Lighting a path through CANCER'S WOODS
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A journey with guides

In his best-selling book *The Emperor of All Maladies*, oncologist Siddhartha Mukherjee, M.D., recounts the history of man’s experience with cancer. At one point in the book he writes that when it comes to cancer “dying, even more than death, defines the illness.”

While it is true that our journey to understand and achieve cures for cancer has taken us through more dark forests than bright meadows, we do have reason for optimism. More people are living after a cancer diagnosis than at any time in history. And the numbers are trending upward.

The implications of this fact both for patients and for the health care system are profound. If more people are living longer after a cancer diagnosis, how best do we help make their lives more comfortable and productive?

In the cover story of this issue of *Forefront* we highlight a handful of innovative “survivorship” programs available at Mayo Clinic Cancer Center designed to help patients improve their quality of life.

If you’re looking for proof that people can live full lives after a cancer diagnosis, look no further than the Spotlight section of this issue. There we highlight Don Wright, a Mayo patient who was diagnosed with multiple myeloma in 2004 at age 72. Don defines the term cancer survivor. Just prior to his diagnosis, he ran his first marathon. Don recently completed his 73rd marathon and he has no plans to stop.

Stories like those of Don Wright inspire us to work harder to improve the treatment and quality of life of our patients. A cancer diagnosis begins a complex and challenging journey for patients and our role as clinicians and researchers is to be trusted guides on that journey.

I invite you to read all the stories in this issue of *Forefront* to learn more about what we’ve been up to at Mayo Clinic Cancer Center.

“More people are living after a cancer diagnosis than at any time in history. And the numbers are trending upward.”

— Robert B. Diasio, M.D.
t’s a familiar refrain, we treat, we cure and we may treat again if the cancer returns. While much progress has been made developing new cancer treatments, there is more need than ever to provide ongoing treatment options for patients diagnosed with cancer. Survivors can face a host of physical, psychological, emotional, social, spiritual and economic struggles throughout the course of their disease and treatment. A few of the major concerns include fear of recurrence, fatigue, pain, stress, sleep issues and living with uncertainty.

Researchers at Mayo Clinic Cancer Center are teaming up to study and advance the science of quality of life for cancer survivors.
Symptom Control and Quality of Life
For 20 years, Mayo Clinic Cancer Center, along with other cancer research organizations, has been advancing the science of symptom control and quality of life for cancer survivors. This effort has continued, despite funding challenges and other obstacles, because of strong, dedicated and determined leadership. Charles Loprinzi, M.D., the Regis Professor of Breast Cancer Research, and Debra Barton, R.N., Ph.D., are two Mayo Clinic researchers leading the way.

Dr. Loprinzi’s primary research focus has been the study of cancer-related symptom control and doctor-patient communication. In fact, his research team was the first to demonstrate that certain antidepressants could decrease hot flashes, which is now a standard non-hormonal treatment for bothersome hot flashes. While Loprinzi and Barton have investigated many different symptoms, including appetite and weight loss, hot flashes, fatigue, nausea, vomiting, bone loss and sexuality issues, a prominent research focus in recent years involves a major side effect of chemotherapy agents — peripheral neuropathy.

Chemotherapy-Induced Peripheral Neuropathy
Chemotherapy-Induced Peripheral Neuropathy (CIPN) is a serious side effect associated with several common chemotherapeutic agents, including platinum agents, taxanes, vinca alkaloids, thalidomide, bortezomib and ixabepilone. CIPN is reported by 30 to 40 percent of patients receiving these types of chemotherapy. Many times, chemotherapy dosing is reduced due to symptoms of CIPN, which can mean that patients don’t always receive the therapeutic dose needed to treat their cancer.

The most common symptoms associated with CIPN are sensory neuropathies, including paraesthesias (burning, tingling and numbness) and pain starting in the fingers and toes and spreading proximally. CIPN can begin weeks to months after initial treatment and reach a peak at, or after, the end of treatment. In some cases, the pain and paresthesias completely resolve after treatment is stopped. However, in most cases, CIPN is only partially reversible and can be permanent. Patients living with CIPN may suffer from pain and difficulty with everyday activities, which translates into a major quality of life factor during and after treatment.

“Cancer is a life changing experience. Our job is to help patients successfully manage that change.”
— Sheryl Ness, patient educator
The Mayo CIPN research program encompasses a number of treatment areas. One of these relates to more accurately defining and measuring chemotherapy neuropathy syndromes. For example, paclitaxel is a chemotherapy drug that often causes pain for a few days after each dose. In the past this pain was thought to be related to muscle or joint problems. However, Mayo Clinic data strongly supported the theory that the pain was a manifestation of nerve injury. Drs. Loprinzi and Barton and colleagues also developed a scale to determine the degree of neuropathy patients are experiencing. These efforts have improved the ability of investigators to facilitate effective CIPN research.

Another aspect of their work has been trying to better define which patients are at higher risk of developing CIPN. Working with Andreas Beutler, M.D., another Mayo investigator with a research focus on chronic pain, they are studying the DNA of patients receiving chemotherapeutic agents that commonly cause neuropathy. Preliminary data from this work supports the hypothesis that a patient’s genetic compositions may hold the clue to determining which ones may be more prone to chemotherapy neuropathy. Further work to refine these findings is ongoing.

In addition, the group continues to evaluate promising therapies to alleviate CIPN. This work, using randomized, placebo-controlled studies, has helped better define agents that do not appear to be helpful and newly discovered agents that look more promising. While no markedly effective therapies have been identified for treatment of established CIPN, the group continues to explore new and promising agents.

This work has included the study of the value of using an electrocutaneous nerve stimulation device, called MC-5A Calmare®, also known as “scrambler therapy.” The MC5-A Calmare® device provides cutaneous electrostimulation by simulating nerve action potentials and directly stimulating peripheral nerves. The MC5-A Calmare® device is not thought to act just by inhibiting pain transmission, but instead by substituting “pain” information with “non-pain” information. It is thought that it does this by mixing another signal into the pain signal transmission, which replaces the original pain information, thus the term, “scrambler therapy.” Based on pilot data from another group of investigators, supporting that this therapy was useful in patients with chemotherapy neuropathy, Mayo is evaluating this treatment in patients with chemotherapy neuropathy and other pain states. Initial data from Mayo support that this treatment looks promising and deserves to be evaluated in a placebo-controlled, randomized study.

In addition to studying possible CIPN treatments, Mayo investigators have lead efforts to study prevention. Early information from pilot trials suggested that both vitamin E and a combination of intravenous calcium and magnesium may be helpful for preventing chemotherapy neuropathy. However, the largest placebo-controlled trials of these agents, recently completed by Mayo investigators, did not support the benefit of using these approaches.

“We are blessed to have an incredibly talented and diverse team of healers who try to tailor therapeutic approaches to meet the patient’s needs. While one patient may benefit from acupuncture, the next patient might be best served by massage therapy. Another might need both.”

— Brent Bauer, M.D.
Complementary and Integrative Medicine

Most cancer patients have some degree of stress and anxiety as they deal with the aftermath of their treatment and worry about the possibility of recurrence. It’s important that every patient is given a chance to explore different stress management strategies until one is found that works for them.

Brent Bauer, M.D., director of the Complementary and Integrative Medicine (CIM) program at Mayo Clinic says, “We are blessed to have an incredibly talented and diverse team of healers who try to tailor therapeutic approaches to meet the patient’s needs. While one patient may benefit from acupuncture, the next patient might be best served by massage therapy. Another might need both.”

In 2012, more than 1,000 cancer survivors were referred to the CIM program with questions on how to improve quality of life and deal with cancer-related symptoms. Dr. Bauer explains that the program’s focus is on helping each patient find their path to optimize their resiliency. This involves a strong focus on nutrition, exercise, stress management and connectedness. Bauer says when patients optimize these aspects of their lives, it can have a positive impact on their quality of life and their overall sense of well-being.

Managing Stress

According to Dr. Bauer, “Reaching out to over-stressed family members and friends is an obvious extension of how we care for the survivor.” That is where Mayo’s Stress Management and Resiliency Training (SMART) program can be helpful. SMART is an innovative program that focuses on enhancing quality of life by addressing the physical and emotional effects of cancer and cancer treatment.

“Fear of recurrence and living with uncertainty is a major concern for cancer survivors,” explains Amit Sood, M.D., who developed the SMART program. He says the residual effects of treatment, both physical and emotional, can have negative effects on the brain, which can cause negative thoughts and excessive worry, adding to the overall stress level.

Dr. Sood goes on to say that the SMART program is designed to help patients understand this stress phenomenon by focusing on training their attention to cultivate positive emotions through being in the present and focusing on gratitude, compassion, acceptance, positive meaning and forgiveness.

The goal of SMART is to help patients see their cancer diagnosis as a transformational event so they find even greater meaning in life after cancer.

A study assessing the effectiveness of the SMART program for increasing resiliency and decreasing stress and anxiety among breast cancer survivors found a considerable improvement in resilience, perceived stress, anxiety and overall quality of life.

The SMART program uses a four-step approach:

**STEP ONE:** Validate the patient’s feelings. Explain that their feelings and emotions about cancer are natural and to be expected after what they’ve been through.

**STEP TWO:** Help patients understand the brain and how the mind can cause a decrease in quality of life.

**STEP THREE:** Inspire patients to transform themselves to reach a better emotional place.

**STEP FOUR:** Empower them with the practical skills to help them experience a better quality of life.
Education
Through its Cancer Education Center, Mayo Clinic Cancer Center now offers classes to support patients’ move forward after cancer treatment. The classes are designed to help patients:
- Develop a healthy lifestyle after treatment
- Manage difficult emotions
- Identify potential long-term or late effects of cancer treatment
- Understand the importance of becoming an active participant in follow-up care

“Cancer is a life changing experience,” states Sheryl Ness, a patient educator in Mayo’s Cancer Education Center and editor of the Living with Cancer newsletter and blog. “Our job is to help patients successfully manage that change.”

For more information and online and virtual support, cancer survivors can connect to Mayo Clinic experts and other cancer survivors through the Living with Cancer newsletter and blog at www.mayoclinic.com/livingwithcancer/

Cancer Survivorship Clinics and Care Plans
Hematologist Carrie Thompson, M.D., is a champion of a newly created cancer survivor clinic for lymphoma patients at Mayo. Her research and clinical initiatives have a strong focus on the well-being of cancer survivors and their caregivers.

According to Dr. Thompson, “Traditional quality of life programs focus on the time during active cancer treatment, but we know that the other areas are just as important and often can become more important as patients transition from treatment to survivorship.” In the Lymphoma Survivorship Clinic, a standardized questionnaire is administered in-person to comprehensively assess quality-of-life components. Issues covered include depression and anxiety, post-traumatic stress disorder symptoms, spirituality concerns, sexuality, relationships, financial concerns and physical and functional symptoms. “By asking these questions, we give patients a chance to open up about their cancer experience, which can be very therapeutic.” Thompson says caregivers may also be profoundly affected by the cancer experience, so the program addresses their well-being as well.

“Traditional quality of life programs focus on the time during active cancer treatment, but we know that the other areas are just as important and often can become more important as patients transition from treatment to survivorship.”

— Carrie Thompson, M.D.
Colon cancer is slow to start. Polyps can take a dozen years to turn into full-blown cancer, giving people ample time to spot the disease — possibly before it develops. Yet, because half of Americans forgo colonoscopy screening, colon cancer remains the second biggest cancer killer in the United States. Even those who do submit to the invasive test have no way of knowing if any polyps discovered during the procedure could eventually turn cancerous.

Two researchers at Mayo Clinic think they can do better. They are tapping into the latest in genetics and genomics technologies to more easily detect the disease and predict its course, all with one goal: to stop colon cancer in its tracks.
Laying new tracks

When David Ahlquist, M.D., a gastroenterologist at Mayo Clinic, began treating colon cancer patients three decades ago, it had already been ten years since the first colonoscopy had been performed. Since then, he has used the colonoscopies to prevent and detect thousands of cases of colon cancer. But for every case that he caught, others were missed because people were reticent or unwilling to undergo such an invasive and costly test. Dr. Ahlquist began to wonder if he were to do it all over again, what it would take to build the ideal colon cancer screening tool.

Dr. Ahlquist, the Carol M. Gatton Professor of Digestive Diseases Research Honoring Peter Carryer, M.D., started ticking off the attributes of his ideal tool — the test would be noninvasive, highly accurate in detecting both cancer and precancerous lesions, affordable, not involve any preparation or change in diet or medication, and could be conducted at home. Instead of examining the colon itself to spot precancerous lesions, Dr. Ahlquist thought a better test would look for cancer cells that had been shed from the lining of the colon and passed into fecal matter.

To test his hypothesis, he searched stool samples for constituents of cancer cells — including protein, RNA, and DNA — that indicated cancer was present. Dr. Ahlquist soon detected structural changes in DNA that could serve as a signature of cancer or polyps. In a recent large study of this method, published in 2012 in the journal Gastroenterology, the DNA stool test detected 87 percent of early stage cancers and 64 percent of precancerous polyps. After several rounds of tweaks, Dr. Ahlquist says a next-generation version of the test recently detected nearly all (98%) of colon cancers in referred patients. For precancers, the polyps that can turn into cancer, the sensitivity was highest for the largest lesions with the greatest likelihood of progressing to cancer.

“If we could get these same detection rates in a screening program, the implications would be enormous,” says Ahlquist. “When screening for cancer the test has to be sensitive, because you may have only one chance to detect the disease. But in screening for polyps — the kind that are the large dangerous ones — there is a longer window and it is the cumulative sensitivity that is critical. We estimate that the sensitivity of the stool DNA test for large polyps should approach 100 percent after the second or third round of

“We hope a test like this can break down those barriers and get more people screened.”

— David Ahlquist, M.D.
screening, much like Pap smear achieves for precancers of the cervix, which is only 50 to 60 percent sensitive at one point in time. Repeated cervical Pap smears have essentially eliminated cervical cancer in the women who are screened. We believe that if the DNA stool test is used widely and regularly as has been accomplished with cervical Pap smear screening, then we can start talking about eradicating colon cancer.”

Dr. Ahlquist and Exact Sciences, the company commercializing the test, recently completed a multicenter study, along with academic center collaborators, to assess whether the test worked as well in the general population as it did in referred patients. More than 10,000 patients were screened for colon cancer and precancerous lesions with both the DNA stool test and a colonoscopy. Most of the results are under wraps while the study is being examined by the Food and Drug Administration as part of the test’s pre-market submission approval; however, the publicly available top-line data shows that the DNA stool test detected 92.3 percent of cancers, essentially equivalent to the reported detection rates of colonoscopy. It also outperformed another colon cancer screening test, fecal immunochemical testing.

For the first time in history, the Center for Medicare and Medicaid Services and the FDA are conducting simultaneous reviews of the stool DNA test, rather than waiting first for FDA approval. Dr. Ahlquist thinks that this unprecedented parallel review by the two large regulatory bodies could accelerate the test’s availability for patients. “We have now demonstrated that the stool DNA test can deliver the same results as colonoscopy but with a non-invasive and less resource dependent approach,” explains Ahlquist. “Many people do not undergo screening because they are squeamish about complying or they are limited by geographic or financial barriers. We hope a test like this can break down those barriers and get more people screened.”
On the Right Track

The vast majority of polyps that turn up during screening might never evolve into colon cancer, says Lisa Boardman, M.D., an associate professor of medicine at Mayo. But there is no good way to discern the 5 to 10 percent that will become aggressive, aside from crude measures like gauging the size of the polyp or looking for abnormal features under the microscope. Such uncertainty undermines efforts to broaden screening programs and makes it unclear when those who are screened should return for follow-up.

Boardman’s research is focused on developing a more accurate method to pinpoint the polyps that are the most dangerous. Since 2000, she has been collecting colon tissue from Mayo’s Biobank for Gastrointestinal Health Research (BGHR) to find out what sets apart the polyps that turn cancerous from the ones that remain cancer-free. Dr. Boardman is most interested in a unique subset of polyps that contain both cancerous and noncancerous cells, because they offer a glimpse into the molecular switch that puts a polyp on track to become cancer.

“If you think of a slow motion film, we are catching the polyp in the frame before it turns completely into cancer so it has the premalignant and malignant right in same tissue,” said Boardman. “We can look for different kinds of signatures that represent these different molecular fates.”

Dr. Boardman plans to use microarray or gene “chip” technology to assess these signatures on a global scale. First she will look at the genome, placing particular focus on 20 genes that are known to be associated with the development of colorectal cancer. Then she will analyze the methylome, the methyl tags that serve as “on-off” switches of genes, for insight into any environmental events at work. Finally, Boardman will study the transcriptome, representing all the genes that are turned “on” at any given time, to understand what players are active in the cell when it becomes cancerous.

Right now, Dr. Boardman’s laboratory is hard at work getting the samples ready for these genomic arrays. This process is time-consuming, as the researchers have to dissect and scrape cancerous and noncancerous portions of polyps as small as a pea. Still, Boardman hopes to have accumulated, tested and analyzed the first 50 cancer-free and 50 cancer-adjacent polyps this year. The results could uncover molecular signatures to predict which polyps are more innocuous and which are on track to become cancer.

“Colon cancer is a disease that we can catch and STOP from developing, but only if people come in to be screened. I hope knowing what the tipping point is for developing cancer will be the incentive for more people to take control of their health.” — Lisa Boardman, M.D.

free. Dr. Boardman is most interested in a unique subset of polyps that contain both cancerous and noncancerous cells, because they offer a glimpse into the molecular switch that puts a polyp on track to become cancer.

Though it can take a long time for polyps to develop into cancer, not all patients with the disease are elderly. About 15 percent of colon cancer patients get the disease before they turn 50. Boardman wondered if those people are more susceptible to colon cancer because they are actually biologically older than their healthy counterparts. She decided to look at telomeres, the molecular tree rings that get shorter and shorter as people age.
In 1997, Mayo Clinic Cancer Center received its first Specialized Program of Research Excellence (SPORE) grant for brain cancer research. The SPORE grant application built on the work of Brian Patrick O’Neill, M.D., who helped establish Mayo Clinic’s Brain Cancer Program that same year.

In 1999, Lynn Hartmann, M.D., led a team of Mayo Clinic Cancer Center researchers to provide the first published evidence that bilateral prophylactic mastectomy reduces the incidence of breast cancer by more than 90% among women with a family history of breast cancer. She is the Blanche R. and Richard J. Erlanger Professor of Medical Research.

In 2003, the NCI approved the extension of Mayo Clinic Cancer Center’s designation as a Comprehensive Cancer Center in Rochester to Mayo campuses in Florida and Arizona. Mayo became one of the first multicenter health care institutions in the country to establish an integrated national cancer center.

In 1994, Franklyn Prendergast, M.D., Ph.D., became Director of Mayo Clinic Cancer Center and oversaw significant changes, including the expansion of the cancer center to Florida and Arizona campuses and the establishment of cancer population sciences research, cancer education and cancer control and prevention programs. He is the Edmond A. and Marion F. Guggenheim Professor.

In the late 1980s, Robert Abraham, Ph.D., discovered and characterized mTOR (mammalian target of rapamycin), a protein that’s present throughout the body that is critical to the growth of cancer cells. The discovery provided new insight about how to block its function and led to the creation of new tumor-fighting drugs.

In 1986, John Kovach, M.D., succeeded Dr. Moertel. He focused on expanding Mayo Clinic’s cancer research base and recruited 18 laboratory investigators with an interest in basic cancer research.

In 1977, Mayo Clinic Cancer Center was a founding partner in the North Central Cancer Treatment Group, an outreach project designed to bring high-quality cancer care and research to community clinics. The group also included a cancer clinical trials cooperative, which allowed promising scientific ideas developed at Mayo Clinic to be tested in communities across the country.

In 1974, Robert Kyle, M.D., was awarded a program project grant by the National Institutes of Health (NIH) to study disorders related to multiple myeloma. The grant was funded throughout his career and generated discoveries that turned Mayo Clinic into a Mecca for blood cancers.

In 1973, Mayo Clinic Cancer Center became a designated NCI cancer center under the direction of Charles Moertel, M.D.

In 1901, the Mayo brothers hired Henry Plummer, M.D., to direct the development of Mayo’s clinical laboratories.

In 1905, Louis Wilson, M.D., perfected a method of staining and rapidly freezing tissue samples that delivered a diagnosis within five minutes.

In 1920, Albert Broders, M.D., another pioneering pathologist, described a system of microscopically grading cancers based on a numerical system. The least malignant cancers were designated Grade 1; the highest, Grade 4. Dr. Broders’ study of 537 cases led to tumor staging, a practice adopted worldwide.

In 1989, Mayo Clinic Cancer Center became the first recipient of the U.S. Public Health Service Comprehensive Cancer Center designation.

In 2006, the Mayo Clinic Cancer Center doubled the number of endowed professors, increased its NCI funding and increased its research focus on genomics-based cancer research under the direction of Robert Diasio, M.D.

In 2013 and beyond, with the availability of more comprehensive human genomic data and with the ability to sequence individual patient tumor samples, Mayo Clinic Cancer Center is involved in therapeutic trials in multiple disease types that will build on our understanding of cancer and lead to new therapies.

In 1977, Mayo Clinic Cancer Center, with a grant from the Howard Hughes Medical Institute, became the first cancer research institute in the nation to provide research training for graduate students.

In 1997, Mayo Clinic Cancer Center was awarded its first P30 grant by the NCI. The P30 grant provided support to an internal review committee for investigators to propose and develop research initiatives.

In 1999, Mayo Clinic Cancer Center was awarded its first SPORE grant by the NCI. The SPORE grant provided support to investigator-initiated research to enhance Mayo’s cancer research efforts.

In 2003, the NCI awarded the designation of Mayo Clinic Cancer Center as a Comprehensive Cancer Center to Mayo Clinic campuses in Rochester, Florida and Arizona. The designation allowed Mayo to establish an integrated national cancer center.

In 2006, the Mayo Clinic Cancer Center was awarded its first P30 grant by the NCI. The P30 grant provided support to an internal review committee for investigators to propose and develop research initiatives.

In 2013 and beyond, with the availability of more comprehensive human genomic data and with the ability to sequence individual patient tumor samples, Mayo Clinic Cancer Center is involved in therapeutic trials in multiple disease types that will build on our understanding of cancer and lead to new therapies.
Patients come to Mayo Clinic for help with the diagnosis and treatment of a difficult medical problem, having the confidence that they are being evaluated with the latest diagnostic methods and treated with the latest and best therapeutic approaches.

Robert Diasio, M.D., Director, Mayo Clinic Cancer Center

The past 40 years, cancer practices at both the Florida and Arizona sites have grown at a rate of 22 percent per year, and have more than doubled the number of patients treated. Mayo Clinic’s cancer operations in Arizona were launched in May 2003, and its Phoenix campus opened in January 2006. The Mayo Clinic Arizona Cancer Center is dedicated to providing comprehensive, state-of-the-art cancer care in a collegial environment.

The Mayo Clinic Cancer Center, located on Mayo Clinic’s campuses in Minnesota, Arizona and Florida, has been among the nation’s leaders in cancer care, research and education for the past 40 years. The Mayo Clinic’s cancer programs have achieved a national reputation for research excellence and clinical care. Patients from around the world come to Mayo Clinic for the highest-quality, most advanced cancer care.

When Dr. Diasio assumed the leadership of the Mayo Clinic Cancer Center, he introduced the vision of a patient-centered approach to cancer care. He believed that patients deserve to receive the best possible care based on the latest scientific evidence. This approach has led to the development of the Mayo Clinic Cancer Center’s new model of care, which focuses on the patient and their family, and emphasizes the importance of collaboration across all disciplines.

The focus on patient care at the Mayo Clinic Cancer Center is evident in the center’s approach to cancer treatment. The center’s multidisciplinary teams work together to provide comprehensive care that is tailored to each patient’s needs. This approach has led to significant improvements in patient outcomes and quality of life.

The Mayo Clinic Cancer Center is committed to advancing the field of cancer research. The center has invested heavily in research, and has established partnerships with leading research institutions around the world. These partnerships have allowed Mayo Clinic researchers to make important breakthroughs in cancer biology and treatment.

The Mayo Clinic Cancer Center is also committed to training the next generation of cancer researchers. The center has established a number of training programs, including fellowships and residencies, to prepare the next generation of cancer researchers. These programs have helped to attract a talented group of researchers to the Mayo Clinic Cancer Center.

The Mayo Clinic Cancer Center is a leader in cancer care, research and education. The center’s commitment to patient-centered care, research and education has led to significant improvements in patient outcomes and quality of life. The center continues to be a leader in the field of cancer care, and is committed to advancing the field of cancer research for the benefit of patients around the world.
Dr. Johnson quickly assembled a team of Mayo Clinic radiologists, biostatisticians, computer programmers, gastroenterologists and colorectal surgeons and set out to push the imaging technology. According to Dr. Johnson, “No medical software was available for image data at the time, so we had to create it.”

His team’s efforts over the last several years have refined the technology that the press likes to call a “virtual colonoscopy,” though Dr. Johnson and colleagues prefer the term “CT colonography.” After the group evaluated, improved and validated the technique, Johnson led the National CT Colonography trial, which recruited 2,600 patients among 15 medical centers. The results, published in the New England Journal of Medicine, showed that for identification of patients with biologically important polyps (those larger than 6 millimeters) CT colonography is as effective as colonoscopy. The astounding imaging technology, now available around the country, is one of several being developed and tested at Mayo Clinic to improve the diagnosis and treatment of some of the hardest-to-detect cancers.

An Easier Test, With More Information
For patients who can’t undergo a colonoscopy because of a fragile colon or difficulties with the bowel prep, CT colonography is a simpler test. After undergoing a lighter prep, patients hold still for two breath-holds on a CT scanner. If the images show polyps that need to be removed by a gastroenterologist, patients schedule a colonoscopy. (A streamlined process at Mayo Clinic enables patients to head upstairs the same day for a traditional colonoscopy.)

While colonoscopy inspects only the interior space of the colon, CT colonography assesses the bowel wall and the contents of the abdomen. The test has revealed unsuspected cancers, such as lung and ovarian cancers, abdominal aortic aneurysms, and in one patient, a small bowel parasite. Dr. Johnson’s team continues to refine the test, including an approach that involves no bowel prep at all. Ultimately he hopes the ease of the exam will encourage more patients to undergo colon cancer screening.
Detecting the Tiniest Recurrence

When radiologist Val Lowe, M.D., was brought in to lead the positron emission tomography (PET) scan center 14 years ago, he recognized that prostate cancer was a critical problem to tackle. Other cancers, like lymphoma or breast, are traceable with PET scans because the cells take up glucose, which can be radioactively tagged, while prostate cells remain invisible to the scans. Then, as studies around the world suggested the prostate cells might metabolize choline, the vitamin B complex found in broccoli and eggs, Lowe’s group felt they’d found their target.

Creating a choline compound with a radioactive tag, known as Choline C-11, they saw results in animal models and then clinical patients. “It was pretty immediate,” Lowe recalls. “Tiny tumors lit up well.” Now, if men have rising prostate specific antigen (PSA) levels, suggesting prostate cancer is present, but the tumors don’t turn up on MRI, CT or bone scans, doctors have another tool to detect lesions as small as 3 millimeters. So far, more than 1,500 men have undergone Choline C-11 PET screening at Mayo Clinic; approximately 30 men are requesting the test each week. Upcoming research will look at how well the test affects patient survival after five years, but the scan is clearly providing another opportunity to address the disease. “We’ve had people come to us who’ve had chemotherapy because the recurrence was suspected in the body, even though other scans couldn’t find it. The choline scan showed it sitting right in the bed of the prostate. Our doctors have gone in and surgically removed residual disease, and the patients’ PSA values have dropped to essentially zero,” Lowe says.

Changing the Management of Lung Cancer Patients

Even though a national trial in 2011 showed that CT screening led to a 20 percent reduction in lung cancer deaths, the technology still presents some challenges. “Ninety-five percent of all pulmonary nodules detected by radiologists during screening are not cancer,” explains pulmonologist Tobias Peikert, M.D. “In addition, a significant subgroup of the screening-detected lung cancers may have an indolent course. Aggressive therapy may cause more harm than benefit for these patients.”

As it happened, biophysicist and computer scientist Richard Robb, Ph.D., director of Mayo’s Biomedical Imaging Resource Lab, had been collaborating with radiologist Brian Bartholmai, M.D., on developing CT imaging software capable of distinguishing densities of tissue and visual patterns in the lungs. Their program, called Computer-Aided Lung Informatics for Pathology Evaluation and Rating (CALIPER), had already shown it could detect and quantify diffuse lung diseases, such as emphysema. Dr. Peikert and pulmonologist Fabien Maldonado, M.D., were hopeful the technology could
be useful for evaluating lung nodules, but were skeptical about how well it would work. Over the last two years, Dr. Robb and his team, imaging scientist Srinivasan Rajagopalan, Ph.D., graduate student Sushraya Raghunath and programmer Ronald Karwoski, developed a new algorithm, based on CALIPER, to examine pulmonary nodules and provide risk analysis. How aggressively will the nodules grow? As it became clear what the new test could do, Dr. Peikert says, “I was won over. It was very exciting.”

The lung nodule characterization software is known as CANARY, which stands for Computer Assisted Nodule Assessment and Risk Yield. Patients undergo a chest CT without intravenous contrast, and then the sophisticated software is introduced. The computer detects density characteristics of each pixel in the image of the nodule, creating a color-coded radiologic profile of each one. These color-coded “signatures” aren’t just descriptive, but correspond to features pathologists typically only see after the lesion is removed and can reliably predict the aggressiveness of nodules. “Significantly, CANARY may allow patients to take a wait-and-see approach rather than jump to surgery, the standard of care, to remove an entire lobe of lung,” explains Dr. Peikert.

The CANARY research team is now gathering data to see how well this technology distinguishes between benign and malignant nodules. It ultimately may be applicable to diseases in other tissues, such as the liver or kidneys, and possibly for detection of subtle changes in density that occur in the brain from stroke or dementia. “There are many steps ahead before CANARY receives Food and Drug Administration approval for clinical use,” says Dr. Robb, the Zbigniew and Anna M. Scheller Professor of Medical Research in Honor of Dr. Thomas J. McDonald. “But I have no doubt that this will become an extremely significant tool in management of lung cancer patients.”

Using high-resolution CT images, CANARY automatically identified nine unique patterns that represent differential tissue signatures of adenocarcinoma tumors in the lungs. The distribution of the color-coded patterns is characteristic of the varied type and nature of the tumors. 

The figure shows three different axial CT sections (top row) from three different patients with three different tumor types automatically detected and classified by CANARY. Tissue signature patterns are overlaid on each detected tumor image (center row) and 3D color-coded renderings of each tumor (bottom row). The three tumor types are: (A) indolent adenocarcinoma in situ, (B) minimally invasive adenocarcinoma, and (C) aggressively invasive adenocarcinoma.
Cells that Light Up During Surgery

For patients with ovarian cancer, survival can hinge on whether all tumor cells are removed during surgery. To be cautious, surgeons may remove healthy tissue around the malignancy. But they may also miss cancer cells that cannot be seen or palpated. That’s why gynecologic oncologist Sean Dowdy, M.D., has taken on the challenge of tagging ovarian cancer cells to make them visible while surgery is taking place. “Ideally with this technique you could see where the tumor stops, and you could tailor resection just a little bit outside where the tumor is to spare normal structures,” Dowdy explains.

He was impressed with the fluorescence tagging technique presented by Purdue chemist, Philip Low, Ph.D., and thought it might be ideal for ovarian cancer. Ninety percent of ovarian cancer cells express a marker called folate receptor alpha, which doesn’t appear in normal cells (lung and endometrial cancers also express it). But Dowdy quickly faced a two-part challenge, first tagging the receptors and then refining cameras to properly visualize them. In a recent trial of 25 patients with ovarian cancer, he found that tagging folate receptor alpha with a fluorescent agent worked well in some women, but not in others, suggesting that the folate receptor alpha levels may vary between patients. This experience prompted a new effort that’s now under way to enhance the technology — both the fluorescence tag and the series of filters in the camera — to illuminate tumors even on a microscopic level, as small as 50 microns.

“It’s very innovative” says Dowdy. “You label cancer cells but not normal cells, and you can see it in real time during surgery.”

But he’s aware that the new technology, like the other Mayo Clinic innovations that have homed in on detecting a particular type of cancer, may also have far-reaching effects in the future.“This approach may apply to thoracic and colorectal surgery. When we refine the technology in the treatment of ovarian cancer, we’ll have a responsibility to introduce it to other specialties, so that those patients can get benefit from it as well.”

“You label cancer cells but not normal cells, and you can see it in real time during surgery.”

— Sean Dowdy, M.D.
forefront / by the numbers

National ranking of Mayo Clinic Cancer Center campus in Minnesota in 2013-14 U.S. News & World Report rankings of top health care institutions.

Number of new DNA sequences associated with ER-negative breast cancer discovered by research team led by Fergus Couch, Ph.D., of Mayo Clinic Cancer Center as part of the Collaborative Oncological Gene-environment Study (COGS), an international research collaboration involving investigators from Europe, Asia, Australia and North America.

Number of patent filings for intellectual property developed by Mayo Clinic Cancer Center members over the past five years.

Number of patients who come to Mayo Clinic Cancer Center campuses in Arizona, Florida and Minnesota annually for cancer management.

Number of manuscripts from Mayo Clinic Cancer Center (MCCC) programs accepted by MCCC for publication in high-impact (impact factor greater than 10) basic, clinical and population science journals over the past five years.
Aubrey Thompson, Ph.D., mined the cells of colon cancer for years before shifting to elusive breast cancers. Now, he says, technological advances in genetics “have taken my breath away” and are dramatically improving the ability to navigate the many-faced crossword puzzle of cancer.

In Florida, Thompson is co-director with Edith A. Perez, M.D., of the Mayo Clinic Breast Cancer Translational Genomics Program, which uses genomics to explore a patient’s cancer and develop individualized treatments — not just for breast cancers but also pancreatic, lung, thyroid and renal cancers.

“We do a lot of deep-sequencing analyses of breast tumors to try to figure out how to treat certain kinds of patients who have tumors that are particularly difficult to treat,” Dr. Thompson explains. “My first love in life is gene structure and gene function, and how changes in these affect malignancy.”

Dr. Thompson credits, “very generous support” from the “26.2 with Donna Foundation,” a non-profit foundation in Northeast Florida that hosts the nation’s only annual marathon dedicated solely to raising funds to end breast cancer, for helping to launch the translational genomics program at Mayo.

That support, says Thompson, a former runner, has helped his team — clinicians, biologists, biostatisticians, bioinformatics specialists, computational biologists, database managers and physicians — isolate previously unseen gene mutations in breast cancer.

Dr. Thompson, a native of Texas, is a laboratory researcher, but he works closely with clinicians. Dr. Perez oversees patient care, and Yan Asmann, M.D. heads computational efforts. Patients always come first.

“My job has been to assemble a bunch of smart people and see to it that they have the resources they need, and then stand out of their way,” Dr. Thompson says. “We all get up early in the day, knowing that our patients need us. That applies more to the physicians than me, but there are things I can do that physicians can’t do to help patients in the long run. That’s the team concept. Each of us has our own expertise, and all of us work together to benefit the patient.”

“What keeps me going,” he says, “is this ability to look at a tumor and a patient, and try to understand the interactions involved. This is like the biggest puzzle you could ever imagine. If we can fit the pieces together, we can make a picture that we understand, and from that picture we can benefit the patient. That’s what it’s all about.”
Barbara A. Pockaj, M.D.
Marshaling the knowledge of researchers and clinicians to tackle challenging cancers

Barbara Pockaj, M.D., of Mayo Clinic Arizona, is, by her own admission, a busy person. She is a cancer surgeon, a senior surgical consultant, a medical researcher and chair of the Section of Surgical Oncology. She also leads the Breast Cancer Interest Group (BIG), which includes researchers from Mayo Clinic, Arizona State University, and the Translational Genomics Research Institute. But her patients always come first.

“If you look at breast cancer in today’s world, we’ve made tremendous progress but there are still challenges,” she explains.

“While there are many options for treatments for some types of breast cancer, others including triple negative breast cancer (estrogen receptor negative, progesterone receptor negative and HER2 negative) and endocrine resistant estrogen positive breast cancer are clinically more challenging. These are the hardest to treat and the most aggressive, so this is where we need to make our biggest clinical impact.”

BIG is part of Mayo Clinic’s efforts to do just that. Clinicians and basic scientists work together on translational projects to develop individualized treatments. “Research takes a village,” Pockaj says. “Our [BIG] members have special abilities and insights. I’ve done research but with a very clinical focus. I think the Ph.D. researcher sometimes understands the details of science to a degree that I cannot, but that person sometimes doesn’t see how that science translates into the clinical picture. This helps the discussion, going back and forth, looking for what best helps our patients.”

Pockaj’s commitment recently was tested by the death of her best friend — of breast cancer. “It was ironic,” she recalls. “It makes you want to do more. It pushes you to say you still have a lot to learn. You can do everything and know everything, but sometimes you cannot beat the cancer. That’s the toughest part. Cancer is still smarter. We just have to get smarter than the cancer.”

As a daughter of working-class parents who came to the United States from Slovenia — from an area that is now Croatia — she embraces the challenges. Born and raised in Ohio, she wanted, like many children from immigrant families, to make a difference. She developed an early interest in medicine. Her first clinical rotation in medical school at Vanderbilt University, in surgery, became her passion.

Dr. Pockaj’s next major stop was at the NCI, part of the NIH, which she calls an amazing place. “People were so dedicated to advance the science of medicine, really selflessly.” Three years later, she joined Mayo Clinic in Arizona, where she has been for almost 18 years.

Despite her long hours on the job, Dr. Pockaj says, she still has “a need for balance with her home life, which includes a husband and child, and a network of good friends.”
Manish Kohli, M.D.

Individualizing therapy for advanced-stage prostate cancer

As a young boy in India, Manish Kohli, M.D., came face to face with cancer when his father, age 37, died of stomach cancer. He knew then, at age 9, he says, that he wanted to be a cancer doctor. That motivation would lead him to the Mayo Clinic Cancer Center in 2008.

His road began at Maulana Azad Medical College at the University of Delhi. With few opportunities in oncology in India, he moved to the United States, where he completed an internship in internal medicine at Cook County Hospital in Chicago, a fellowship at the University of Arkansas in Little Rock and a faculty appointment at the University of Rochester in New York before landing at Mayo Clinic in Rochester, Minn.

Today Dr. Kohli is part of the Prostate Cancer Medically Optimized Genome-Enhanced Therapy (PROMOTE) study, a Mayo Clinic initiative that is targeting a wicked opponent called castration-resistant prostate cancer — an advanced stage of prostate cancer that ranks second in cancer deaths among men in the United States.

Separately, Kohli also examines blood samples from patients with kidney and testicular cancers in pursuit of genetic markers that might guide treatment strategies to help patients with these tumors.

“At Mayo Clinic we take this very seriously for the sake of our patients,” Dr. Kohli explains. “Their care comes first and last, before and above our research. The whole circle of what we do revolves around them, with the research woven in a way that we can bring it back to the patient.”

The last three years, says Kohli, associate professor of oncology, have brought six new treatments for late-stage prostate cancer. But, as in all cancers, a treatment that works in one patient doesn’t always work in another, and some treatments that initially are effective fail or must be stopped because of toxicity.

“Not only do we try to develop new treatments, but what is more critical and important is that we try to find out which treatment will serve which individual patient the best, and that often is a tall order to figure out,” he says. “Individualized or precision treatment is the next big challenge and opportunity in the world of oncology. How to individualize a treatment so that the treatment’s benefits outweigh the risk is the basic drive.”

PROMOTE aims to do this, Kohli says, by sequencing the cancer DNA and RNA from tumor sites and then growing the patient’s tumor in animal models — he calls them “avatars” — for experimental treatment that can be brought back to the patient in the future.

A goal, Dr. Kohli says, is to find genetic signatures that will help fine tune individual treatments. “I tell my patients that this, first of all, is research. Like all research, we don’t know the answers yet to what we will find and bring back to them, but the potential is tremendous.”
Blood Cancer Just Another Bump in the Road

Don Wright was diagnosed with multiple myeloma at the age of 72 in 2004. Multiple myeloma is a blood cancer that affects cells in the bone marrow and can damage bones. There is no cure. However, new drugs and new treatments are helping some patients manage the disease. Don takes oral pomalidomide, which frees him to travel around the country without visiting a clinic for chemotherapy treatments.

Just prior to his diagnosis, Don had completed his first marathon, Grandma’s, in Duluth, Minn. With the help of his Mayo Clinic physician, Martha Lacy, M.D., Don has managed his disease and has completed 73 marathons since his diagnosis, including his most recent finish at the Med City Marathon in Rochester, Minn. last May.

That run marked his return to Minnesota after having completed his goal of running a marathon in all 50 states in December 2012. Don now has a new goal of running 100 marathons.

You can follow Don on Facebook: http://www.facebook.com/E-Race-Cancer, on Twitter @eRaceCancer, or you can read his blog posts at http://minnesotadon.blogspot.com or http://myelomahope.blogspot.com/.

Proton Beam Therapy Closer to Reality

Construction on the Mayo Clinic Proton Beam Therapy facilities in Minnesota and Arizona is moving closer to completion.

Construction on the Richard O. Jacobson Building, future home of the proton beam therapy program in Rochester, is progressing, with the completion of the exterior face of the building and rapid progress on the mechanical and electrical work on the interior of the building. In May, the building was the site of a traditional Japanese ceremony to mark the beginning of equipment installation. Guests at the event included major benefactors Lawrence and Marilyn Matteson; Takashi Hatchoji, chairman of Hitachi America; Fumio Nakamura, general manager of Hitachi’s particle therapy division; and Toshiyuki Akaho, corporate officer and general manager of Hitachi’s energy systems division. Hitachi is the equipment manufacturer for both facilities.

In March, Mayo Clinic Arizona marked the installation of the last steel beam for its proton beam therapy facility, which will reside on the lower level of the new Mayo Clinic Cancer Center Building, now under construction on Mayo’s Phoenix campus.

The milestone was celebrated with a small ceremony in which staff signed the beam before it was lifted into place.

The Rochester facility is on track to open its doors to patients in 2015, followed by the Arizona opening in 2016.
Mayo Clinic Arizona Cancer Center Consolidation

Mayo Clinic Cancer Center in Arizona is consolidating operations in a new state-of-the-art facility in Phoenix. The new building will offer patients the convenience of seeing all their cancer specialists at one location, without having to shuttle back and forth between the Scottsdale and Phoenix campuses.

A new proton beam therapy facility will occupy 165,000 square feet on the lower levels and concourse of the building, including four treatment rooms, patient exam rooms, offices and public areas. Three floors above the concourse will include 215,000 square feet of outpatient and support space, including Cancer Center specialties, hematology and oncology, an infusion area, exam rooms, the Breast Clinic, a pharmacy, cafeteria and patient education library. The building will also include an outpatient surgery area, a GI endoscopy suite and a Pain Clinic.

Planners worked closely with patients to design a next generation building that complements Mayo’s multi-disciplinary practice. Innovative features that will be part of the new building include:

- Patient-centered care pods built around multidisciplinary teams.
- Exam rooms that will allow for better interaction between physicians and patients.
- Easy access to the Mayo Clinic patient portal so patients can review personal information and educational materials.
- A digital kiosk that will allow patients who prefer to check themselves into appointments the opportunity to do so.

Mayo Clinic Cancer Center in Arizona is the largest in the Southwest with more than 200 staff members, including internationally known hematologists, medical and radiation oncologists, surgeons, diagnostic radiologists, pathologists, researchers and scientists.

The new building will begin to be occupied in 2015 and will be open to patients in 2016.

Mayo physicians Identify Reasons for the High Cost of Cancer Drugs

A virtual monopoly held by some drug manufacturers in part because of the way treatment protocols work, is among the reasons cancer drugs cost so much in the United States, according to a commentary by two Mayo Clinic Cancer Center physicians published earlier this year in Mayo Clinic Proceedings. The physician say value-based pricing is one potential solution.

“Cancer care is not representative of a free-market system, and the traditional checks and balances that make the free-market system work so efficiently in all other areas are absent when it comes to most cancer treatment,” wrote authors Mustaqeem Siddiqui, M.B.B.S., an oncologist, and Vincent Rajkumar, M.D., a hematologist.

For example, when it comes to over-the-counter painkillers or antibiotics, a physician or patient can choose from multiple drugs. But cancer drugs are administered to patients sequentially or in combination, creating a virtual monopoly for each drug. This is one of the principal reasons for the high cost of cancer therapy.

Other factors, explain the two physicians, include the expense of drug development; the high price that patients and insurers are willing to pay for even modest improvement in outcomes; and a lack of regulations, such as a cost-effectiveness analysis to account for economic and value-based considerations in the drug-approval and pricing process.

Mayo’s Nicotine Dependence Center Celebrates 25 Years

The typical cigarette contains the naturally addictive chemical, nicotine, and a variety of additives. Tobacco smoke contains a deadly mix of over 7,000 chemicals, including formaldehyde, arsenic, hydrogen cyanide, carbon monoxide and ammonia. Hundreds of these chemicals are toxic, and more than 70 have been directly linked to cancer.

As Mayo Clinic’s Nicotine Dependence Center (NDC) celebrates its 25th anniversary of helping people overcome nicotine addictions, success stories abound. The stories range from tobacco-using individuals who overcame addictions to the NDC hosting its 20th internationally acclaimed tobacco conference; from establishing the only residential treatment program in the United States, to taking a leading role in the legal fight against Big Tobacco in the 1990s.

Today, the NDC continues to be a pioneer in innovative treatment programs for tobacco users, backing its patient care and multilayered education programs with critical findings from an active and aggressive research team.

Still, when the staff of the NDC comes to work every day, they are keenly aware of the fact that tobacco use is the single most preventable cause of premature death in the United States.

“Tobacco use in the U.S. kills more people than if three fully loaded 747s crashed every day with no survivors,” explains Richard Hurt, M.D., NDC founder and executive director.”Why do we tolerate something that kills so many people?” Hurt says ending tobacco use is going to happen sometime and he wants to start talking about it now.
New DNA Sequences Shed More Light on Breast and Ovarian Cancer Risk

Researchers at Mayo Clinic Cancer Center have identified new DNA sequences associated with breast and ovarian cancer. The findings, published earlier this year in three studies in the journals Plos Genetics and Nature Genetics, will help reveal the underlying causes of these diseases and help researchers build better risk models to support prevention strategies.

In the first study, published in PLoS Genetics, researchers studied variations across the genomes of 14,351 BRCA1 mutation carriers and found two new DNA sequences associated with breast cancer risk and two new DNA sequences associated with ovarian cancer risk. One sequence associated with ovarian cancer is the first known BRCA1-specific risk sequence for the disease. The researchers were then able to use their results to estimate the risks of both cancers for each BRCA1 mutation carrier. These new results may soon be incorporated into clinical management of patients.

“Women with mutated copies of the BRCA1 or BRCA2 gene have markedly increased but highly variable risks of breast and ovarian cancer,” says Fergus Couch, Ph.D., a Mayo Clinic investigator who co-authored the study. “To put this into perspective, a woman with a BRCA1 mutation has about a 65 percent lifetime risk,” explains Couch. “Risk models will help her make decisions by indicating if her true risk is liable to be closer to 90 percent — in which case she may choose prophylactic surgery — or closer to 40 percent — in which case frequent monitoring may be most appropriate.”

The second study, published in Nature Genetics, focuses on women susceptible to estrogen receptor-negative (ER-negative) forms of breast cancer. Couch’s team discovered four new DNA sequences that were associated with ER-negative breast cancer but not ER-positive breast cancer. The discovery was based on integrated results from three genome-wide association studies of 6,514 ER-negative breast cancer patients and 41,555 healthy controls.

“Women have a worse prognosis if their tumors are ER-negative because these cells grow more rapidly,” explains Dr. Couch. “They also have fewer treatment options.” He says the new DNA sequences will yield new information about the biology of the disease, which could eventually help researchers develop new treatments.

The third study, also published in Nature Genetics, reports the findings of the largest genome-wide association study of any cancer to date. Researchers found 41 new DNA sequences associated with breast cancer. Incorporating the DNA sequences into risk models is expected to considerably improve the ability to predict which women are at greater risk of developing breast cancer.
Mayo Researchers Discover Genomic Variant That Increases Risk of Brain Tumors

People who carry a guanine (G) instead of an adenine (A) at a specific spot in their genetic code have roughly a sixfold higher risk of developing certain types of brain tumors, a Mayo Clinic and University of California, San Francisco, study has found. The findings, published online in Nature Genetics, could help researchers identify people at risk of developing certain subtypes of gliomas, which account for about 20 percent of new brain cancers diagnosed annually in the United States. The findings also could lead to better surveillance, diagnosis and treatment.

Researchers still have to confirm whether the spot is the source of tumors, but if it’s not, “it is pretty close,” said senior author Robert Jenkins, M.D., Ph.D., a pathologist at the Mayo Clinic Cancer Center and the Ting Tsung and Wei Fong Chao Professor of Individualized Medicine Research at Mayo Clinic. “Based on our findings, we are already starting to think about clinical tests that can tell patients with abnormal brain scans what kind of tumor they have, just by testing their blood.”

“Being able to tell people that the mass in their brain is this type of tumor is actually good news, because it has a much better prognosis than other brain tumors,” Jenkins explained. “So what is it that predisposes people to develop less aggressive, but still lethal, gliomas? That makes understanding the function of this variant even more important.”

New Multiple Myeloma Treatment Guidelines Personalize Therapy

Researchers at the Mayo Clinic Cancer Center have developed new guidelines to treat recently diagnosed multiple myeloma patients who are not participating in clinical trials.

The guidelines give physicians practical, easy-to-follow recommendations for providing initial therapy, stem cell transplant and maintenance therapy. The guidelines were published in the April issue of Mayo Clinic Proceedings and represent a consensus opinion of hematologists at Mayo Clinic Cancer Center sites in Arizona, Florida and Minnesota.

“Multiple myeloma is an incurable blood cancer that affects more than 20,000 people in the United States each year,” explained Joseph Mikhael, M.D., a hematologist at Mayo Clinic Cancer Center in Arizona and lead author of the guidelines article. “Over the past decade we have made great progress in understanding the disease, developing drug therapies and increasing overall survival. However, as a medical community we haven’t done as good a job at optimizing therapy based on a patient’s individual risk factors.”

The new guidelines help patients with low-risk disease avoid the harsh side effects of therapy and reserve more intense therapy for patients with aggressive disease.

Researchers Identify Gene Variations That May Guide Preventive Therapy for Breast Cancer

A Mayo Clinic-led team has discovered new genetic variations that may help predict breast cancer risk in women who receive preventive therapy with the drugs tamoxifen and raloxifene. A study highlighting the findings was published in the June issue of the journal Cancer Discovery.

“Our findings are important because we identified genetic factors that could eventually be used to select women who should be offered the drugs for prevention,” said James Ingle, M.D., an oncologist at Mayo Clinic and the Betty J. Foust, M.D., and Parents’ Professor. Dr. Ingle and collaborators at the National Surgical Adjuvant Breast and Bowel Project (NSABP) and the RIKEN Center for Genomic Medicine conducted a genome-wide association study involving 592 patients who developed breast cancer while receiving preventive therapy and 1,171 matched controls.

The researchers analyzed participants’ DNA to identify variations in their genetic makeup and identified two genetic variations, or single nucleotide polymorphisms (SNPs), that were associated with breast cancer risk in or near the genes ZNF423 and CTSO. They discovered that women with favorable variations in these genes were more likely to respond to preventive therapy with the drugs, while women with unfavorable variations may not. In addition, women with unfavorable variations had a fivefold increased risk of developing breast cancer.

“This is a major step toward truly individualized prevention of breast cancer,” says Dr. Ingle. “Our findings provide clear direction as to which women are likely and which women with unfavorable variations may not. In addition, women with unfavorable variations had a fivefold increased risk of developing breast cancer.

“This is a major step toward truly individualized prevention of breast cancer,” says Dr. Ingle. “Our findings provide clear direction as to which women are likely and which are unlikely to benefit from tamoxifen or raloxifene.” Ingle explains that the findings provide the basis for a reinvigoration of research efforts in breast cancer prevention.
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**CANCER RESEARCH PROGRAMS**

**Cancer Prevention and Control**
Scott Leischow, Ph.D. Program Co-Leader
Charles Loprinzi, M.D. Program Co-Leader

**Cell Biology**
Panagiota Anastasiadis, Ph.D. Program Co-Leader
Jan van Deursen, Ph.D. Program Co-Leader

**Developmental Therapeutics**
Scott Kaufmann, M.D., Ph.D. Program Co-Leader
Zhenkun Lou, Ph.D. Program Co-Leader

**Gastrointestinal Cancer**
Kenneth Wang, M.D. Program Co-Leader
Mark McNiven, Ph.D. Program Co-Leader

**Genetic Epidemiology and Risk Assessment**
James Cerhan, M.D., Ph.D. Program Co-Leader
Alexander Parker, Ph.D. Program Co-Leader

**Gene and Virus Therapy**
Evanthia Galanis, M.D. Program Co-Leader

**Hematologic Malignancies**
Leif Bergsagel, M.D. Program Co-Leader
Thomas Witzig, M.D. Program Co-Leader

**Immunology and Immunotherapy**
Richard Vile, M.D. Program Co-Leader
Larry Pease, Ph.D. Program Co-Leader

**Neuro-Oncology**
Joseph Loftus, Ph.D. Program Co-Leader
Brian O’Neill, M.D. Program Co-Leader

**Women’s Cancer**
Sean Dowdy, M.D. Program Co-Leader
James Ingle, M.D. Program Co-Leader

**SPECIALIZED PROGRAMS OF RESEARCH EXCELLENCE (SPOREs)**

**Brain Tumor SPORE**
Brian Patrick O’Neill, M.D. Principal Investigator
Robert Jenkins, M.D., Ph.D. Co-Principal Investigator

**Breast Cancer SPORE**
James Ingle, M.D. Principal Investigator

**Lymphoma SPORE (Shared with the University of Iowa)**
Thomas Witzig, M.D. Co-Principal Investigator

**Ovarian Cancer SPORE**
Lynn Hartmann, M.D. Principal Investigator
Scott Kauffmann, M.D., Ph.D. Co-Principal Investigator

**Pancreatic Cancer SPORE**
Gloria Petersen, Ph.D. Principal Investigator

**AFFILIATIONS AND COLLABORATIONS**

*Academic and Community Cancer Researchers United
Alliance for Clinical Trials in Oncology
American Cancer Society
American College of Surgeons Oncology Group
Biosign Institute - Arizona State University
Cancer and Leukemia Group B
*Cancer Prevention Network
Children’s Oncology Group
Coalition of National Cancer Cooperative Groups
Eastern Cooperative Oncology Group
GLOIogene
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Indian Health Service
Minnesota Partnership for Biotechnology and Medical Genomics
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Ontario Institute for Cancer Research
Pancreatic Cancer Genetic Epidemiology
Pharmacogenetics Research Network
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*Phase II Consortium
Radiation Therapy Oncology Group
Translational Genomics Research Institute (TGen)
*Based at Mayo Clinic

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forefront/ parting shot

STAY OUT OF THE SUN RUN The eighth-annual Stay Out of the Sun Run was held on Friday, May 17 in Rochester, Minn. Proceeds from the run support melanoma research and patient education at Mayo Clinic Cancer Center. This year’s run was followed by the third biennial Melanoma Patient Education Symposium at Mayo Clinic Cancer Center on May 18, 2013.