FOREFRONT
MAYO CLINIC CANCER CENTER Vol. 7 2017

CYCLING THROUGH
ANDY GORDON'S FIGHT AGAINST MULTIPLE MYELOMA
IN PERSPECTIVE

Cancer is still the second-leading cause of death worldwide. Yet we do have reason for optimism. The deeper we continue to dig into the makeup of cancers, the more targets we have for treatment. A convergence of advances gives me new hope that we can make significant progress against almost all cancers.

The discovery in the past decade that cancer tumors shed DNA into the bloodstream coupled with tools that now have the analytical sensitivity to detect tiny amounts of DNA allows us to screen for cancer in new ways. This includes a colorectal cancer screening test that patients can use in the privacy of their homes. More than half of all colorectal cancers are diagnosed at advanced stages due to low screening rates. This noninvasive, inexpensive home test is one way we will improve participation in screening. In this edition, you can read more about this test and some of the others our researchers and clinicians have collaborated on to detect cancers when they are most likely to be curable.

We are also improving the way treatment is administered. You will read about a breast cancer surgeon and a radiation oncologist at Mayo Clinic who were determined to find a better option for their early-stage breast cancer patients. They developed a protocol to decrease the length of treatment from three to six weeks to only nine days.

Overcoming obstacles is something we face down every day. This edition illustrates how a neurosurgeon and a lab director at Mayo Clinic collaborated to overcome two major obstacles and create a promising therapeutic vaccine for patients with glioblastoma, the most aggressive form of brain cancer and one of the most difficult tumors to treat. We are forging ahead in many ways to attack cancer at a genetic level. You will read about a genetic marker in some types of colon cancer that a Mayo Clinic gastroenterologist and oncologist is using to target the cancer with a new immunotherapy drug.

You will also meet Andy Gordon, who received a diagnosis of multiple myeloma 12 years after his first wife died from the same disease in less than a month. Fortunately, because research has evolved over the last decade, Andy’s multiple myeloma is in remission. Today, he is a grateful grandfather.

This is an incredibly exciting time for cancer research. Stories like those of Andy inspire us to work harder to improve treatment for our patients. New findings are released every day with real impacts. More people are living after a cancer diagnosis than at any time in history.

At Mayo Clinic Cancer Center, whether researching and developing the next breakthrough cancer treatment or administering expert care with compassion, it takes the best efforts of everyone involved to provide hope and save lives. I am deeply grateful for your commitment to cancer research and the role you play in making a difference for patients everywhere.

Thank you, and enjoy this edition of Forefront.

Robert B. Diasio, M.D.
Director
Mayo Clinic Cancer Center
William J. and Charles H. Mayo Professor
Game Changers
  Innovative Tests for Cancer Detection

Cycling Through
  Andy Gordon’s Fight Against Multiple Myeloma

A Molecular Abnormality
  Colon Cancer Trial Focuses on Biomarker

Just Five Days
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Labnotes

Meet the Investigators
GAME CHANGERS

FIVE INNOVATIVE TESTS FOR CANCER DETECTION

Finding cancer as early as possible is critical to saving lives. Mayo Clinic is creating a new era in health care with tests that make early and accurate detection of common cancers easy. Many are minimally invasive, convenient, cost-effective and widely available, removing the barriers that prevent people from getting treatment.
Breast cancer can’t hide in dense tissue

Mammography may not be enough to spot breast cancer for about half of all women who are screened. These women have dense breast tissue. They can be helped by a breast imaging technique pioneered at Mayo Clinic that nearly quadruples detection rates of invasive breast cancers in dense breast tissue.

On a mammogram, both dense tissue and tumors appear white. Spotting a tumor in dense tissue is like looking through a frosted glass window. Molecular breast imaging, or MBI, provides a clearer picture.

“MBI can uncover the reservoir of cancers that remain undetected on screening mammography because of masking by dense breast tissue,” says Deborah J. Rhodes, M.D., a Mayo Clinic Breast Clinic physician and a member of the team that developed the supplemental test.

In MBI, a short-lived radioactive tracer is injected into the vein. If tumor cells are present, they absorb the tracer like a sponge and illuminate on the image.

A Mayo Clinic team of physicists, radiologists and internists has spent nearly 15 years developing and evaluating MBI, including three clinical trials with over 5,000 women.
Recurrent prostate cancer lights up

Prostate cancer is the most common cancer among men, and about 30 percent of those diagnosed will experience a recurrence. These recurrences can often be difficult for physicians to find.

A Mayo Clinic research team developed an imaging method known as Choline C-11 positron emission tomography, or PET, scan that can find recurrent prostate cancer earlier than other tests.

“It’s a way of looking at the body three-dimensionally so you can see through the body and around the body to find cancer,” says Mayo Clinic radiologist Val J. Lowe, M.D., who helped create the new technology.

Choline C-11 uses a radioactive form of the vitamin choline, which is readily absorbed by cancer cells. The drug is injected into the patient who then has a PET scan.

“Choline C-11 lets us pinpoint at a very early interval where the cancer is returning,” says Mayo Clinic urologist Eugene D. Kwon, M.D., who was part of the team that developed the test. “Based on what we see in the PET scan, we can more intelligently design the patient’s next therapy.”

In about one-third of men, Choline C-11 PET scanning picks up metastatic lesions that aren’t seen with traditional imaging.
Colorectal cancer is the second-leading cancer killer in the U.S.

Yet many people who should get screened skip it. Colonoscopy, the most widely used screening method, is expensive and requires bowel prep, sedation and time off work.

Mayo Clinic researchers co-developed a test, now called Cologuard, that screens for colorectal cancer by measuring tumor DNA in stool. Cologuard is mailed to patients at home and requires only a stool sample, with no bowel preparation, medication or dietary restrictions. A patient mails the sample to a lab for analysis, and results are sent to the prescribing physician. In published studies from the screening setting, this noninvasive, inexpensive test detected 94-100 percent of early, curable-stage colorectal cancers.

Mayo Clinic became the first health care organization to offer Cologuard. Mayo Clinic gastroenterologist David A. Ahlquist, M.D., and his research team collaborated with Exact Sciences Corp. to develop Cologuard.

Among the first 100,000 patients to send in tests, 42 percent had never been screened for colorectal cancer by any approach.

“That’s exactly what we were hoping for — improving screening participation rates should lead to more effective cancer detection at the population level,” Dr. Ahlquist says.

Dr. Ahlquist and Mayo Clinic have a financial interest in Cologuard. Neither Mayo Clinic nor Dr. Ahlquist receives royalties for Cologuard tests ordered for Mayo Clinic patients by Mayo Clinic physicians.
Developing a test for esophageal cancer

Over four decades, esophageal cancer cases have increased 600 percent in the U.S.

“Compared with all other, more common cancers, incidence of esophageal cancer has skyrocketed,” says Mayo Clinic gastroenterologist Prasad G. Iyer, M.D. The cancer can be very deadly.

A sedated endoscopy at a gastroenterology lab is the recommended screening test today.

Dr. Iyer is collaborating with Exact Sciences Corp. and Mayo Clinic gastroenterologist David A. Ahlquist, M.D., to develop a new screening test that scans for DNA biomarkers of precancerous conditions in the esophagus. The biomarkers are picked up on a capsule sponge that a patient swallows. When the gelatin shell of the capsule dissolves, the released sponge is pulled out, providing cellular samples of the esophagus lining.

The sample can be gathered in a primary care office without the expense and side effects of an endoscopy, Dr. Iyer says. It’s sent to a lab for biomarker analysis.

Early data from studies show very high rates of sensitivity and specificity for predicting the presence of Barrett’s esophagus, a precursor for cancer. The capsule sponge was swallowed by over 90 percent of participants and was safe and well-tolerated. A phase II clinical trial is underway now at Mayo Clinic.

When esophageal cancer is caught early, survival is 80–90 percent.

“That tells the story of why early detection is the best. That’s the whole rationale for early screening,” Dr. Iyer says.
Soon, women may be using tampons to screen for the most common gynecologic cancer in the U.S.

An increasing number of women are diagnosed each year with endometrial cancer. Mayo Clinic gynecologic oncologist and surgeon Jamie N. Bakkum-Gamez, M.D., is attempting to change that trend.

“When this cancer is detected early, it has a very high cure rate,” Dr. Bakkum-Gamez says. “But when it’s detected at advanced stages, it’s almost always lethal. And we don’t have a screening test.”

In a 2015 study, Dr. Bakkum-Gamez showed it is possible to detect endometrial cancer using tumor DNA picked up by ordinary tampons. Now her team is working to develop the first early-detection test for endometrial cancer using tampons. This would be a prescribed, self-administered mail-in test, similar to Cologuard.

“We’re keeping the patient at the center of this. We want to make sure this is a test that provides wide access to care,” Dr. Bakkum-Gamez says. Her team is working on a commercially available test.

“This is an exciting time in women’s health, as we’re on the brink of introducing a life-changing test for cancer.”
MULTIPLE CYCLING THROUGH
Meet Andy Gordon, a health care litigator, dad, husband, cyclist, philanthropist and one in 14 million.
It was Labor Day 2009 when Andy received the same diagnosis his wife had heard 12 years earlier — a one in 14 million possibility. Andy’s wife Sue was diagnosed on April 11, 1997, with multiple myeloma, and she died on May 1. She never came out of the hospital. Their kids were 12 and 14 at the time.

Multiple myeloma is a blood cancer that forms in a type of white blood cell called a plasma cell. Plasma cells help you fight infections by making antibodies that recognize and attack germs. Multiple myeloma causes cancer cells to accumulate in the bone marrow, where they crowd out healthy blood cells.

“I was living in Washington, D.C., and riding my bike a fair amount when I started to have back pain,” recalls Andy. “I thought it was just middle-aged stuff.” The pain became unbearable while he was in Guantanamo Bay, Cuba, working for the U.S. Department of Homeland Security. In and out of planes and boats, he chalked it up to his activity, but he scheduled an appointment when he returned to the states just to make sure.

When the doctor couldn’t figure out the source of the pain, she sent Andy for a CAT scan. “I could tell just from the look on her face this is not going to be terrific news,” Andy says. The doctor told Andy he needed to be hospitalized immediately.

Andy had just turned 60 when an oncologist in the Washington, D.C., area confirmed he had multiple myeloma. Andy began chemotherapy right away. “I knew the most important thing for me was for my kids to know that what happened to their mom was not going to happen to me,” Andy declares.

### The Journey for Treatment

Three months before his diagnosis Andy married Patti Evans, a friend he had known for years. “If you get sick, you want Patti on your team,” he says. Patti was caring for her ailing father in Phoenix and was unable to fly to Washington while Andy was undergoing chemotherapy, so instead she secretly called friends and asked them to visit him. “Patti’s just one of those people who is a problem solver. When you’re facing a cancer for which there’s no cure, that’s particularly important,” Andy says.

The chemotherapy was working, and Andy’s cancer was decreasing enough to make him a candidate for a stem cell transplant. On the advice of his physician in Washington, Patti and Andy began to look for a medical center where he would get the transplant. They had consultations with several top medical centers in the U.S., but found their reputations to be different than what he experienced as a patient.

“I can close my eyes and actually see our first visit to Mayo Clinic and my initial interview with Joe — the sense was completely different than what I’d gotten from some of these other places,” Andy emotionally recalls. Joseph R. Mikhael, M.D., is a hematologist at Mayo Clinic in Arizona. He has conducted extensive research on multiple myeloma and is one of the world’s foremost leaders on the disease.

More than 60 hematologists at Mayo Clinic care for patients and conduct research to improve treatment of hematologic diseases including myeloma, lymphoma and leukemia. Our multiple myeloma research and practice group is one of the largest in the world.

The Arizona myeloma team of Leif Bergsagel, M.D., Rafael Fonseca, M.D., Joseph Mikhael, M.D., and Keith Stewart, M.D., is advancing the science and finding innovative ways to care for patients living with blood-related disorders and cancers.
Changing the Outcome

Multiple myeloma research has evolved incredibly over the last 10 to 15 years. Today there are new approaches, drugs and transplants that can be used to bring multiple myeloma into remission. In 1997, when Sue Gordon was diagnosed, the use of combining chemotherapy drugs was just in the experimental stages.

The revolution in multiple myeloma over the past two decades has been fueled by giant leaps in the understanding of its pathogenesis and the development of several novel agents. Today, patients like Andy are living healthier lives, and overall survival has doubled.

Because multiple myeloma is a complex and wide-ranging disorder, it must be managed individually based on multiple interacting disease- and patient-related factors. Mayo Clinic was instrumental in the development of carfilzomib and pomalidomide, two new drugs approved by the U.S. Food and Drug Administration for multiple myeloma in 2012. The last time the federal agency approved a novel myeloma therapy was in 2006. This approval was based primarily on the results of a large Mayo-led clinical trial that took place at multiple centers across the U.S.
“Mayo researches, it treats, it cares, it raises funds for multiple myeloma. Thanks to Mayo Clinic, this world has changed from a place where my first wife died within 22 days of diagnosis to a place where I’ve gotten to see our first two grandchildren and will hopefully see many more grandchildren, bat and bar mitzvahs, and maybe a wedding or two along the way.”

— Andy Gordon

Back on the Bike
Andy underwent a combination of high-dose chemotherapy and an autologous stem cell transplant, which means his own stem cells were used. Andy stayed in remission for more than four years.

“I got on with my life. I went back to work and back to riding. I wanted to do something to help find a cure for blood cancers. That’s why I got involved in the Arizona Chapter of the Leukemia and Lymphoma Society,” Andy says. He raised more than $150,000 through cycling fundraisers. Mayo Clinic’s Arizona campus has received grant funds from the Leukemia and Lymphoma Society, which provides research funds to organizations to find cures for blood cancer.

During those four years, multiple myeloma treatments continued to improve. Dr. Mikhael relied on a similar chemotherapy treatment and a second autologous stem cell transplant, putting Andy into a deep remission.

One year after the second transplant, Andy got back on his bike and completed a 100-mile ride around Lake Tahoe. And he’s back to working as an attorney and professor at Arizona State University Sandra Day O’Connor College of Law.

Andy’s children are now 32 and 34. “My greatest joy,” says Andy, as he wipes a tear, “is that I’ve gotten to see our first two grandchildren and will hopefully see many more grandchildren.”
Pioneer shapes treatment of multiple myeloma

The groundbreaking work of Mayo Clinic hematologist Robert A. Kyle, M.D., changed the treatment of multiple myeloma, a cancer of the plasma cells.

For more than 60 years, Dr. Kyle has reviewed patient histories and recorded the data of all patients with monoclonal plasma cell disorders into a large database. Several hundred thousand blood samples have been collected and frozen for research on patients.

In 1978, Dr. Kyle made a major discovery about a common condition that may progress to multiple myeloma or a related disorder. He described monoclonal gammopathy of undetermined significance (MGUS). The condition can progress to smoldering multiple myeloma (SMM), a precancerous form that Dr. Kyle also described, with his colleague, Philip Greipp, in 1980. MGUS can also progress to symptomatic multiple myeloma, Waldenstrom’s macroglobulinemia or primary amyloidosis. Before his work, MGUS was considered benign and long-term follow-up was not recommended.

Patients now have a much clearer idea of whether or not their condition will progress to myeloma and, if so, at what stage in life they can expect to develop symptoms. Physicians understand that the benign and intermediate forms are best carefully monitored but left untreated to avoid the potentially debilitating side effects of therapy.

Dr. Kyle has received the top two awards in hematology and oncology — the David Karnofsky Award from the American Society of Clinical Oncology and the Wallace Coulter Award from the American Society of Hematology. In his acceptance speech for the latter, he said, “Keep your eyes open, keep working and don’t give up.”

At 89, Dr. Kyle practices his advice and continues to do research. He is part of several studies being published this year.
Microsatellite instability (MSI) might sound like something a NASA engineer would study. But it’s actually a molecular abnormality found in 15 percent of colorectal cancers, explains Mayo Clinic medical oncologist and gastroenterologist Frank A. Sinicrope, M.D., who is testing an immunotherapy drug that could help patients with this subtype of colorectal cancer.

Just recently, researchers discovered why colorectal cancer with MSI can evade the body’s immune system, grow and become lethal: checkpoint proteins present on MSI tumors allow the cancer to manipulate the body’s defenses.

Armed with this knowledge, Dr. Sinicrope and his team will conduct a national clinical trial to test whether a drug called an immune checkpoint inhibitor can prevent the cancer from dodging death. The trial will enroll patients with stage III colon cancer with MSI who have already had surgery to treat the cancer.

“There is a great deal of interest in the trial and a lot of optimism based upon remarkable results seen for immune checkpoint inhibitors in patients with metastatic colorectal cancers,” Dr. Sinicrope says.

**Escaping attack**

Colorectal cancer with MSI is typically diagnosed at an earlier stage, and patients do better than those without the molecular abnormality. But the survival advantage is lost once the cancer spreads to other sites in the body.

MSI has a genetic basis. It results from the loss of function in one of the genes that repair errors in the DNA sequence when DNA is replicated. Tumors with MSI mutate rapidly, acquiring hundreds to thousands of mutations. This causes the immune system to kick into high gear. It recognizes the tumor and dispatches an army of T cells to attack. Yet the cancer has developed ways to escape this attack. Researchers observed this for many years and didn’t understand how it was possible.
Researchers now know that colorectal cancer with MSI can tap into checkpoints, an immune system pathway used to distinguish foreign cells from normal cells and signal whether or not to attack cells. Checkpoint proteins present on MSI tumors bind to receptors on T cells so those T cells can’t be activated in an attack. By exploiting the immune system’s checkpoints, MSI tumors can fly under the radar.

Immunotherapy prompts the immune system to refocus on fighting cancer. Immunotherapy drugs are new, but the idea of immunotherapy is not. Some of the foundational discoveries in checkpoints were made two decades ago in a series of experiments performed by Mayo Clinic researchers.

An immunotherapy drug called an immune checkpoint inhibitor is an antibody that blocks the cancer from evading attack and boosts immune response against the cancer. Such drugs have shown promise in clinical trials on metastatic colorectal cancer with MSI — when the cancer has spread to other sites in the body and is often fatal. The U.S. Food and Drug Administration approved in May 2017 the use of one immune checkpoint inhibitor for patients with this kind of cancer who have no other options for treatment.

“This is the exciting area of precision oncology.”

— Frank A. Sinicrope, M.D.
More research needed to better predict treatment

New immunological drugs are helping many cancer patients. But more research is needed to know who could benefit from this dynamic area of treatment.

A recent Mayo Clinic study investigated the accuracy of a current assessment method for immunotherapy treatment. The presence of PDL1, a protein on the membrane of some cancer cells, is used to determine whether immunotherapy will be effective for lung cancer patients. Mayo Clinic researchers led by oncologist Aaron S. Mansfield, M.D., showed in the study that PDL1 is not a reliable indicator.

“PDL1 comes, it goes, it’s expressed here but not there,” Dr. Mansfield says. “And based on how you assess its expression, you may miss patients who may benefit from immunotherapy.”

Dr. Mansfield and his colleagues examined biopsies over two decades of 73 patients with both primary lung cancer and lung cancer-related brain metastases. In the samples, the presence of PDL1 changed between biopsies from the same patient at different times. PDL1 can vary based on the size of the biopsy, specific tumor, time between tests and therapies the patient has undergone.

“Immunotherapy is moving to the frontline treatment of lung cancer for a subset of patients,” Dr. Mansfield says. “And that makes our work even more critical. But what we’ve done with our research is poke a hole in the use of PDL1 to select patients. We need a better biomarker than PDL1.”

Biomarkers are molecular substances in body tissues or fluids that can predict the effectiveness of treatments. Dr. Mansfield and his colleagues are now working to identify other biomarkers to predict who will benefit from immunotherapy.

Predicting treatment

In addition to seeking better therapies for patients, Dr. Sinicrope’s research focuses on cancer biomarkers.

Biomarkers are molecular substances found in body fluids or tissues that can alert doctors to disease. They are used increasingly in screening for the early detection of cancer. Biomarkers can also predict the likelihood of the recurrence or spread of cancer. And they can indicate whether treatment, like immunotherapy, may work in certain patients.

MSI is considered a predictive biomarker for treatment with checkpoint inhibitors, Dr. Sinicrope says. Testing for MSI at the time of a colorectal cancer diagnosis is increasing around the U.S. and now is recommended for all newly diagnosed patients. MSI is seen in a range of other cancers as well, including endometrial cancer.

Discovering biomarkers like MSI and categorizing the immune composition of tumors can help transform patient care, Dr. Sinicrope explains. In the case of MSI tumors, the evolving perspective is to treat the molecular abnormality — not necessarily the tumor type, he says.

“This is the exciting area of precision oncology.”
Imagine a bucket of sand. Every grain of sand in the bucket is white — except for one.

That one grain is darker than the rest. You may not be able to see it on first glance, but sift through, and you can find the one rogue grain of sand.
When applying this bucket of sand analogy to early-stage breast cancer, it illustrates the importance of radiation after breast-conserving surgery.

Breast-conserving surgery, also known as lumpectomy, is a type of operation to remove cancer from the breast while preserving a normal-appearing breast. Unlike a mastectomy, only a portion of the breast is removed. During a lumpectomy, a small amount of normal tissue around the lump, called a margin, is taken to help ensure that all the cancer is removed. However, Tina J. Hieken, M.D., a breast cancer surgeon at Mayo Clinic, cautions, “Just because you can’t see the cancerous cells anymore — even under a microscope — doesn’t mean there might not be a rogue cell that could grow and cause recurrence in the future.” Hence, the dark grain of sand.

That’s why radiotherapy after lumpectomy is the standard of care for most patients with early-stage breast cancer.

When breast cancer recurs, it typically appears in the site or the same portion of the breast where the original cancer was found. Therefore, the goal of whole-breast radiation therapy after lumpectomy is to decrease local recurrences and improve patient outcomes.

And it does. Over the years, gold-standard randomized trials involving thousands of women with early-stage breast cancer have been conducted to compare mastectomy with lumpectomy followed by radiation. These studies demonstrated that both approaches are equal in terms of their effect on survival.

However, 10 to 45 percent of patients who have breast-conserving surgery do not complete postoperative radiation therapy. So if radiotherapy decreases the chance of recurrence, then why are some women omitting this portion of their therapy?
“Good question,” acknowledges Sean S. Park, M.D., Ph.D., a Mayo Clinic radiation oncologist who specializes in breast cancer. “The standard whole radiotherapy treatment lasts somewhere between three and six weeks. That’s almost a month and a half of being away from their family or home and can pose a financial burden.”

Also, women may avoid radiotherapy because of the logistics of traveling to a radiation therapy facility five days per week for a month, the potential side effects to the lungs and heart, and the possibility of undesirable cosmetic changes.

Determined to find a better option for their patients, Drs. Hieken and Park began studying accelerated partial breast irradiation. With this approach, radiotherapy is directed to a small portion of the breast that is at the highest risk of cancer recurrence. With focused radiotherapy deposited to the lumpectomy bed and immediate surrounding breast tissue, partial breast irradiation is delivered in just five days.

The research team identified that the best method for sparing normal tissue might be brachytherapy, which involves placing a catheter device to deliver the radiotherapy. In general, this device is placed two to three weeks after an operation, once final pathology confirms complete removal of the breast cancer with negative margins and no cancer in the lymph nodes.

However, Drs. Hieken and Park developed a protocol to bypass this extra wait using a revolutionary technique developed at Mayo Clinic.

“Because we use intraoperative frozen section pathology, we can clear our margins and place the catheter in one operation,” Dr. Hieken explains.

Mayo Clinic is one of the few medical centers in the nation to routinely use a tissue freezing process for analyzing operating room tissue samples. The process enables pathologists to rapidly analyze and diagnose tissue samples with 98 percent accuracy, while the patient is still in the operating room. The rapid turnaround of results saves patients time and money, since one surgery at Mayo can take the place of two or three procedures at other institutions.

The day after lumpectomy and the placement of a catheter, radiation treatment planning begins, and the final pathology report is verified. Radiotherapy is completed within nine consecutive days of the patient’s operation.

Drs. Hieken and Park recently published the results of the first 123 patients treated on this protocol, of which 110 participants, or 90 percent, successfully underwent intraoperative catheter placement. Of those patients, 99 percent completed their radiation within nine days of surgery.

“We were able to assess one-year complication rates in the majority of patients and found it to be reassuringly low,” says Dr. Hieken. “Early cancer outcome data shows 98 percent of patients remain cancer-free.”

The duo now plans to analyze the cost of this approach versus standard treatment for early-stage breast cancer and find a way to shorten the treatment schedule even further.
Jane’s Story

Jane Brandhagen has always feared mammograms, because she’s always been the one to get called back. One day in May 2016, that call back confirmed she had early-stage breast cancer.

“It turned out to be cancer, and I was so angry. I work out every day, eat healthy and take really good care of myself,” Jane says. “I thought I would just have a double mastectomy because I never wanted to deal with this again.”

However, while talking to her doctor about her options, Jane was told she would be a perfect candidate for the brachytherapy radiation study conducted by Drs. Hieken and Park. And that’s when Jane felt the stars began to align.

Knowing this study would cut down the radiation treatments from 20 over four weeks to less than a dozen in one week tipped the scales for Jane.

She admits that it was a little “uncomfortable for one week or less — more like five days — but that was the trade-off for not having 20 radiation treatments, which might have damaged healthy tissue and my lung. That was huge.”

Now, Jane says her advice to other women is to get a mammogram.

“I feel so lucky to be here,” she says. “It was a good find because the cancer was just three little dots. Who knows what would have happened if I waited another year.”
Glioblastoma, also known as glioblastoma multiforme, is the most aggressive form of brain cancer and one of the most difficult tumors to treat. Even with surgery, radiation and chemotherapy, the average survival is about 15 months. “This tumor is a very bad actor. You don’t need to see too many patients with glioblastoma before you really want to do something more,” says Ian F. Parney, M.D., Ph.D., a neurosurgeon at Mayo Clinic.

For over 20 years, Dr. Parney has searched for the right technology that would help him fight this disease. Now, in collaboration with Allan B. Dietz, Ph.D., director of the Mayo Clinic Human Cellular Therapy Laboratory, Dr. Parney believes they’ve finally identified a promising therapeutic vaccine for patients with glioblastoma.

Things you need to build a better mousetrap. One: Obtain the most advanced technology. Two: Find the right “cheese.” Three: Identify a formidable foe, like a coy mouse or, in this case, an infiltrative tumor.
Therapeutic vaccines combine tumor antigens, or proteins, with dendritic cells, which are created from white blood cells called monocytes, to boost the patient’s immune system to eliminate the tumor. Therapeutic vaccines typically require samples of a patient’s tumor to provide antigens.

Unfortunately, the supply of glioblastoma tumor antigens from an individual patient’s sample is limited. This is because neurosurgeons like Dr. Parney do not have the luxury of removing large amounts of brain tissue due to the sensitive location of the tumor.

Successful vaccine treatments also require mature dendritic cells. But standard methods for culturing dendritic cells, which are developed using monocytes from healthy blood donors, generate a higher number of immature dendritic cells when applied to monocytes from glioblastoma patients. Immature dendritic cells weaken the vaccine’s potency because they work to suppress the immune system.

To overcome these obstacles, Drs. Parney and Dietz built a better mousetrap.

They created a library of clinical-grade brain tumor cell lines from patients, eliminating reliance on tumor samples from each individual to obtain antigens. Also, Drs. Parney and Dietz developed a better technique to culture dendritic cells from patients’ white blood cells. “We spent four years optimizing this drug,” Dr. Dietz explains. “Before we even started the first trial, we spent the time to make sure we had the best drug we could possibly make.”

Now, the dendritic cell vaccine is in the final stages of a pilot clinical trial involving patients with newly diagnosed glioblastoma. Patients were enrolled on the trial after undergoing surgery to remove as much of the tumor as possible. Then, standard radiation therapy was administered. Upon completion, patients were given a combination of chemotherapy and vaccine for six months, followed by another six months of only vaccine injections.
Driving innovation forward

In an era of landmark discoveries and expanding knowledge of the brain, patients need innovators on the frontlines armed with extensive training and equipped with the latest tools.

Mayo Clinic’s Precision Neurotherapeutics Innovation Program, a collaboration between the Neurosurgery Simulation and Innovation Laboratory, led by Bernard R. Bendok, M.D., and the Mathematical Neuro-Oncology Laboratory, and Kristin R. Swanson, Ph.D., unites a group of physicians, scientists and mathematicians to identify reliable ways to predict the future path of a person’s brain tumor growth in a unique, new way — using mathematics. Analyzing data from MRI scans and other pathology from individual patients, researchers can simulate and calculate how fast and where a patient’s brain tumor is likely to spread. This allows doctors to develop a treatment plan for the specific patient, rather than a one-size-fits-all therapy.

These more precise therapies succeed because of the innovative technologies used to superimpose the knowledge and data into the operating field. The Precision Neurotherapeutics Innovation Lab enables physicians to practice a surgery before operating on a patient using 3-D printed or holographic models to improve patient outcomes.

“At Mayo Clinic, our goal is to evolve from conventional surgery to individualized precision surgery,” Dr. Bendok says. “This goal can be achieved through innovations that will result from integrating simulation science, advanced imaging and robotics into the surgical environment.”

Often with vaccine trials, patients only receive three or four vaccine injections. However, this improved technique enabled Drs. Parney and Dietz to treat patients with up to 15 vaccine injections over the course of a year.

“Everybody is enrolled, and the final patient only has a few more treatments,” Dr. Parney says. “Although we don’t have final results yet, we’re seeing a couple of very interesting and exciting things. First, it’s quite feasible to treat a lot of patients with this treatment. The second is that it appears to be safe. [The] third thing is that we are seeing evidence in the lab that we’re stimulating immune responses against tumor proteins. The final and most exciting thing is that we are seeing some evidence of biological activity that may be helping people. For example, it seems there is a group of patients who have no progression of their tumor for a long period of time.”

The team anticipates that final analysis of the trial will be ready in fall 2017. Once the final results come in, Drs. Parney and Dietz hope to build a larger clinical trial with the goal of obtaining U.S. Food and Drug Administration approval.

“We’re phenomenally excited about the other opportunities that really just mean taking this technology a half step to the left or the right,” Dr. Dietz explains. “If you’re looking for an area to make a difference in a reasonable time frame, you know that if you can move the needle even a little bit in glioblastoma, you’ve made significant progress.”

In the future, they expect the technology to fight glioblastoma will just keep getting better.

“We’re better now than we were a year ago or five years ago, and we’re going to be better in a year from now and five years from now,” Dr. Parney says. “I firmly believe this is a tumor that we’re going to make really significant strides in and get better outcomes for people. So stay tuned.”
Mayo Clinic breast cancer study sheds significant light on tumor sequencing and response to chemotherapy

After years of anticipation, Mayo Clinic researchers reported the results of a prospective tumor sequencing study in women receiving chemotherapy prior to breast surgery.

The Breast Cancer Genome-Guided Therapy (BEAUTY) study used comprehensive sequencing data derived from the tumor and the host genome — genes inherited from a person’s biological parents — in women with high-risk breast cancer requiring chemotherapy prior to surgery. From March 2012 to May 2014, BEAUTY enrolled 140 patients across Mayo Clinic’s campuses in Arizona, Florida and Minnesota.

The main findings of the BEAUTY study, published in the online issue of Journal of the National Cancer Institute, demonstrated that the most common genetic changes were not more commonly observed in chemotherapy-resistant tumors compared to chemotherapy-sensitive tumors. Mayo Clinic investigators also noted that the luminal androgen receptor subtype of triple negative breast cancer, an uncommon type of aggressive breast cancer, was less likely to respond to chemotherapy. It was also more likely to contain a unique type of mutation in p53, a tumor suppressor gene commonly mutated in triple negative breast cancer.

As a result of the study researchers now know that:
- The most common and recurrent genomic alterations observed in the BEAUTY study were equally as likely to be observed in patients who responded to chemotherapy as those who did not respond.
- Many uncommon genomic alterations were observed, and much larger studies will be needed to determine whether these unique alterations identify groups of patients who are more or less likely to respond to chemotherapy.
- The development of patient-derived xenografts, or mouse avatars, using needle biopsies from the primary breast tumor prior to surgery is feasible and is a powerful tool for studying new therapeutic strategies.
- Treatment of the avatars with the same chemotherapy that the patients received demonstrated the response in the avatar mirrored the response in the patient.

“Using the data generated from this study, the Mayo BEAUTY team will launch a successor study bringing forward new drugs to women with chemotherapy-resistant tumors,” says Judy C. Boughey, M.D., breast surgeon and co-chair of the BEAUTY study.

The research team’s goal is to bring forward the most promising drugs to patients who have tumors resistant to current therapies.

Immunotherapy to be tested on advanced pancreatic and breast cancers

A new technique that raises armies of cancer-fighting immune cells will be tested soon in a clinical trial.

“We have a way of growing T cells that is very different from the way people are doing it currently,” says Peter A. Cohen, M.D., a Mayo Clinic immunotherapist who co-led the study with Sandra J. Gendler, Ph.D., a Mayo Clinic immunologist, and Mary L. (Nora) Disis, M.D., a University of Washington immunotherapist.

The immunotherapy will first be used to treat patients with advanced pancreatic and breast cancers in a phase I/II clinical trial led by Mayo Clinic that is expected to start by late 2017 or early 2018.

The researchers discovered a new culture method that unlocks the natural fighter function of immune T cells when they are passing through the bloodstream. This allows T cell armies to be raised directly from blood that naturally recognize and target the proteins present on most human cancers.

It was difficult to unleash T cells’ natural ability to recognize and target cancer cells. The researchers found that T cells traveling within the bloodstream naturally remained locked in a resting state unless they were exposed to natural alarm signals normally triggered only by serious infections.
Once outside the body, the T cells could be exposed to such alarm signals to unleash their fighter function. When the T cell cultures were also exposed to cancer-associated proteins, such as MUC1, it required three weeks to grow armies trained to recognize and target cancers expressing these proteins.

“The cancer-associated proteins we have tested so far already target the majority of human cancers, and it is likely that this culture method will extend to many additional proteins present on cancer cells,” Dr. Gendler says.

The treatment is also expected to make new immunological drugs, such as checkpoint inhibitors, work even better, Dr. Cohen says.

Drs. Cohen and Gendler’s collaboration to target cancer cells through their expression of MUC1 was last highlighted in Vol. 6 of Forefront.

Vaccine designed to provide immune response against early breast lesions

Only about 35 percent of precancerous breast lesions become cancer if untreated, but physicians cannot identify which are potentially dangerous.

So all women diagnosed with ductal carcinoma in situ, a very early stage of breast cancer, undergo traditional therapy of surgery and possibly hormonal therapy and radiation.

Now, Mayo Clinic researchers are about to test a vaccine that is designed to establish lifelong immunity against development of these precancerous lesions. They hope it will replace traditional therapies and prevent recurrence for some, if not all, these patients.

If ultimately successful, the vaccine could become part of a routine immunization schedule in healthy women.

“We’re taking a very unique approach here,” says Mayo Clinic immunologist Keith L. Knutson, Ph.D., who designed the vaccine. “We ultimately want to move our vaccines into primary prevention.”

Dr. Knutson has received a $3.7 million grant from the U.S. Department of Defense to conduct a phase II clinical trial to test the vaccine. It is targeted against human epidermal growth factor 2 (HER-2), an oncogene known to play a role in the development and progression of an aggressive subtype of breast cancer known as HER-2 positive.

Dr. Knutson suspects that excess HER-2 proteins are expressed in all subtypes of breast cancer, including the most common one: estrogen-positive breast cancer. The vaccine is designed to stimulate production of T cells that target initial development of ductal carcinoma in situ.

In 2017, Dr. Knutson and his colleagues at Mayo Clinic campuses in Florida and Minnesota will test the vaccine in 40–45 patients diagnosed with ductal carcinoma in situ. These patients will be treated with the vaccine first. Six weeks later, they will receive surgery (lumpectomy or mastectomy) and other standard therapy. During the initial six weeks, physicians will monitor patients to see if ductal carcinoma in situ lesions reacted to the vaccine.

“Our goal is to determine whether or not the vaccine can see very early disease and get rid of it,” Dr. Knutson says.

Eliminating ductal carcinoma in situ would reduce the overall breast cancer burden significantly.

“Ductal carcinoma in situ is a significant health problem, accounting for about 20 percent of U.S. cases of breast cancer,” Dr. Knutson says.

High doses of immune cells help non-Hodgkin’s lymphoma patients

High doses of patient’s own immune cells significantly increase the chances of disease-free survival in non-Hodgkin’s lymphoma, a clinical trial at Mayo Clinic shows.

The finding led to a change in patient care.

“Because of this phase III trial, we have already changed our practice to collect higher immune cells for transplant to any patient with lymphoma,” says Mayo Clinic hematologist Luis F. Porrata, M.D.
In the trial, Dr. Porrata and his team collected different types lymphocytes, or immune cells, from two groups of patients who had either diffuse large B-cell lymphoma, follicular lymphoma or mantle-cell lymphoma.

One group received high doses of lymphocytes when they underwent transplants of their own stem cells. Stem cell transplants restore a patient’s ability to make normal blood cells after high-dose chemotherapy. Two years later, the survival rate for the group was 92 percent, and the rate at which the cancer returned was 24 percent.

The other group of patients received small doses of lymphocytes in stem cell transplants. The group’s survival rate was 68 percent, and rate for recurrence of the cancer was 50 percent.

The trial also showed that high doses of a particular type of lymphocyte called natural killer cells were associated with better outcomes for patients. Natural killer cells play a major role in limiting the spread of tumors and infected cells. They are among the immediate defenses that make up the body’s innate immunity.

This finding suggests that early recovery of innate immunity is important to the survival of lymphoma patients undergoing stem cell transplants, Dr. Porrata says.

He adds that further studies are underway to understand the underlying mechanism of how innate immunity and natural killer cells affect outcomes for patients in stem cell transplants.

**Study looks at uterine microbiome to detect endometrial cancer triggers**

Endometrial cancer triggers remain elusive, despite continued research. But given the typical inflammatory profile, microbes in the uterine environment are suspected of playing a role in the development of this disease.

The National Cancer Institute defines a microbiome as a collection of microorganisms and viruses that live in a specific environment in the human body. Mayo Clinic researchers set out to discover whether there is a microbiome component in the malignancy of tumors and if its appearance in patients diagnosed with the disease is distinguishable from that of patients without malignancy.

According to Marina R. Walther-Antonio, Ph.D., lead author of the first direct-assessment uterine microbiome study, researchers now know that the uterine microbiome and the microbes present in the vaginal environment of women with endometrial cancer are different from women without endometrial cancer.

“The populations of microbes found throughout the reproductive tract were shifted in the presence of cancer and hyperplasia (enlargement of an organ or tissue), and were distinct from the noncancerous cases,” says Dr. Walther-Antonio.

Because of the modifiable nature of the microbiome, this discovery also holds the promise of a critical advance in endometrial cancer prevention. Researchers are investigating the possibility of using vaginal swabs as an early screening tool for endometrial cancer and noncancerous endometrial biopsies to identify patients who will develop endometrial cancer in the future.

“These findings provide important insights into the causes of the disease with broad implications for development of a measurable indicator in the early detection of, and screening for, endometrial cancer,” says Dr. Walther-Antonio.

**Shorter chemotherapy could spare patients**

For patients with stage III colon cancer, a shorter course of oxaliplatin-based chemotherapy following surgery was associated with fewer and less severe side effects.

This is one of the key findings of the International Duration Evaluation of Adjuvant chemotherapy (IDEA) study, which comprised six separate clinical trials of nearly 13,000 patients from 12 countries. Results of the IDEA study were presented recently at the 2017 annual meeting of the American...
Society of Clinical Oncology in Chicago by Mayo Clinic researchers.

“Chemotherapy after surgery, also known as adjuvant therapy, is a standard treatment to increase the cure rate of patients with colon cancer who have undergone surgery and had cancer spread to lymph nodes,” says Axel Grothey, M.D., an oncologist at Mayo Clinic and senior author of the study. “The current standard adjuvant therapy, which was established more than a decade ago, is a combination of two or three drugs, one of which is called oxaliplatin, given for about six months.”

Dr. Grothey says the key side effect of oxaliplatin is nerve damage that may result in permanent numbness, tingling and pain in the hands and feet even after the chemotherapy is discontinued. He says the likelihood of developing neurotoxicity and its severity is closely related to the duration of the therapy and the total dose of oxaliplatin received over time.

“The goal of our study was to investigate if a shorter three-month duration of oxaliplatin-based therapy is as effective in reducing the risk of cancer recurrence as the standard six-month duration,” says Qian Shi, Ph.D., a biostatistician at Mayo Clinic.

Dr. Grothey says a shorter duration of therapy could spare patients potentially unnecessary toxicity and lead to substantial savings in health care expenditures, and become the new standard of care in the postoperative management of patients with stage III colon cancer, which affects approximately 400,000 patients worldwide every year.

Liquid biopsies offer hope for earlier treatment of ovarian cancer

Ovarian cancer is one of the hardest cancers to diagnose and treat, because it often cannot be found until the late stages. Now, Mayo Clinic researchers have found a promising new way to monitor and treat recurrence of ovarian cancer. George Vasmatzis, Ph.D., a researcher with Mayo Clinic’s Department of Laboratory Medicine and Pathology, finds that liquid biopsies from a blood draw, along with DNA sequencing, can show a return of ovarian cancer long before a tumor reappears. This finding could lead to earlier and more effective individualized treatment.

“With liquid biopsies, we don’t have to wait for tumor growth to get a DNA sample,” says Dr. Vasmatzis. “This important discovery makes it possible for us to find recurrence of the disease earlier than other diagnostic methods. We can repeat liquid biopsies to monitor the progression of the cancer. That gives hope of a better treatment plan over time.”

The study was done on 10 patients in advanced stages of ovarian cancer. Blood was drawn before and after surgery. Investigators compared DNA from the blood to DNA tissue samples from the tumor. If, after surgery, DNA matched that of the tumor, patients were found to have a recurrence of cancer.

“In this study, the blood drawn before and after surgery, and the surgical tissue, was used to identify DNA fragments with abnormal junctions that can only be seen in this patient’s tumor DNA,” Dr. Vasmatzis explains. “This allows us to shape treatment to the individual patient rather than using a standard treatment that may not work for everyone.”

Ovarian cancer has one of the highest death rates of all gynecological cancers. Most patients go into remission after initial treatment, but the tumor returns 75 percent of the time. The next stage of ovarian cancer that develops typically does not respond to chemotherapy.

Dr. Vasmatzis’ research, “Quantification of Somatic Chromosomal Rearrangements in Circulating Cell-free DNA From Ovarian Cancers,” is published in the July 2016 edition of Scientific Reports.
Long before national news outlets documented his determined rise from migrant farmworker to Harvard Medical School and world-renowned neurosurgeon, Alfredo Quinones-Hinojosa, M.D., was an inquisitive boy who loved staring at the nighttime sky and stars from the roof of his family’s home near Mexicali, Mexico. And when he talks about his career in medicine and cancer research, it becomes clear that curiosity and imagination are close companions — or even the foundation — for the determination that is perhaps considered his hallmark.

“The brain is the unexplored frontier of medicine,” says Dr. Quinones-Hinojosa, who chairs Neurosurgery on Mayo Clinic’s Florida campus and is a William J. and Charles H. Mayo Professor. “I didn’t fully understand that until medical school, when a neurosurgeon pulled me into an operating room to watch one of his surgeries. I saw the brain and heart dancing together, and I realized that, right in front of me, was the organ that makes each of us who we are. My knees just buckled.”

His research career launched in a similarly fundamental way — in basic neuroscience research with lobsters. As a medical student, he successfully cloned a complex receptor in the brain that was linked to aggressiveness in those animals. Later, he started investigating cancer cells and says he was captivated by how they hijack the body’s basic mechanisms to spread.

He started his own lab with a $30,000 grant during his neurosurgery residency. Today, his lab has 17 staff members and several grants from the National Institutes of Health to study glioblastoma, a lethal and aggressive brain cancer.

Patients with glioblastoma have a median survival of about 15 months, and there is no cure. Dr. Quinones-Hinojosa is trying to change that through research that aims to diagnose the disease earlier, better predict how it spreads and develop new treatments.

In the treatment arena, his team is combining stem cells and nanomedicine to develop a new technique for treating glioblastoma during the surgery. Stem cells have an innate ability to migrate to areas of injury, including glioblastoma lesions, which makes them a perfect vehicle for delivering treatments, Dr. Quinones-Hinojosa says.

“Our strategy is very simple,” he says. “After we remove a tumor and while the patient is still in the operating room, we’ll deliver stem cells that carry a treatment molecule. We’ll send the modified stem cells to the areas just beyond the surgery site to find and kill cells that migrated from the tumor. We’ll harvest the stem cells from the patient — from their own fat cells — before the surgery. So the stem cells will act like a Trojan horse to improve the effectiveness of our surgeries.”

If effective, the strategy would address one of the main challenges to improving glioblastoma outcomes. Typically, the cancer reappears quickly after surgery, and it spreads rapidly. Dr. Quinones-Hinojosa’s team has studied it in animal models and used a protein called BMP4 as the treatment molecule for the stem cells. Their studies in animals show that stem cells packed with BMP4 shrink tumors and make glioblastoma cells more susceptible to chemotherapy, which may help reduce recurrence of the disease.

That strategy is only one of many the team is investigating. They have also expanded their focus to include cancer metastasis — more specifically, how cancers spread from their sites of origin to the brain. And highlighting only one area of the team’s research is a challenge, says Dr. Quinones-Hinojosa, who is married and has three children. “It’s like asking me to choose my favorite child,” he says.
What makes a one-of-a-kind researcher? In the case of Mayo Clinic hematopathologist Lisa M. Rimsza, M.D., it is drive, determination and a lot of what one mentor called “moxie.”

It is also something inherent. Dr. Rimsza says she recalls a department chair at the University of Arizona who once said: “You can just tell someone who’s obsessed with research. They start that way, and it’s a phenotype they never give up. I think you’re one of those people.”

Today, Dr. Rimsza is a professor of laboratory medicine and pathology at Mayo Clinic College of Medicine and Science in Scottsdale, Arizona. Her most recent research accomplishment has drawn attention from across the globe.

Dr. Rimsza led a team of researchers on a yearslong effort to create, publish and commercialize a lab-ready test that can identify the individual genomic makeup of cancer tissues in patients with diffuse large B-cell lymphoma, the most common form of non-Hodgkin’s lymphoma.

The test, called the Lymph2Cx assay, was offered for the first time in the U.S. in December and is available only at the Molecular Diagnostic Arizona Laboratory, of which Dr. Rimsza is director. Mayo Clinic plans to offer the test to patients at its Rochester, Minnesota, and Jacksonville, Florida, campuses, as well by sending their samples to the Arizona laboratory.

The path that took Dr. Rimsza from research to publication of the Lymph2Cx test has had its share of twists and turns. Through it all, she has relied on a relentless work ethic and that innate passion for discovery.

“I just love seeing the long-term goal,” she says. “It has just always been in my mind — just don’t ever give up.”

Prior to obtaining her medical doctor degree, Dr. Rimsza worked as a pharmacist and regularly mixed chemotherapy drugs for cancer patients. She says she saw ample opportunity to improve outcomes for patients with diffuse large B-cell lymphoma, which represents as many as 30,000 new cases per year.

The cancers of diffuse large B-cell lymphoma patients can be grouped into two subtypes with a test of the genetic expression of tumor cells. But the most widely used genetic test, in practice and in research, is still only about 83 percent accurate.

“There are not many people that would accept an 83 percent chance that they’re getting the right therapy,” Dr. Rimsza explains.

In 2007, Dr. Rimsza was elected principal investigator on the Lymphoma and Leukemia Molecular Profiling Project. With her typical determination, she and her team set out to standardize a genetic assay for diffuse large B-cell lymphoma.

The program’s issuance of the Lymph2Cx test, with Dr. Rimsza as co-creator, has improved the accuracy of genetic testing for diffuse large B-cell lymphoma tissues in a timely and widely replicable manner. The test will help ensure patients with the appropriate cellular function are directed to experimental treatments that could lead to breakthrough therapies.

Dr. Rimsza is now engaged in the work of shepherding the test through U.S. Food and Drug Administration trials and the processes for intellectual property and licensing.

“It’s just been a feat of determination, and it’s been one thing after another,” she says.

As her mentor described it, Dr. Rimsza simply has “moxie.”

Lisa M. Rimsza, M.D.

Driven to Discover
For Mark J. Truty, M.D., a Mayo Clinic surgical oncologist, fighting pancreatic cancer isn’t just his job — it’s personal. “When I was a teenager, my dad died in my arms from the ravages of pancreatic cancer.”

Years later, when Dr. Truty became a hepatobiliary and pancreatic cancer surgeon, he realized the medical field was still employing the same methods used to treat his father. Nothing had changed in decades.

“I have a higher risk than the general population for this disease, so I want to make sure we are moving the field forward.” To make this a reality, Dr. Truty is identifying how to use chemotherapy, radiation and surgery to combat this deadly cancer — something he calls “total neoadjuvant therapy.”

At the time of his father’s diagnosis and, in most cases, today, the standard treatment for patients whose tumors are localized is surgery. Patients whose tumors have spread or are vascularized receive only chemotherapy and radiation and are typically considered inoperable. None have good long-term outcomes.

But Dr. Truty is trying to change this. “We are expanding the available options and improving outcomes for these patients,” says Dr. Truty, whose new treatment sequence gives patients more successful options.

The first step for these patients is a multiagent chemotherapy administered by Mayo Clinic oncologists. Dr. Truty explains that pancreatic cancer spreads early and aggressively, despite initial staging scans. Starting with chemotherapy right after diagnosis targets the spreading cancer that might not yet be detectable.

Dr. Truty follows the chemotherapy with radiation treatment to kill cancer cells at the site of the future operation. Creating a sterilized field gives the surgeon the greatest chance of having a negative margin, which means no cancer cells are left behind. Finally, Dr. Truty and his surgical colleagues operate to remove the tumor. During the procedure, tumor samples are immediately reviewed by dedicated pathologists who quick-freeze the tissues and examine them for any remaining cancer — a technique developed at Mayo.

“But because of this specific series and order of treatments, we are now able to offer surgery to many patients who were deemed inoperable previously,” he says.

However, this does not mean that each pancreatic cancer patient’s process is the same. This protocol is based on integrative care that is individualized to the patients and their tumors. The sequence of chemotherapy, radiation and surgery is consistent, but the type and duration of chemotherapy and radiation and the extent of surgery depend on the individual.

The unique nature of the surgeries makes for a time-intensive process. The average surgery takes around six hours, but more than 25 percent of the surgeries are more than 10 hours long. However, the time is worth it to Dr. Truty. “We are finally seeing patients who have survived beyond five years after surgery.” This is a surprising result for a diagnosis for which the predicted survival usually is calculated in months.

Dr. Truty is not stopping now. Along with co-investigators from Mayo Clinic Department of Oncology and the Center for Individualized Medicine, Dr. Truty is researching the different mutations of pancreatic cancer to help predict which chemotherapy drug will be most effective for each patient.

One thing is clear: Dr. Truty does not give up, and he believes people who are diagnosed with pancreatic cancer shouldn’t either. “Fight for your health,” Dr. Truty says. “Don’t take no for an answer. There are now options out there. There is hope.”

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**Mark J. Truty, M.D.**

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To relieve the burdens of cancer by promoting basic and clinical research on the incidence, causes and progression of cancer and translating discoveries into improved methods for prevention, detection, diagnosis, prognosis and therapy.

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