too much pressure on his leg but says he feels the best physically



and mentally he has in five years.

Mullinax presented the trial's results at the annual Connective Tissue Oncology Society meeting in Ireland in November 2023. The results showed 71% of the patients enrolled were successfully treated and TIL therapy stalled disease progression in all treated patients to varying degrees, with Hernandez achieving the longest response at more than a year. The trial accomplished its goal to prove that TIL is safe and feasible for sarcoma patients.

"The next iteration or next step is: How do we make TIL therapy more effective for sarcoma patients? Now that we know it's safe and feasible and we have proven the skeptics wrong who said this approach wouldn't work, now how do we make a better TIL product?" Mullinax said.

Mullinax is studying how to optimize the TIL product for effectiveness and is hoping to secure funding to open a phase 2 trial based on his lab results.

HEAVY ARTILLERY in the -**Battle Against Brain Tumors**

By Corrie Benfield Pellegrino | Photos by Nicholas J. Gould



A lot of life's biggest moments can happen in a short span of time. An unforgettable wedding. A jubilant baby announcement. A milestone birthday celebration. A lifechanging brain surgery.

Robert Roggeman started out the summer of 2023 with a carefree calendar. He and his wife, Lisa, had traveled to a family friend's wedding in Huntsville, Alabama, the first week of June. The celebration was beautiful. But on the flight back home to Tampa, the retired Army colonel experienced a jolting end to the trip. On the plane's descent, he was hit with a splitting headache, the pain so intense it made his eyes water.

The one-time tank commander had traveled all over the world in the course of his military career, and he had experienced headaches on planes before. He was not one to rush to a doctor. But the next morning, Robert's eye was red and swollen shut. Worried that he'd had a stroke, his wife insisted he get checked out.

"Usually I'd fight her because I don't want to go to the doctor," Robert said. This time, he reluctantly agreed.

"Usually I'd fight her because I don't want to go to the doctor."

Robert's primary care doctor examined his eye and, at Lisa's request, sent him for an MRI to check for signs of a stroke. He also referred Robert to an ophthalmologist. The eye doctor cleared Robert, but the MRI results showed something unexpected. Robert hadn't had a stroke. Instead, there was a suspicious spot on his brain.

The couple and their daughters, Julie and Maggie, were nervous. The family had been through the stress of the unknown before with deployments. Julie, 29, feared the worst. Maggie, 27, reassured her dad everything would be fine.

Robert and Lisa made an appointment at Moffitt Cancer Center.

Diagnosed by chance, **Robert Roggeman came to Moffitt** at just the right time, becoming the first patient to benefit from the new intraoperative MRI

'VERY FORTUITOUS'

In July 2023, Robert and Lisa met with Michael Vogelbaum, MD, PhD, chief of neurosurgery and leader of the Neuro-Oncology Program at Moffitt. Vogelbaum explained that the MRI results had revealed a brain tumor called a glioma.

"He told us: 'You guys are very fortuitous,'" Robert remembered. "No. 1, you listened to your wife. No. 2, you took some action. No. 3, the incident on the plane has nothing to do with the brain tumor."

"He told us: 'You guys are very fortuitous."

It turns out the headache and the swollen eye were symptoms of unrelated sinus pressure. The brain tumor was not causing any symptoms yet. But the MRI had caught it early.

"Fortuitous" is a word that stuck with Robert. His father had died of a glioblastoma, an aggressive type of brain tumor, when he was 80. By the time his father had symptoms, it was too late to operate. Because Robert's tumor was diagnosed early, his prognosis was much better.

In light of his family history, Robert opted to do genetic testing so he could better prepare his daughters if there was any risk for them down the line. He quickly learned his girls were fortunate - there was no genetic linkage.

The timing of Robert's diagnosis was also serendipitous. In July, the cancer center opened its new state-of-theart Moffitt McKinley Hospital, which houses an innovative intraoperative magnetic resonance imaging (iMRI) system. The iMRI allows doctors such as Vogelbaum to conduct realtime imaging during delicate brain surgeries without moving the patient. It improves the surgeon's ability to remove as much of the cancer as possible.

Robert's brain surgery was set for Aug. 8, 2023. He would be the first patient to benefit from the iMRI

'MILLIMETERS MATTER'

An internationally recognized leader in neurosurgical oncology, Vogelbaum has been using various forms of imaging technology in surgery for decades. He has experienced the evolution of the iMRI technology and been a champion for bringing the system to Moffitt, knowing it would improve outcomes for patients like Robert.

Traditionally, brain surgeons have been guided by imaging that is done preoperatively. Vogelbaum explains that in the early years of his career, a preoperative CT scan or MRI image would be displayed on a light board in the OR and used to estimate where on the head the opening should be made.

"And when you were removing the tumor, all you had were visual cues and an understanding of where the tumor had been in the anatomy," he said.

A revolution occurred with computerized image guidance technology, which uses preoperative MRI scans and patient positioning data to help surgeons better pinpoint tumor locations. But that technology also has its limitations.

"The brain is not rigid," Vogelbaum explained. "As time goes by and the brain relaxes while we are working on it, that image guidance becomes less and less accurate because it's based on a preoperative MRI. And in our world, millimeters matter."

That's why the intraoperative MRI is a gamechanger. It allows surgeons to get real-time imaging on a patient while the person is still in the operating room and under anesthesia. If the scan shows that there is abnormal tissue remaining, the surgeon can continue to operate and remove it.

"The intraoperative MRI helps us to do the best we can in terms of removing the tumor so we can be more confident that we've accomplished that," Vogelbaum explained. "There are situations where we cannot remove all of the tumor safely. But we want to eliminate the situations where we could have removed all of the tumor but didn't."

HAPPINESS AMONG HARD TIMES

Robert and Lisa were impressed with Vogelbaum's experience and expertise. They trusted that they were in good hands, but the weight of what was to come hung heavy over them.

With Robert's surgery scheduled, Lisa immediately began rallying the troops to support the family. For years, she had led and been a part of Family Readiness groups that support service members and military families during deployment, relocations and unexpected emergencies. This time, she assembled a group of family members, friends and close neighbors as a support system.



Michael Vogelbaum, MD, PhD, is chief of neurosurgery and leader of the Neuro-Oncology Program at Moffitt. He has experienced the evolution of the intraoperative MRI technology and been a champion for bringing the system to Moffitt.

"We know about grieving," Robert said. "We were hoping for the best but preparing for the worst."

Amid the shock, stress and sorrow, though, life's bright moments continued to shine through.

The week before surgery, the couple got some uplifting news. Their younger daughter, Maggie, was pregnant. The baby would be their first grandchild.

On the Saturday before the surgery, the family celebrated another milestone - Robert's 60th birthday. Lisa and the girls threw him an epic party at the historic Centro Asturiano in Ybor City. Relatives flew in from all over. Old military buddies rallied by his side. Robert was inundated with personalized mementoes and engulfed in decades of friendship.



Robert Roggeman's brain surgery took three hours and included intraoperative imaging that helped guide his surgical team to continue resecting the tumor.

The glow of the party carried

Robert and Lisa through the weekend, old stories and new memories taking front stage.

By Monday, though, the family's focus turned to surgery preparations. And on Tuesday morning, Robert was rolled into the operating room.

THE TOUGH PART

Once Robert was taken back for surgery, Lisa sat on edge in the family waiting area, anxious for updates on her husband of 32 years. She knew Robert was tough, but waiting is never easy.

Vogelbaum's initial work to remove the tumor took about an hour. The surgical team reported back to Lisa regularly to let her know that everything was going well.

Once Vogelbaum reached the point where he needed an updated image of the surgical area, the team prepared Robert for the iMRI. Vogelbaum made sure there was no active bleeding, filled the surgical cavity with saline and performed a temporary closure. The team then carefully covered Robert with sterile towels and a large plastic drape, essentially cocooning him to protect the sterile field.

Housed in a shielded diagnostic space between two operating rooms, the iMRI is a multiton device that hangs from a track on the ceiling. It can smoothly glide into the ORs on either side for intraoperative imaging. Before the massive magnet could enter the operating room, though, a host of safety checks needed to be performed.

Ferromagnetic materials and equipment had to be pushed outside of the safety zones marked on the operating room floor, indicating where they were safe from the iMRI's powerful magnetic forces. Monitors, carts and other equipment were rolled away from Robert and out of the magnet's reach. Surgical lights, which are mounted on large arms attached to the OR walls, were swung back to the edges of the room for safety. Robert himself had already been carefully checked to ensure there was no risk of burns from metallic implants.

With the patient and the operating room prepped, a specially trained safety officer ran through a final checklist to make sure everything was in place for the iMRI's entrance. When the safety officer gave the all clear, the iMRI bay doors opened and the magnet moved into place, perfectly incapsulating Robert. The team performed a new scan, and then the iMRI receded back into its space.

"Most of the time, when I use the intraoperative MRI, I don't end up removing additional tissue," Vogelbaum explained. "However, the few times I do end up removing additional tissue, I'm grateful for the fact that I was able to discover that intraoperatively instead of postoperatively."

In Robert's case, the intraoperative imaging made a difference. With a new, more accurate view of the surgical area, Vogelbaum went back to work resecting the tumor.

All told, the surgery took three hours. When it was complete, Robert was rolled out of the operating room and into the intensive care unit to begin his recovery.



Robert and his wife, Lisa, had prepared for a tough recovery. But he was ready to go back to work the same week after his surgery.

Robert reassured his girls: "I feel great. Don't worry about me. You guys take care of Mom. I'll be fine. It's time to go home."

Anticipating a rough recovery, Robert had taken the rest of the week off from his job as vice president of operations for a local defense company. Julie, who lives in New Smyrna Beach, was staying at the house to help. Maggie, who lives nearby in Tampa, was also at his side. Friends and family members were on standby to assist.

But Robert, with 24 staples in his head, didn't feel like laying around. He was able to walk and get around normally. He wanted to go back to work.

"My family was flabbergasted," he said.

He decided to work the rest of the week from home. The next week, he hadn't been cleared to drive yet, so he got a ride into the office from a co-worker who lives nearby.

"To me, it's amazing that I could recover so quick and get back to normal," he said.

And there was more reason for optimism. When the pathology reports came back, Vogelbaum explained that the tumor was a grade 2 glioma. The outlook was positive.

"It was the best-case scenario," Robert said. "They explained it's not a real aggressive type of tumor. We think we got it all. And we will continue to monitor."

Vogelbaum was also pleased with the outcome and has high expectations for the benefit the iMRI holds for future patients with brain tumors.

"We have ever-growing bodies of evidence showing that the more we can remove safely, the better the patient is likely to do in terms of maximizing survival," he explained.

For Robert, ongoing monitoring requires a follow-up MRI every three months. He had his first in early November, and everything looked good.

"For me, this is a second chance or a continuation to live a good life," he said, "to be healthy and try to do good."

"To me, it's amazing that I could recover so quick and get back to normal."

November marked five months since the fateful plane ride that led to Robert's diagnosis. The family had packed in a lot of joy, tears, trepidation and hope in that relatively short amount of time.

Robert and Lisa were ready to move forward. The week after his first follow-up scan, the couple set sail on a weeklong cruise to the eastern Caribbean. In early December, the

a good life."



After a summer dominated by a cancer diagnosis and brain surgery, Robert and his family are ready to look to the future. He will continue to be monitored with MRIs every three months.

BACK TO LIFE

One of the first things Robert thought about when he woke up from brain surgery was lunch. The nurse gave him a menu and asked about his pain level. He estimated it at a 3.

"When I woke up, I didn't have a lot of pain. I didn't have a splitting headache like I thought I was going to have," he said.

Vogelbaum had told Robert that most patients stay in the hospital for two nights after brain surgery, but Robert was ready to go home immediately.

"What do I have to do to get out of here?" he asked the nurse.

First, he needed a postoperative MRI to make sure everything was looking good. After one night in the ICU, though, he was cleared to go home.

The discharge was an emotional experience for the family. So much pent-up distress.

family traveled to Boston to catch the Army-Navy game. By Christmas, the incision scar across the front of Robert's skull had faded to be almost invisible, a faint reminder of the family's big battle.

With the whirlwind of the summer in the rearview, Robert and Lisa were looking forward to the new year. And of course life's next major event: the birth of their first grandbaby.

SURVEILLANCE — for a — Silent Killer

Moffitt's new Pancreatic Interception Center aims to catch a disease that often goes undiagnosed until it's too late

By Sara Bondell | Photos by Nicholas J. Gould

Editor's note: To protect his family's personal health information, we are not publishing Don's last name.

During the sweltering summer heat, Don walks the length of his Longboat Key building lobby. Back and forth. Fourteen loops, 16 loops, sometimes 18 loops.

He's tall, thin and built like an athlete. He moves with the grace not often seen in a 77-year-old, most likely thanks to years of playing football and basketball and running track and field.

Watch him walk, and you'd never know. Don is battling pancreatic cancer.

DON Cancer Survivor





After a chance DNA test showed Don's daughter carried a BRCA1 mutation, Don and his wife got tested. When Don tested positive for the $mutation, his\ doctor\ recommended\ annual\ cancer\ screenings,\ which\ ultimately\ led\ to\ an\ early\ diagnosis\ of\ pancreatic\ cancer.$

HAD IT NOT BEEN FOR A TWIST OF FATE, Don wouldn't be walking the lobby, fighting his disease one step at a time. Instead, the disease could still be secretly growing inside him, only making itself known when it was too late.

About 10 years ago, Don's daughter sent her DNA to a private genetic testing service on a whim. The results showed she carried a BRCA1 mutation. The mutation is passed down from a parent and carries an increased risk for breast, pancreatic, ovarian and prostate cancers. Ashkenazi Jewish women like Don's daughter are more than 10 times more likely to have a BRCA1 or BRCA2 mutation than women in the general U.S. population.

Don and his wife, Randi, thought their daughter inherited the mutation from Randi, who had a history of breast cancer. However, she tested negative for the mutation. That left only one other possibility.

"It was a body blow, a shock," Randi said of Don testing positive for the BRCA1 mutation.

Don's internist recommended annual mammograms and abdominal scans. Year after year, his scans showed nothing. Then, on May 3, 2023, radiologists identified a pancreatic tumor on his scan.

"It was a wrenching, lifechanging bit of news, no matter what," Randi said. "He was taking these tests every year like a dental cleaning, but when we heard it was cancer and then pancreatic cancer, it's a very big emotional adjustment for us and our family."

A DISEASE ON THE RISE

Pancreatic cancer is rising in incidence and is now the 10th most common cancer in the United States. Pancreatic cancer is also the third leading cause of cancer-related deaths in the U.S. and is projected to be the second leading cause by 2040. While the five-year relative survival rate has increased to 12.5%, symptoms can be vague - abdominal or back pain, unintentional weight loss, loss of appetite, itching, yellowing of skin and the whites of the eyes. Most patients present with later-stage disease.

The cause for most pancreatic cancers is still unknown. In addition to factors such as age, sex, race and family history, modifiable factors shown to increase the risk for pancreatic cancer include smoking and being overweight or obese. Other lifestyle factors that may influence pancreatic cancer risk include diets with high amounts of red and processed meats, heavy alcohol consumption and physical inactivity.

Having a personal history of conditions including chronic pancreatitis (inflammation of the pancreas), new-onset or chronic type 2 diabetes and precancerous pancreatic cystic lesions also increase the risk.

Pancreatic cancer tends to run in families, with about 10% to 15% of pancreatic cancers occurring as a result of an inherited genetic mutation that is passed from generation to generation.

The five-year survival rate for stage 4 pancreatic cancer that has spread to other organs is 3%. If diagnosed at stage 1, or when the cancer hasn't spread outside the pancreas, the five-year survival rate is 44%.

Although most pancreatic cancers are difficult to detect early, individuals like Don with a known genetic mutation or identified pancreatic cysts have the best chance at prevention and detection of early, operable disease and improved survival. To help these people, Moffitt Cancer Center opened a Pancreatic Interception Center in March 2023 that offers a comprehensive surveillance program, pushing pancreatic cancer prevention into the forefront.

A VISION DRIVEN BY FAMILY

Jennifer Permuth, PhD, vice chair of research for Moffitt's Gastrointestinal Oncology Department, knows firsthand that prevention is the best way to fight pancreatic cancer. Her father has a history of intraductal papillary mucinous neoplasms (IPMN), the most common type of precancerous pancreatic cyst. Thanks to the incidental finding of the cyst 15 years ago and surgery at Moffitt to remove it, he is alive today.

Permuth's sister, Rachel, passed away from colorectal cancer in 2022 at the age of 44. Genetic testing revealed Rachel inherited a mutation that causes Lynch syndrome, the most common cause of hereditary early onset colorectal cancer, from their mother's side of the family. Permuth subsequently tested positive for the mutation, putting her at higher risk for colorectal, gynecological, pancreatic and other cancers associated with Lynch syndrome.

"I am at very high risk, and even before my father's and sister's diagnoses, I wanted our Moffitt team to offer a top-notch

> "I am at very high risk. ... I wanted our Moffitt team to offer a top-notch surveillance clinic for individuals and families at increased risk for pancreatic cancer."

surveillance clinic for individuals and families at increased risk for pancreatic cancer," Permuth said. "I always wanted a place where I could feel that I was being watched closely and could empower myself with the tools to make sure that if a cancer is detected, it's as early as possible."

Permuth has spent the past few years trying to shape this vision. When therapeutic endoscopist and functional medicine expert Shaffer Mok, MD, joined the Gastrointestinal Oncology team in 2022, the pair were able to make the firstof-its-kind surveillance clinic a reality. The clinic monitors people with genetic mutations that predispose them to pancreatic cancer as well as those with pancreatic cysts.

"This is standard across many centers in the United States. but the difference between us and those centers is that we are giving people a comprehensive lifestyle prescription of things that are based on evidence that they can do to kind of reclaim their disease and potentially impact their disease state and risk of pancreatic cancer in the future," Mok said.

The number of people with pancreatic cysts is rising, mostly because people are living longer, doctors are ordering more imaging for patients and imaging techniques have improved. Cysts can be benign, premalignant or malignant. Most patients have IPMNs, premalignant precursors to pancreatic cancer that carry a risk of 3% to 60% for becoming cancerous. Because the risk range is so large, it's important to have all the pieces of the puzzle when surveilling these patients.

The Pancreatic Interception Center uses endoscopic ultrasounds for the most accurate diagnostics. The procedure is more likely to detect cysts that are commonly missed on a standard MRI. It is also one of only 12 centers in the U.S. that uses an endoscopic technique that can look at the lining of the cyst in real time. Tissue samples and advanced genetic testing are also used to better individualize surveillance plans.

Since the Pancreatic Interception Center opened, it has seen more than 1,200 patients, the majority with pancreatic cysts. The center has performed more than 150 endoscopic procedures, and about 30 patients have had surgery to remove high-risk cysts. All the patients, whether they have cysts or a genetic predisposition, are offered educational

- Jennifer Permuth, PhD



material and an individualized lifestyle plan, which could include tobacco cessation counseling, diet templates, supplement recommendations and exercise programs. The goal is to reduce anxiety and determine the best course of action for each patient.

"Just because you have a cyst in your pancreas doesn't mean it's the end of the world. Just because you have a genetic condition that can make you at risk for pancreatic cancer doesn't mean you're going to get it," Mok said. "But getting somewhere like the Pancreatic Interception Center that will allow you to take it off your plate and let your providers watch it for you is most important."

EXPANDING THE RESEARCH

In addition to following and treating patients, the Pancreatic Interception Center is focused on research. While the surveillance program offers hope for patients with genetic mutations or cysts, the two patient populations make up only a small portion of pancreatic cancer patients.

Permuth is the co-founder of the Florida Pancreas Collaborative, a statewide initiative that aims to advance research for individuals with or at risk for pancreatic cancer, with emphases on early detection efforts and addressing the disproportionate burden of disease among Black people. With funding from the National Cancer Institute and collaborations among several institutions, she is co-leading a study with abdominal radiologist Daniel Jeong, MD, that focuses on finding a better minimally invasive way to distinguish between high- and low-risk IPMNs. The study uses an approach that combines computer-detected features that cannot be seen with the naked eye along with biomarkers, called microRNAs, from a blood test.

"In the future, as we monitor high-risk individuals over time in our Pancreatic Interception Center and counsel patients about their medical management, it will be really helpful to see if levels of these biomarkers are changing and/or if the computer is telling us that imaging features associated with more aggressive lesions are detected," Permuth said.

Preliminary data show this novel approach has superior sensitivity and specificity compared with standard classification methods and may more accurately predict high-risk cysts.

"I want to see us save lives by preventing the disease altogether, or if we catch it, catch it as early as possible," she said.

Moffitt will also be the first institution to incorporate various biomarkers with a natural agent to help prevent IPMN progression to malignancy. Through a National Cancer Institute-sponsored chemoprevention trial, doctors are aiming to find a new way treat IPMNs beyond the traditional "watch and wait" approach.

"If we can prevent the cyst from either growing or progressing, it could delay the development of something bad and could be an option rather than surgery," said Mokenge Malafa, MD, a gastrointestinal surgeon and lead investigator of the phase 2 trial.



Mokenge Malafa, MD

Patients on the trial will be randomly

assigned to a placebo group or a group that receives a special form of vitamin E that was created in Malafa's lab. In the lab, the vitamin E compound was able to selectively kill cancer cells without affecting normal cells. It also could help boost the immune system.

The trial will enroll more than 200 patients with low-risk IPMNs. They will take a pill twice a day for three years in hopes that those who receive the vitamin E compound will see cysts shrink or not progress.

"This is very exciting for us. Because of the interception center and the way we have the infrastructure, we are able to screen these patients, and that gives us a unique population," Malafa said. "As you can imagine, this is very tricky to manage in the regular clinics because there are just so many factors."



"We are giving people a comprehensive lifestyle prescription ... that they can do to kind of reclaim their disease and potentially impact their ... risk of pancreatic cancer in the future."

- Shaffer Mok, MD

After a more than 20-year career in pancreatic cancer at Moffitt, Malafa says the trial and the Pancreatic Interception Center are the biggest steps forward he has experienced in disease prevention and early detection.

'I AM FIGHTING FOR TIME'

Because Don was originally diagnosed with stage 1 pancreatic cancer, he was a candidate for Whipple surgery, a complex procedure that removes the head of the pancreas, a portion of the small intestine, gallbladder, part of the bile duct and occasionally a portion of the stomach.

The surgery comes with a laundry list of potential long-term side effects, such as decreased pancreatic function, diabetes and difficulty digesting. But it's a pancreatic cancer patient's best chance at survival. With Don's history of comorbidities - diabetes and congestive heart failure - he wanted to be treated at a specialized cancer center.

At Don's first meeting with his care team at Moffitt, his surgeon, Malafa, said he would be a good candidate for robotic surgery. He had the Whipple surgery in July 2023 and had a remarkable recovery that landed him back home only five days later.

However, during the surgery, the surgical team discovered the cancer had spread to some lymph nodes, changing Don's diagnosis to stage 3. It was a devastating blow, but he stayed focused on his recovery and next treatment steps.

"There's the physical recovery and there's the mental recovery. You know what the numbers are, you looked something up that you wish you hadn't," Don said. "I am fighting for time and quality of life with my kids and grandkids. If I fight it right and do everything they want me to do, it gives you a reason to keep living and maybe you will be one of the people who can get through it."

After his surgical drains were removed, Don excelled in physical therapy. He changed his diet and began walking the lobby of his building. In the fall of 2023, he began chemotherapy and immunotherapy treatment. He feels fatigued at times but has returned to playing golf and spends as much time with his two children and four grandchildren, ages 14 to 20, as he can.

The family is also dedicated to spreading awareness about screening and finding more ways to prevent pancreatic cancer.



"If we could get more people to be screened like I did, it could save more lives," Don said.

They want to see genetic testing become more accessible and more testing and scans suggested at annual checkups. They hope research ultimately leads to a blood test that can detect pancreatic cancer before an individual is symptomatic and the disease has spread.

"Pancreatic cancer is just dreadful," Randi said. "We need to summon the medical army together and find a way to find it earlier."

Even though they've been married for 56 years, Randi says she is seeing a totally new side of her high school sweetheart. His bravery and determination have been unmatched, and the pair have decided not to take any time for granted.

"It makes you think big thoughts. It changes you," Randi said. "For a while, we were grieving for this path that we are on, but I said, 'Nobody has a crystal ball to know when anything may happen. We have to focus on the fact that we are living. Let's embrace this and find moments of joy every day."

> *"If we could get more people"* to be screened like I did, it could save more lives."

"Waking up and realizing that I had two breasts again brought tears of joy. I felt normal again."

"A mastectomy is an emotional scar, and a lot of healing takes place, not just surgical but psychological," Dayicioglu said. "Some patients feel fine without any reconstruction and are happy to be done with surgeries. Everyone is different, and that's OK."

AN IMMEDIATE CONTINUATION OF CARE

In Stout's case, Dayicioglu supported her choice to have breast reconstruction. Her second surgery would involve removing her left breast and then undergoing full reconstruction on both breasts. This would all be done in one eight-hour surgery, which would make recovery easier.

Stout, a resident of Plant City, Florida, is among a growing number of breast cancer patients who have had both treatment and reconstruction surgery done at Moffitt. For Stout, having reconstruction done in the same building where she underwent treatment made sense.

"I am beyond thankful that I was able to receive continuation of care from start to finish at Moffitt," the 46-year-old said. "I have an amazing oncology team, and knowing how connected my team was when it came to my transition of care from one phase of my treatment to the next was important to me."

Stout's surgical oncologist, Nazanin Khakpour, MD, who performed her original mastectomy, returned to the operating room in May 2022 and removed her remaining left breast. Dayicioglu and her team then stepped in and performed a deep inferior epigastric perforator flap procedure (DIEP flap) to re-create both breasts.

In this type of surgery, a section of abdominal skin and fat, along with blood vessels, is removed and attached to the chest to create a breast through microsurgical techniques.

"Breasts can be reconstructed in many ways, mostly with implants," Dayicioglu said. "But in Angela's case we were able to remove fatty tissue off the body, save the muscles, reconstruct the breasts and get a slim stomach at the same time."

Less than 10% of breast reconstruction patients are eligible for this specific procedure, which takes longer than implants and requires a longer recovery period. It's especially useful in patients like Stout, who had undergone radiation as part of her cancer treatment.

"Tissue changes with radiation," Dayicioglu said. "We see more scarring around an implant when there is radiation, and in the long-term this population of patients experiences asymmetries. Due to those reasons, using a patient's own

Reconstructing a Sense of Normalcy

By Steve Blanchard

Photos by Nicholas J. Gould

ANGELA STOUT Cancer Survivo

Reconstruction surgery after a mastectomy brought Angela Stout's life back into focus

Angela Stout remembers her first thought when she awoke from breast reconstruction surgery at Moffitt Cancer Center.

"I looked down, and I was very excited that there were two again!" she said.

For 12 months, Stout had lived as "half flat," as she calls it.

In May 2021, Stout had a mastectomy on her right breast at Moffitt after she was diagnosed with invasive ductal carcinoma, HER2-positive breast cancer. Afterward, she underwent 25 rounds of targeted radiation therapy, so reconstruction had to wait.

"I lived that way for a whole year, and it played with my whole mental focus," Stout said. "Looking in a mirror for a year and seeing only one breast and the scars where my

right breast used to be impacts how you feel about yourself. I don't know if the other breast had been taken right away if that would have changed things or not."

After completing months of radiation, though, she had a choice.

"My doctors talked to me about a mastectomy to remove the noncancerous left breast because of my family history," Stout said. "Even with a breast prosthetic, I still felt uneven and felt everyone could see it."

Stout said it even impacted her self-esteem around her husband, to the point that she would avoid letting him see her without a top on. "And I'd avoid looking at myself in the mirror," she said.

That's a common feeling among patients, reconstructive surgeon Deniz Dayicioglu, MD, explains. Many patients find that reconstruction improves their well-being.

tissue like in a DIEP flap is a better choice in the right candidates."

When Stout first heard of this procedure, she started researching it online and even joined Facebook groups for women who had either undergone the surgery or were considering it. She was happy to learn she was a candidate for this type of reconstruction.

"Waking up and realizing that I had two breasts again brought tears of joy," Stout said. "I felt normal again even though I was still healing."

reconstruction surgery performed by Deniz Dayicioglu, MD, was done right after her second mastectomy. The combined operation made <u>Stout</u>'s recovery easier.

> *"Some patients feel fine"* without any reconstruction and are happy to be done with surgeries. Everyone is different, and that's OK."

> > - Deniz Dayicioglu, MD

RECONSTRUCTION GOES BEYOND BREAST PATIENTS

John Kiluk, MD, leader of the Reconstructive Oncology Program at Moffitt, says that having plastic surgeons like Dayicioglu on site at Moffitt allows surgeries to proceed that would be much more challenging elsewhere.

"At Moffitt, we see some of the toughest cancers in the state," Kiluk said. "Having plastic surgery expertise like we have here really allows us to do resections that we otherwise couldn't do. The plastic surgery team can come in following a resection and help us close the wound."

Plastic surgery, he added, helps in so many different aspects of patient care, including minimizing the emotional trauma of losing a breast or decreasing the risk of lymphedema.

"Our plastic surgeons are experts at improving quality of life," Kiluk said.



Rogerio Neves, MD, PhD, a plastic surgeon and senior member in the Department of Cutaneous Oncology at Moffitt, notes that the plastic surgery team is involved in all types of procedures outside of breast reconstruction, as well. The team works closely with surgical oncologists in many departments across Moffitt.

"Skin cancers often require many surgeries, and depending on the size and location of that procedure, plastic surgeons may be called in to minimize any deformity," he said. "Often, at a later time, after surgery or radiation therapy, a reconstructive procedure may be scheduled to restore a patient's function

and appearance as much as possible."

Head and neck, gynecologic, sarcoma, gastrointestinal, genitourinary, neuro and cutaneous oncology surgeons may also call on a reconstructive surgeon to assist in a patient's treatment, Neves said.

Currently, Moffitt utilizes the talents of 10 plastic surgeons across multiple disciplines to improve patient outcomes.

"These surgeons are an amazing asset to our institution and to our patients," Kiluk said. "Together, we are able to minimize the impact of cancer on our patient's lives."

A PERSONAL DECISION

For Stout, the decision to undergo reconstruction surgery after her mastectomies was very personal. She realizes it's not a decision every woman makes.

"I think there's a preconception that reconstruction is tied with vanity," Stout said. "I'm thrilled with the results from the reconstruction, and I'm very happy with my appearance. It has also helped me heal emotionally and psychologically. I no longer avoid looking in the mirror, and I have learned to love my body again."

Dayicioglu agrees that reconstruction ultimately depends on the patient's preference. The goal, she said, is for a patient to be happy, comfortable and satisfied with treatment following cancer.

"For us, as long as the patient is satisfied with the results, we're happy," she said. "If they have any doubt or are looking for a correction, we can discuss it and look at options."

Patients who have had reconstruction may want to come back and fine-tune some things, Davicioglu said, adding that there is always room for revision. Those follow-up procedures are much simpler and take 30 minutes or so compared to the more in-depth reconstruction that Stout experienced.

Stout has returned to Dayicioglu to have some scar revisions and grafting done to establish a more symmetric look, for example. In February 2023, Stout visited Dayicioglu again to construct nipples on her new breasts.

Although she originally considered tattoos to re-create her nipples, Stout ultimately decided reconstructing her nipples would help her reclaim even more of her femininity.

"At Moffitt, we see some of the toughest cancers in the state. Having plastic surgery expertise like we have here really allows us to do resections that we otherwise couldn't do."

– John Kiluk, MD





"I had breasts again," she said. "But without nipples, it just felt strange."

BEING A RECONSTRUCTIVE ADVOCATE

Today, Stout shows "no evidence of disease," meaning there is no sign of cancer in her body.

Since she was first diagnosed, Stout has been active on social media and has connected with other women who have undergone a variety of breast cancer treatments. She even created her own Facebook page called "Angela's Journey: Kicking Breast Cancer's Butt" to share and document her cancer story.

In another group, she and other women share their reconstructive journeys following mastectomies and even compare notes and photos about their experiences.

"I'm part of a DIEP flap support group on Facebook, and we encourage each other and talk about our doctors and our journeys," Stout said. "I use that platform to share different resources, take what I learn from these women and share with others in different groups. It's all about supporting each other, complimenting each other and showing that no one is alone, no matter what they decide in their treatment."

Stout's experience at Moffitt has also triggered her creative side. She has counted 227 appointments at Moffitt since her "I have my breasts, but I don't have any breast tissue," she diagnosis. During that time, she has collected inspirational said. "So no more mammograms for me."

"You have to use humor and turn bad news into a positive attitude when you can."

T-shirts and other items that reflect positivity and humor, encouraging anyone who is on a cancer journey.

She even created a piece of art in honor of her Clinical Research Unit team at Moffitt's McKinley Campus to mark the end of her active treatment in January 2022. In that painting, a flamingo poses near the words "Flocking Fabulous." She also has another favorite design: a skeleton that says, "Check your boobs, mine tried to kill me."

"You have to use humor and turn bad news into a positive attitude when you can," Stout said.

Talking about reconstruction, or breasts in general, can be uncomfortable for a lot of people. But Stout encourages women to embrace the journey and look at all the options available to them.

While she'll continue to be monitored following her treatment at Moffitt, an experience she says she's happy to continue, she is relieved that she will get to avoid one uncomfortable experience.

RUNNING for a LIFELINE

One step at a time, patient Kathryn VonAldenbruck and the doctors and researchers at Moffitt fight to beat lung cancer

By Jonesa Rodriguez and Corrie Benfield Pellegrino

Photos by Nicholas J. Gould

Kathryn VonAldenbruck wouldn't call herself a hardcore runner. She picked up running in her early 40s and considers it a sporadic pastime.

Elsa Flores, PhD, doesn't consider herself a runner either. She actually prefers working in the lab on new therapies for cancer patients.

But on this warmer than usual Saturday morning in November 2023, both women found themselves at the starting line of the same 5K, surrounded by thousands of running enthusiasts, energetic joggers and spirited walkers. The event was an important one for both women, not for setting personal records or finishing first, but for the work it fuels and the triumph it represents.

For VonAldenbruck, a patient at Moffitt Cancer Center, Miles for Moffitt gave her a chance to show what it looks like to be a survivor.

For Flores, associate center director for Basic Science at Moffitt, the event and the money it raises bring her and her fellow researchers closer to finding the lifesaving treatments that patients like VonAldenbruck are counting on.

For both, the 2023 event marked five years into two separate journeys for a cure.



KATHRYN VONALDENBRUCK Cancer Survivor

STARTING FROM THE BEGINNING

When VonAldenbruck first took up running, she would often participate in a string of 5Ks and then not run for a couple of years while the duties of raising three children took first place.

In 2018, her kids were getting older, and she was ready to pick up the pace again. She signed up for the Treasure Coast Halloween Half Marathon in her hometown of Stuart, Florida, and started to train. But when she couldn't complete a mile or even walk up a flight of stairs, she suspected something was wrong.

"I kept blaming it on everything. Maybe it could be asthma. We had blue algae at the time, and red tide was coming in," VonAldenbruck said.

She made a doctor's appointment and got a chest X-ray. Her primary care physician told her everything was fine and that she should come back in six months. But she knew her body was telling her something.

VonAldenbruck followed up with a pulmonologist for a CT scan. The next day, she got a call to return to the office. The pulmonologist broke the news. Her scan showed signs of cancer that had metastasized to the lymph nodes.

She left the pulmonologist's office in shock and immediately called her husband to tell him the news. At that moment, reality sank in. She couldn't hold back the tears.

"I still hadn't wrapped my head around everything, the diagnosis. I was still thinking: 'I'm not going to see my kids

graduate from middle school and high school. I am going to miss all the important things," she said.

VonAldenbruck was diagnosed with locally advanced stage 3 non-small cell lung cancer. She was 48 at the time, an otherwise healthy nonsmoker. A local oncologist in Stuart referred her across the state to Moffitt Cancer Center.

During her first appointment at Moffitt, VonAldenbruck learned surgery was not possible due to her tumor's location and the extent of the spread. However, she did have treatment options. It turns out she was the perfect candidate for a Moffitt-sponsored clinical trial that paired radiation with an aggressive immunotherapy combination of ipilimumab and nivolumab. Her oncologist, Ben Creelan, MD, was a treating doctor and co-investigator on the trial, which was only available at Moffitt.

VonAldenbruck jumped at the opportunity, becoming the first patient on the trial. She started this intensive treatment the day after Christmas 2018.

PLANTING SEEDS OF HOPE

For patients like VonAldenbruck, the innovative clinical trials and groundbreaking cancer research being done at Moffitt are a lifeline. Each year, new lifelines are launched by the funding that comes from Miles for Moffitt. Since its inception in 2006, the event has raised more than \$12 million for cancer research, with grants providing seed funds for scientists and physicians exploring new avenues to prevent and fight the disease.





"The goal is trying to find therapies that target specific pathways rather than killing every cell, including healthy tissues."

In 2018, the year VonAldenbruck was diagnosed and began her clinical trial regimen. Flores was embarking on a new potential lifeline for patients with lung cancer. The scientist had been awarded a \$200,000 grant from Miles for Moffitt to bring together a team to study how lung tumors metabolize nutrients. The goal was to identify these metabolic pathways and therapeutically target the tumors.

"Common chemotherapy hits all proliferating cells, not just the cancer cells. These dividing cells are present in the intestines and hair follicles. That's why people lose their hair and have a lot of digestive issues. Chemotherapy is very nonspecific," Flores explained. "The goal is trying to find therapies that target specific pathways rather than killing every cell, including healthy tissues."

The metabolic research is promising, but it could take years to complete. The Miles for Moffitt grant was just the beginning. It allowed Flores to bring together a team of top scientists and clinicians who shared an interest in tumor metabolism, immunotherapy and groundbreaking treatments that could be gentler for patients with lung cancer.

"I started exercising right away. It was the one thing I wanted to get back into."

The funding enabled the team to begin setting up the infrastructure needed for research projects, including developing preclinical models to study tumors, training a machine learning tool to grade the aggressiveness of tumors and building a lung cancer data repository for quick analysis. In addition, the grant provided funding to hire a program manager to facilitate collaboration among the scientists.

As the foundations for the research were laid, Flores had her sights set on securing long-term funding through a highprofile National Cancer Institute grant known as a Program Project Grant (P01). A P01 grant brings multiple investigators together to study projects that share a common theme or focus. The application process is complex and requires extensive preparation.

"You're doing all this work before you can get the P01 funding," Flores explained. "So the Miles for Moffitt funding was instrumental in each project getting off the ground."

KEEP IT MOVING

While Flores and her team hustled to launch their research. going into 2019, VonAldenbruck was feeling emotionally drained. She had begun treatment on the clinical trial, which started with 30 sessions combining radiation, immunotherapy and chemotherapy.

"She got all three at the same time - the kitchen sink basically," Creelan said. "We know that for Kathryn's type of cancer, the odds of long-term remission is only 30% with conventional therapy. So adding immunotherapy made sense."

Although she was hopeful, VonAldenbruck was wrestling with the anxiety of whether her treatment would work. Her half-brother, who also was diagnosed with lung cancer in 2016, had just passed away.

"It was a confusing time for me. He had gone through treatment and did everything," she said. "One of the things I kept telling myself was that his journey was not mine. And this is my journey, and I'm going to control it as much as I can."

During her initial treatment, VonAldenbruck stayed in Tampa. She decided to begin an exercise routine, starting with walks to Busch Gardens.

"I started exercising right away. It was the one thing I wanted to get back into. I knew it was good for me not only physically but mentally," she said.

After seven weeks of treatment, VonAldenbruck got the good news that the trial was working. Her scans were showing no signs of cancer. She needed to continue the immunotherapy for a year, and her care team would monitor her progress during that time.

"She did phenomenal on the treatment," Creelan said. "She responded very well."

Back at home on Florida's east coast, VonAldenbruck wanted to get back into running. So she decided to join a running club.



"It's up to us – cancer centers, foundations, donors – to move the needle. ... We want to move the football downfield to the goal for these populations."

"I had to start somewhere. I said I was going to do it, and I put my mind to it," she said. "We started with first walking a half a mile, and we would gradually build it up each week."

Soon, VonAldenbruck was able to alternate walking and running. She signed up for the Pineapple 5K, with a goal of finishing in under 40 minutes. She finished in 36.

"I was ecstatic that I could do it," she said.

The accomplishment pushed her to keep going. At her next race, she met a fellow survivor who shared a similar journey in battling breast cancer. The two bonded instantly.

"We did our first 5K together. And then I said if we can do this, we can do a 10K. Next thing you know, we're doing a half-marathon and then a full marathon," VonAldenbruck said.

"I kept telling myself ... this is my journey and I'm going to control it as much as I can."

GAINING MOMENTUM

Fueled by two additional Miles for Moffitt grants in 2019 and 2020, Flores' team was also picking up the pace during this time. The team had already traveled to the National Cancer Institute (NCI) in Washington, D.C., to pitch this research to program officers and get guidance on submitting for the P01 grant. They had received positive feedback but were told that more research needed to be done.

The additional Miles for Moffitt grants gave the researchers the funds they needed to accelerate the data required for the resubmission. Perhaps most importantly, the funding kept the research moving forward when COVID threatened to bring everything to a standstill in 2020.

"We were working in shifts. We knew we needed to get data out," Flores remembered. "So having that funding helped keep the team together and working on the project."

In 2021, the team resubmitted the application and got good news. The NCI awarded the group a five-year \$10.2 million

The team, known as the Lung Cancer Metabolism Working Group, is focused on four overarching projects:

- Flores, who is the principal investigator for the P01, is studying the tumor suppressor gene p53, which is commonly mutated in lung, breast and skin cancers. Her research is focused on understanding that pathway and finding new therapeutics that rewire the metabolism of lung cancer cells.
- Gina DeNicola, PhD, interim chair of the Department of Metabolism and Physiology and leader of the Metabolism Program, is studying the Nrf2 gene, which is also commonly mutated in lung cancer and is known to be involved in metabolism.
- · John Cleveland, PhD, chief scientific officer and center director, and Eric Haura, MD, associate center director for Clinical Science and director of the Lung Cancer Center of Excellence, are studying the myc gene and working to understand the commonalities between the two major types of lung cancer - non-small cell lung cancer and small cell lung cancer – to find common therapies.
- Paulo Rodriguez, PhD, chair of the Department of Immunology and co-leader of the Immuno-Oncology Program, is focused on boosting the immune system and profiling the metabolism of immune cells, looking for metabolic treatments that could improve immunity and treat cancer.

P01 grant. The federal funding now supports the research as the team works together to unveil common metabolic mechanisms regulated by common genetic drivers.

The group meets regularly to discuss what they are learning and to share ideas. The team ultimately hopes to use this research to identify existing drugs that could be repurposed to treat cancer or find new targets for developing drugs. These advances could benefit the full spectrum of patients with lung cancer, including never-smokers, former smokers and current smokers.

More and more, Creelan and his colleagues are seeing younger never-smokers like VonAldenbruck being diagnosed with lung cancer. The Centers for Disease Control and Prevention estimates that 10% to 20% of lung cancer cases diagnosed each year in the United States are never-smokers – defined as people who have never smoked or smoked fewer than 100 cigarettes in their lifetime.



"We don't know why this is happening, but we need solutions. These people are fit. They are motivated. They want to move on with their lives," Creelan said. "So that's where we need the money and the research focus. This is a rising unmet need."

In particular, research funding to explore treatment options for these relatively smaller populations of patients is crucial, Creelan explains. Seed funding like the grants provided by Miles for Moffitt can play a big role. This money is directly translated into new trials at Moffitt.

"It's up to us - cancer centers, foundations, donors - to move the needle. Many drug companies ... ignore never-smoker lung cancer. We want to move the football downfield to the goal for these populations," Creelan said.

PUSHING FORWARD TOGETHER

VonAldenbruck knows firsthand the power of having a team that is always pushing you forward. She now runs with a group of four women who encourage and motivate one another. They've dubbed themselves "GirlGangStrong."

For her New Year's resolution in 2022, VonAldenbruck decided to complete a 5K each month. She stayed on track until November, when after three years of being in remission, she learned her cancer had returned and had spread to her adrenal gland. This time, she was diagnosed with stage 4 lung cancer.

She went back on the immunotherapy regimen and underwent 12 weeks of chemotherapy, but she didn't want to slow down. She decided to keep running.

A year into her second round of treatment, on Nov. 18, 2023, VonAldenbruck and her gang of running partners gathered in downtown Tampa for Miles for Moffitt. Flores and her race team, called the Research Rangers, were there, too.

Together with thousands of other Moffitt scientists, doctors, patients and supporters, they took to the streets. They raised money for the research into new lifelines that Moffitt will continue to incubate. And they ran to send a message, said VonAldenbruck, who is once again responding well to treatment:

"We hold each other up. We are thriving. We are living."

ABOUT MOFFITT CANCER CENTER

Moffitt Cancer Center in Tampa, Florida, has made a lasting commitment to the prevention and cure of cancer, working tirelessly in the areas of patient care, research and education.

MISSION

To contribute to the prevention and cure of cancer

VISION

Create revolutionary breakthroughs and innovations that rapidly impact and save more lives

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Miles for Moffitt 2024

Save the date for the 19th annual Miles for Moffitt!

Join us Nov. 23, 2024, in downtown Tampa or virtually for an inspiring community event that raises money for lifesaving research at Moffitt Cancer Center.

Registration opens April 16, 2024

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