



2011 ANNUAL REPORT



Transforming
Cancer Care through
Science and Technology

UPMC CancerCenter

Partner with University of Pittsburgh Cancer Institute

On the cover, top: UPMC CancerCenter and the University of Pittsburgh Cancer Institute (UPCI) are partners in the continuum of translational cancer care that moves discovery about cancer from the lab to the clinic to the community. Representing the continuum of cancer care are, from left: drug discovery researcher Dr. D. Lansing Taylor; surgical oncologist Dr. David Bartlett; chemotherapy pharmacist Molly McAleer; and Pittsburgh barber Kevin "Bat" Andrews.

Bottom: Lung cancer cells cultured and imaged using a JOEL JEM-6335F SEM at 3000x magnification. Photo © 2012 University of Pittsburgh Center for Biologic Imaging. Used with permission.

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THREE CORNERSTONES OF CANCER RESEARCH AND CARE

For more than 25 years, UPMC CancerCenter and its partner, the University of Pittsburgh Cancer Institute, have been committed to a culture of excellence in all aspects of cancer care — in our research, equipment, facilities, and people. Our work is guided by three inextricably linked tenets that both define and direct the way we practice medicine every day:

Advancing good science

UPCI physicians and researchers are active in all phases of quality scientific endeavor, including basic, preclinical, translational, and clinical research. From studies that expand our understanding of the biological basis of cancer and its progression, to clinical application of that understanding through novel therapies to treat patients with cancer, good science is at the core of all that we do.

Investing in smart technology

The newest technology is not always the best technology. We invest in smart technology — the kind that helps us do our jobs better for the benefit of our patients. That technology comes in many forms: from our Clinical Trial Management Application (CTMA) that tracks every step of the clinical trials process from inception to closure, to our web-enabled clinical pathways that guide clinicians in identifying the best treatment protocols for each patient. From the diagnostic radiologic imaging equipment that helps us find cancers earlier and the advanced radiosurgery devices that enable us to treat the most difficult cancers, to the electronic health record systems that assist us in tracking patient information to help ensure patient safety. Smart technology is technology used wisely to benefit our patients.

Providing “patient-first” care

We put our patients at the center of everything we do. That is why we pursue the best and brightest researchers and practitioners, who provide complete cancer care through in-depth knowledge, skills, and experience in areas such as clinical care, social work, nutrition, behavioral medicine, pain management, palliative care, finance, and many others. The expertise of these individuals is exceeded only by the high level of compassion and dedication to our patients’ needs that they provide on a daily basis.

SHAPING OUR EVERYDAY APPROACH

These guiding principles combine to shape our approach to studying, diagnosing, and treating cancer at UPMC CancerCenter. Each is critical to our mission to prevent, treat, and heal cancer. The stories that follow demonstrate how these three principles help shape our everyday activities as we seek to discover new information about cancer to enable our physicians to provide the best care and, ultimately, the best outcomes for our patients.

Applying good science, investing in smart technology, and putting patients first are the motivational philosophies behind everything we do.

By now you may have noticed a subtle but important change in our name on the cover of this 2011 Annual Report. The move to the UPMC CancerCenter name is meaningful because it represents the totality of UPMC oncology services — from our comprehensive medical, radiation, and surgical services delivered through our network of more than 35 locations, to our specialty women’s, pediatric, and multidisciplinary programs. It also embraces the work of our research partner, the University of Pittsburgh Cancer Institute (UPCI), which is distinguished as western Pennsylvania’s only National Cancer Institute (NCI)-designated Comprehensive Cancer Center.

What’s the relevance of this new logo? Well, it starts with our approach to cancer research and care. As the title of this report states, applying good science, investing in smart technology, and putting patients first are critical to everything we do.

Yet, as part of one of the nation’s largest health systems, UPMC CancerCenter provides many entry points for patients seeking cancer care.

While convenient access through community locations is a cornerstone of our cancer network, this accessibility has led to patients interacting with a variety of different and sometimes potentially confusing entities within our organization as they proceed through our continuum of cancer care. The UPMC CancerCenter name represents the opportunity to create a single entity that offers high-quality cancer care and research programs all with an exacting focus: Providing the best possible outcomes for our patients and their families.

GOOD SCIENCE

While we are excited to move forward with the UPMC CancerCenter brand, we also want to recognize all that we have accomplished over the past year. Our focus on science has led to many remarkable accomplishments, as our scientists have been active across the research spectrum. Among our many highlights last year:

- Recognition of the role of the HMGB1 protein in mitochondrial integrity.
- Use of a natural product to prevent prostate cancer in laboratory models.
- The first report of genome sequencing in head and neck cancers.
- The completion of a trial testing a new type of vaccine against brain tumors.

Great researchers need resources to support their work, and we continued to receive significant National Institutes of Health (NIH) funding and non-NIH funding, as well. The Division of Surgical Oncology received ongoing NIH P01 and NIH R01 grants, as well as a new R01 grant, titled “Improving Vaccines for Peritoneal Tumors: Enhanced Distribution & Immune Evasion.” In addition, its NIH T32 training grant, titled “Postdoctoral Research Training in Biotherapy of Cancer,” was renewed for an additional five years.

We also are proud that our Specialized Program of Research Excellence (SPORE) in Lung Cancer recently was renewed by the NCI for a third five-year term. This highly competitive grant underwrites some of our research to improve lung cancer detection, enhance lung cancer treatment, and identify tobacco-exposed individuals at



highest risk for lung cancer. Led by **Dr. Jill Siegfried, Dr. William Bigbee, and Dr. Joel Weissfeld**, this SPOR validates UPCI as a leader in lung cancer research.

SMART TECHNOLOGY

Embracing smart technology also provides many benefits for our patients. Among the enhancements to the arsenal of cancer treatment equipment available throughout our network last year were:

- One of the nation's first TrueBeam™ STx systems for precision radiation therapy at our Mary Hillman Jennings Radiation Oncology Center.
- New linear accelerators at our joint venture site on the campus of The Washington Hospital and at our cancer centers at UPMC St. Margaret and UPMC McKeesport.
- Additional services, such as Rapid Arc®, gating, and on-board imaging, at the Radiation Oncology Center at Jefferson Regional Medical Center, UPMC/Jameson Cancer Center, UPMC/HVHS Cancer Center at UPMC West, and UPMC Cancer Center at UPMC Passavant.
- A CT simulator at our Beaver cancer center.

Complementing these quality initiatives was our selection of a state-of-the-art, cancer-focused electronic health record (EHR) system that will, over the next year, link select UPMC CancerCenter community sites with Hillman Cancer Center to further our efforts to deliver care more safely and efficiently.

PATIENT CARE

Last year, we continued a major initiative toward quality of care by uniting our centers through a hospital-based practice model and ensuring optimal standards for oncology care across the network through our web-based Clinical Pathways program. In addition, we are in the final steps of certification through the Quality Oncology Practice Initiative (QOPI). UPMC CancerCenter is the largest academic-community partnership in the country to pursue this ambitious accreditation.

To make cancer care more accessible to the patients who need it, we're launching a new joint venture with

St. Clair Hospital, which includes the addition of a second linear accelerator, and opening our newest cancer center at UPMC East in July 2012.

We also announced several significant growth initiatives. Planning is in full swing for the Center for Innovative Science, which is a tripartite partnership between UPCI, the University of Pittsburgh School of Medicine, and UPMC. Tentatively slated to open in 2014, this renovated research building, adjacent to Hillman Cancer Center, will foster the intellectual and physical environment needed to operationalize personalized medical care with a special focus on cancer.

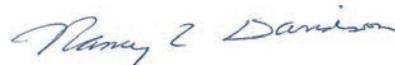
The state-of-the-art Mario Lemieux Center for Blood Cancers will house the clinical and patient services areas and research facilities for hematological malignancies in a dedicated space in Hillman Cancer Center. Set to open in December 2012, this center will be a model for leveraging technology to deliver the highest quality of care while creating the optimal patient experience.

OUR COMMITMENT

This letter demonstrates the vast breadth and scope of our oncology services. The remaining pages of this report provide even further evidence of the tremendous work being done by our researchers, physicians, caregivers, and staff. They are the true heart and soul of everything we do.

Their dedication is one reason we felt it was necessary to unite our services under a single name. As UPMC CancerCenter infers, "For one, we are many. For many, we are one."

Sincerely,



Nancy E. Davidson, MD

Director, University of Pittsburgh Cancer Institute and UPMC CancerCenter



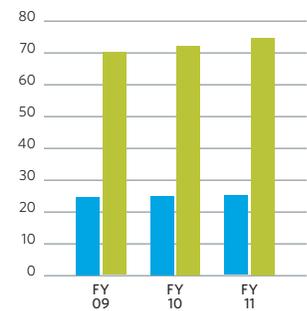
Stanley M. Marks, MD

Chairman, UPMC CancerCenter

UPMC CANCERCENTER PATIENT VISITS*

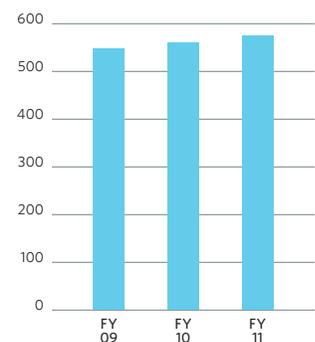
■ New Patients
■ Unique Patients Receiving Services/Treatment

In thousands



UPMC CANCERCENTER TOTAL NUMBER OF PATIENT VISITS*

In thousands



* Fiscal Year running July 1 through June 30. Total includes all patient visit types for medical oncology, radiation oncology, and surgical oncology

Lung cancer specialist Dr. Mark A. Socinski



Transforming Cancer Care through Science and Technology

What does it take to build a world-class lung cancer center? Ask nationally recognized lung cancer specialist **Mark A. Socinski, MD**, and he will share with you a myriad of attributes, ranging from an internationally known thoracic surgical oncology program to a robust research program and strong leadership, all of which are available right here in western Pennsylvania. They are, in fact, some of the reasons Dr. Socinski chose to make Pittsburgh, UPMC CancerCenter, and the University of Pittsburgh Cancer Institute (UPCI) his new home in 2011.

INNOVATIVE APPROACHES TO LUNG CANCER MANAGEMENT

After 16 years at the University of North Carolina, Dr. Socinski joined the UPMC CancerCenter and UPCI team in September 2011. What would make someone leave an institution after being there so long?

“UPMC CancerCenter and UPCI are no secret to those of us in the oncology world,” says Dr. Socinski. “After many site visits and discussions with colleagues around the country, there were many reasons why UPMC CancerCenter and UPCI were a good fit for me and my research, but what really stood out was its strong leadership.”

Under Director **Nancy E. Davidson, MD**, UPCI and UPMC CancerCenter successfully completed their renewal of the National Cancer Institute (NCI) Core Grant in 2010, maintaining the center’s status as an NCI-designated Comprehensive Cancer Center.

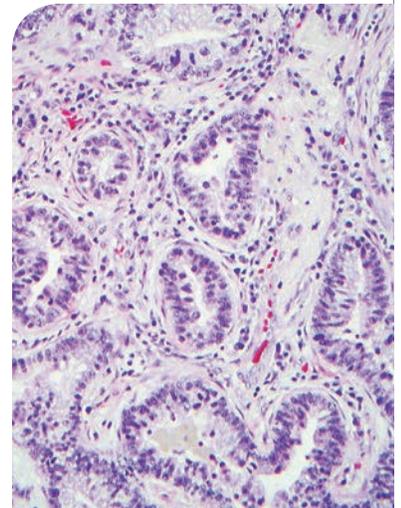
During her three-year tenure, Dr. Davidson has brought on board other talented physicians and researchers, such as Division of Hematology-Oncology Chief **Edward Chu, MD**, who joined the team in late 2010.

ON THE CUTTING EDGE

UPMC CancerCenter’s nationally recognized Thoracic Surgical Oncology Program is led by **James Luketich, MD**, and **Rodney Landreneau, MD**. The newly established Department of Cardiothoracic Surgery consists of 40 faculty members, almost half of whom are dedicated thoracic surgeons. One of the program’s many strengths is its collective expertise in the image-guided and minimally invasive surgical management of lung lesions, which has been shown to preserve lung function and allow for quicker recovery following surgery for many patients.

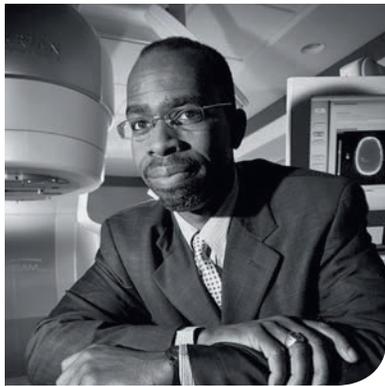
While surgical resection with a lobectomy (removal of a lobe of the lung), whether it be minimally invasive or the traditional open procedure, is the standard treatment in operable lung cancer and offers the best prognosis, lung cancer is still the most common cause of cancer-related death in the United States. With an aging population, many patients have additional health issues that may preclude them from undergoing surgery. Often, conventional external beam radiotherapy is offered as treatment when surgery is not an option, with reported five-year survival rates of only 10 percent to 30 percent, even in early-stage cancers.

Another mainstay of the surgical program is its tremendous strength in research, as UPMC thoracic surgical oncologists are continuously exploring new and innovative technologies for treating patients with lung cancer both inside and outside the operating room.



Above, top: Cardiothoracic surgeon Dr. James Luketich is head of the Department of Cardiothoracic Surgery, which has a particular strength in image-guided and minimally invasive surgical management of lung cancer.

Bottom: Adenocarcinoma is one of the most common non-small cell lung cancers.



Above: Radiation oncologist Dr. Dwight Heron is co-leading a multicenter trial of stereotactic radiosurgery for the treatment of inoperable non-small cell lung cancer.

Below: Cardiothoracic surgeon Dr. Arjun Pennathur led a study of lung cancer patients treated with the CyberKnife® system of stereotactic radiosurgery, which concluded that this technique may offer a reasonable alternative to surgery in high-risk patients.

To improve upon these less-than-satisfactory treatment options for high-risk patients who are not candidates for surgical lobectomy, Dr. Landreneau, Dr. Luketich, **Arjun Pennathur, MD**, and their colleagues are evaluating new and innovative technologies, including video-assisted thoracoscopy (VATS) and limited resection, computed tomography (CT)-guided radiofrequency ablation (RFA), and stereotactic radiosurgery (SRS).

VATS represents a minimally invasive surgical option in which only part of the lung lobe containing the tumor is removed (sublobar resection), preserving lung function for compromised patients unable to undergo complete lobectomy. UPMC's experience in minimally invasive VATS sublobar resection, also called segmentectomy, is one of the largest reported in the United States. Because sublobar-resected patients have a higher risk of tumor recurrence at the site of surgery than lobectomy patients, UPMC CancerCenter

lung surgeons have pioneered the use of intraoperative radiation brachytherapy, in which an implant emits radiation to the tumor internally. We are leading a multicenter, randomized trial sponsored by the American College of Surgeons Oncology Group (ACOSOG) to evaluate the efficacy of this approach.

When even a limited (sublobar) resection isn't feasible, patients may opt for an innovative image-guided therapy, such as RFA or SRS. RFA works by delivering thermal energy into the tumor through an image-guided needle electrode. This technique, performed with image guidance to improve precision, is beneficial because many patients have compromised lung function, making preservation of normal lung tissue all the more critical. Dr. Pennathur, Dr. Landreneau, Dr. Luketich, **Neil Christie, MD**, **William Gooding, PhD**, and colleagues evaluated a CT-guided RFA procedure in 100 consecutive lung cancer patients, representing one of the largest published studies of image-guided ablation for lung tumors in the United States. The research team found that this therapeutic technique is safe, feasible, and reasonably effective, resulting in estimated two-year overall survival of 49 percent in a high-risk group of patients. (*Pennathur et al., Ann Thorac Surg 2009, 88:1601-8*).

Another breakthrough is the partnership with colleagues in radiation oncology to utilize SRS, an innovative form of radiation therapy that focuses high-powered x-rays on a small, targeted area, such as an inoperable tumor. Using a three-dimensional coordinate imaging system, the tumor is precisely localized and subjected to multiple convergent radiation beams. The precision granted by SRS enables the delivery of a much higher dose of radiation than traditional methods, maximizing the effect on the tumor while limiting the toxicity to normal lung tissue. UPMC CancerCenter surgeons published a study of SRS (using the CyberKnife®



system) in 100 consecutive lung cancer patients, and concluded that this technique also may offer a reasonable alternative to surgery in high-risk patients. (*Pennathur et al., Ann Thorac Surg 2009, 88:1594-600*).

Currently, Dr. Luketich and **Dwight E. Heron, MD, FACRO**, director of radiation oncology services for UPMC CancerCenter, are leading a large, national, multicenter prospective trial of SRS for the treatment of patients with high-risk, medically inoperable, early-stage non-small cell lung cancer. To date, the trial has enrolled more than 100 patients. The preliminary results of this study indicate that both local disease control and disease-specific survival are encouraging, with an estimated 90 percent two-year local, progression-free survival. The trial continues to accrue patients to enable a full evaluation of the potential of SRS in this setting.

UPCI SPORE IN LUNG CANCER

In addition to strong leadership and expertise in thoracic surgical oncology, the basic science

research program, led by **Jill Siegfried, PhD**, recently renewed its Specialized Program of Research Excellence (SPORE) in Lung Cancer from the NCI for five more years of funding. Originally awarded in 2001, this multiproject, multi-investigator grant supports the innovative research of UPCI investigators whose overall goals are to improve lung cancer detection and treatment, and identify individuals at highest risk for developing lung cancer. The long-term goal of the UPCI SPORE in Lung Cancer is to conduct clinical trials based on research results from its translational research projects to improve the outcomes of patients diagnosed with lung cancer, and define new biologic tools useful in identifying asymptomatic lung cancer. One of the key aspects of the Lung Cancer SPORE is the collaborative effort between basic scientists and clinicians — thoracic surgeons, oncologists, and pulmonologists — which allows for translation of the basic research efforts into clinical benefits for patients.

I got to know the whole team so well that when my visits started to slow down, I started to miss everyone. That personal touch has been really important to me throughout my cancer journey.

—SANDRA LISOTTO,
PATIENT

PATIENT PROFILE

Sandra Lisotto

LUNG CANCER DIAGNOSIS A SHOCK FOR ASYMPTOMATIC PATIENT

In August 2010, during an appointment with her chiropractor, an x-ray showed nodules at the bottom of her lungs. Concerned about the imaging results, Sandra's chiropractor referred her to a pulmonologist at UPMC Shadyside for further testing.

The nodules were diagnosed as Stage IV, non-small cell lung cancer. At the time, Sandra, a nonsmoker, wasn't experiencing any symptoms, and, in fact, was rarely ever sick. With no warning, she was suddenly dealing with an advanced lung cancer diagnosis. She recalls feeling overwhelmed, but at the recommendations of both her pulmonologist and family doctor, she scheduled an appointment with Dr. Mark

Georgiadis at UPMC CancerCenter at UPMC St. Margaret.

"I was so thankful that they recommended the UPMC St. Margaret location," says Sandra. "Traveling to Hillman every three weeks, sometimes more often, would have been more stressful for me."

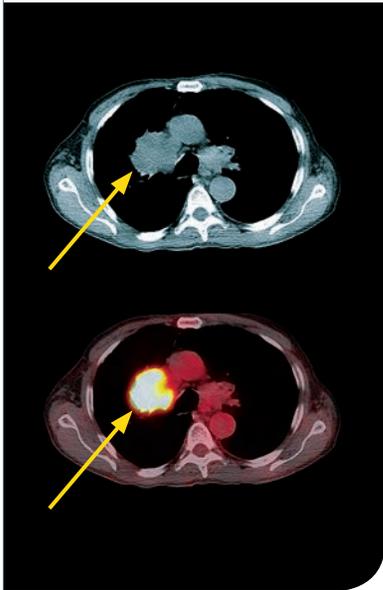
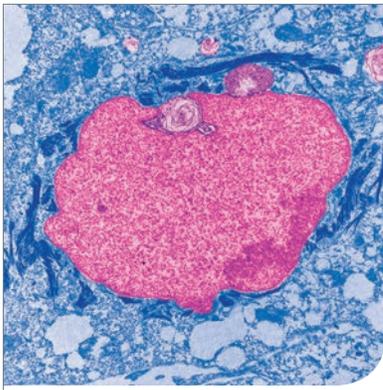
Sandra underwent chemotherapy, which reduced her disease by 43 percent. Because she responded to the chemotherapy so well, Dr. Georgiadis recommended that she participate in a clinical trial evaluating the use of hormones in postmenopausal women with non-small cell lung cancer who have never smoked, and who have had good results from chemotherapy. This

trial is based on the science that has resulted from UPCI's SPORE in Lung Cancer, which is funded by the V Foundation.

Although she was hesitant at first about participating because of potential side effects, Sandra decided to enroll in the clinical trial.

"Dr. Georgiadis talked with me about my concerns and assured me that he wouldn't have recommended a treatment that I would be extremely uncomfortable doing," recalls Sandra.

Although Sandra ultimately had to stop the clinical trial treatment because a CT scan showed growth, she says her experience with the clinical trial, Dr. Georgiadis, and the cancer care team at UPMC St. Margaret has been wonderful.



Above, top: Lung cancer cells cultured and imaged using a JOEL JEM-1101 TEM at 13200x magnification by the University of Pittsburgh Center for Biologic Imaging. Photo used with permission. © 2012

Above, bottom: CT scan, above, and PET scan with arrows showing right upper lobe lung mass invading the mediastinum, the area between the lungs that contains the heart, trachea, and esophagus.

FINDING A SCREENING TOOL

CT screening for lung cancer has been under study for more than a decade. With recent reports from the NCI-sponsored National Lung Screening Trial (NLST) demonstrating a significant reduction in lung cancer mortality associated with CT screening, this detection method may become widespread, resulting in more frequent detection of lung nodules requiring medical follow-up.

Joel Weissfeld, MD, MPH; David O. Wilson, MD; Steven Shapiro, MD; Carl Fuhrman, MD; Dr. Siegfried; and their colleagues have been studying tools to predict which individuals with positive CT scans are at high risk for developing lung cancer — a measure critical to the management of these patients' care. Examining patients through the Pittsburgh Lung Screening Study (PLuSS), the research team determined that tumor doubling time (DT) is a useful measure that could aid in risk stratification and follow-up management. Specifically, a recently published study by Dr. Weissfeld and colleagues determined that volumetric analysis of CT-detected lung cancers is particularly useful in distinguishing adenocarcinomas/bronchioloalveolar carcinomas (AC/BAC), typically found in the slowest-growing subset. Conversely, the squamous cell cancer subtype was found most often in the fastest tumor doubling time group. (*Wilson et al., Am J Resp Crit Care Med 2011, Oct. 13*).

A NETWORK OF CARE

One of the most noteworthy aspects of the UPMC CancerCenter network is its size and ability to offer state-of-the-art care across the entire network, be it at Hillman Cancer Center or one of its convenient, community-based locations.

"UPMC CancerCenter's large network provides the opportunity to reach a large number of lung cancer patients without sacrificing quality of care," says Dr. Socinski.

A majority of cancer care takes place in community settings. UPMC CancerCenter is able to ensure that each patient receives the same quality of care regardless of treatment location through an innovative series of strategies called Clinical Pathways.

Developed by UPMC CancerCenter through its for-profit affiliate, Via Oncology, to define the recommended treatments for the most common types of cancers, Clinical Pathways are evidence-based medical and radiation oncology protocols designed and reviewed by disease-specific committees made up of both academic and community oncologists.

Dr. Socinski and UPMC CancerCenter network oncologist **Mark Georgiadis, MD**, chair the Lung Cancer Committee, which reviews and updates the pathways for managing patients with various types and stages of lung cancer.



CARE CLOSE TO HOME

Although lung cancer treatments throughout our community are the same as they are at Hillman due to the Clinical Pathways program, there are some differences — and those differences often play large roles in how patients decide where to receive their care.

The biggest difference is geography. Community practices are scattered all across western Pennsylvania, affording patients the option of receiving their care closer to home or at Hillman, and allowing them to easily maintain communication with their familiar physicians.

UPMC CancerCenter's integrated network model is designed to facilitate state-of-the-art care at the community sites, while maintaining Hillman Cancer Center as the location with the most diverse, extensive expertise and technological advancements. One of the factors that makes this system work well is communication between the specialists at Hillman and the community oncologists, so that information about patients can easily flow back and forth.

"Patients themselves can move back and forth between their network site and Hillman, as well," says Dr. Georgiadis. If a patient has a stage of disease or a particular complication that requires technologically advanced care that can be offered only at Hillman, the patient can go to Hillman to be treated and then return to

his or her community oncologist. It all happens seamlessly, thanks to extensive interchanges between specialists at Hillman and community oncologists.

The integrated network model affords patients the ability to participate in clinical trials evaluating the latest cancer treatments without having to travel to Pittsburgh. UPCI and UPMC CancerCenter have a rich array of clinical trials and investigational treatments available, many of which also are available at the network sites, where dedicated research nurses and staff help to support interested and eligible patients who choose to participate in a trial.

According to Dr. Georgiadis, location choice can be especially important for patients diagnosed with lung cancer. Many patients with lung cancer already have advanced disease at the time of their diagnosis. Patients with advanced lung cancer often have significant symptoms from their disease, which makes traveling back and forth from a treatment facility far from home both uncomfortable and difficult.

"The ability for patients with advanced lung cancer to participate in clinical trials at their community oncology site is paramount," says Dr. Georgiadis. "It is also one of the strongest elements of our network of community oncology centers: The ability to offer this type of advanced care close to home helps decrease the discomfort and anxiety that comes along with a cancer diagnosis."



Dr. Mark Georgiadis

Pathways help to ensure that all patients receive the same standard of care, regardless of whether they are treated at Hillman or at one of our community locations.

—DR. MARK GEORGIADIS,
MEDICAL ONCOLOGIST

RAISING FUNDS AND AWARENESS

In 2005, the University of Pittsburgh Greek System made a pledge of \$500,000 to support the Lung Cancer Program at UPCI. Since then, the fraternities and sororities at Pitt have worked closely together to raise money and awareness through events held on campus throughout the year, such as Greek Sing and Pittsburgh Dance Marathon. In 2011, they reached their goal and are helping to provide support for a number of UPCI lung cancer research initiatives: the Pittsburgh Lung Screening Study (PLuSS), which is trying to improve the use of CT screening for early detection of lung cancer; a clinical trial using anti-estrogens to treat women who have estrogen receptor-positive lung cancer; and seed money for young investigators who are starting their careers in lung cancer research.



From the moment of diagnosis, through the course of treatment, and into survivorship, medical oncologists serve as the patient's link to the medical treatments and services offered by UPMC CancerCenter.

MEDICAL ONCOLOGY

Over more than 70 medical oncologists across 18 medical oncology locations and 10 combined medical oncology and radiation oncology offices offer the full spectrum of treatment modalities, including conventional chemotherapy, targeted therapies, stem-cell transplants, hormone therapy, biological therapy, and regional perfusion.

But one of the most significant benefits of UPMC CancerCenter's link with the University of Pittsburgh Cancer Institute (UPCI)—western Pennsylvania's only National Cancer Institute (NCI)-designated Comprehensive Cancer Center—is our ability to offer access to clinical trials. Clinical trials are research studies used to develop the most effective new drugs and

treatment models for cancer care, and they are vital to furthering our ability to understand, diagnose, treat, and someday eliminate cancer.

Clinical trials enable doctors to offer patients cutting-edge treatment options months or years before they become available as standards of care. Most clinical trials include the standard of care but add to that another type of medication or radiation therapy that shows promise to improve outcome. Each year, more than 4,500 patients enroll in the roughly 300 active clinical trials we offer. UPMC CancerCenter and University of Pittsburgh Cancer Institute (UPCI) offer clinical trials for many different types of cancer, the majority of which are Phase I, Phase II, and Phase III trials.

PARTICIPATING IN A CLINICAL TRIAL

At UPMC CancerCenter, physicians work closely with research coordinators (RCs), who are not only the links connecting patients to the right clinical trials but work as partners with patients to advance care through clinical trials. At Hillman Cancer Center and Magee-Womens Hospital of UPMC, RCs specialize in certain types of cancers or treatments to which he or she is assigned, and typically enroll and manage patients on clinical trials that are for those specific cancers or treatments.

For example, **Brittini Prosdocimo, RN, BSN, RC**, is a nurse at Hillman specializing in head and neck cancers. She is called upon by the treating physician to discuss clinical trials with patients who are identified at the weekly head and neck multidisciplinary conference (MDC), a meeting of many different specialists who consult together on each patient prior to their visit at the head and neck clinic.

“As our physicians present their cases at our weekly MDC meetings, the team considers all the different treatment options and clinical trials available to that particular patient,” says Brittini. “The doctor then meets with the patient during the visit to present the options the team has developed, along with any clinical trials the patient might be eligible for. If the patient is interested in a trial, the doctor asks me in to explain the study in more detail, and I work with the physician to get the patient’s informed consent and begin the screening process.”

Because of the large number of clinical trials offered at Hillman and Magee, there are more than 30 RCs available to match eligible patients with clinical trials that are open to enrollment. Specialized RCs are available for brain, breast, esophageal, lung, gastrointestinal, and genitourinary cancers, as well as for leukemia, lymphoma, multiple myeloma, sarcoma, melanoma, biobehavior, and bone marrow transplant.

UNDERSTANDING CLINICAL TRIALS

Clinical trials are conducted in phases. Trials at each phase have different purposes and help scientists answer different questions. Each phase builds on research from a previous phase.

THE FOUR PHASES OF CLINICAL TRIALS ARE:

- **Phase I trials** enable researchers to determine the safe dose of a new drug or agent and learn about its side effects.
- **Phase II trials** test the effectiveness of the new drug or agent in stopping or controlling the growth of tumor cells in a certain type of cancer. These studies typically involve 100 to 300 people.
- **Phase III trials** attempt to identify the more effective option between the standard treatment and the experimental treatment. To gather information as quickly as possible, Phase III trials usually involve between 1,000 and 3,000 patients, and often are multicenter studies, meaning that they are performed within the same window of time in cancer research centers across the country.

In many Phase III studies, patients are assigned randomly to receive either the experimental or the standard treatment. From what is known at the time, either of the treatments chosen could be better or of equal help to the patient. Random assignment helps make certain study results are not biased. These studies can also be double-blind studies, meaning neither the doctor nor the patient knows which treatment the patient is getting. Placebos also may be used in Phase III studies — but they are never used instead of a standard treatment. Rather, they may be used instead of the additional new treatment along with the standard treatment. Patients do not know if they have received the placebo while they are on the study, but may find out afterward. Randomization, blinding, and using placebos are standard methods of ensuring that the data collected are objective and unbiased.

- **Phase IV trials** are performed when more information is needed about a drug that has been approved for use. These studies provide information about a drug’s risks and benefits, as well as the best way to use it.

OTHER TYPES OF CLINICAL TRIALS INCLUDE:

- **Biospecimen trials**, which are developed to utilize biospecimens (blood and tissue) for research.
- **Registry trials**, which create a voluntary database of people who are willing to consider future participation in research studies.



Harry Strauser is the research coordinator at UPMC CancerCenter, Uniontown.

At the community sites, however, RCs are generalists and enroll patients on clinical trials for a variety of cancer types. “When I have a new patient, I look at their diagnosis and all of their lab work to complete a clinical trial screening worksheet that helps to evaluate their potential eligibility for the trial,” says **Tammy Enders, RN, BSN, OCN, RC**, a nurse at UPMC Passavant. “I also outline what the study will entail and, once I determine if a study is available, I share that information with the treating physician to see if the study and the patient complement one another.”

Once reviewed and approved, the treating physician presents the study to the patient as a treatment option. If interested, the patient meets with Tammy to discuss the trial, and start the informed consent and screening process.

In community locations further away from Hillman and Magee, the RCs may be the link between patients and clinical trials for an entire region. For example, UPMC CancerCenter, Uniontown, is the only site for clinical trials in southwestern Pennsylvania. **Harry Strauser, RN, BSN, OCN, RC**, is the RC at the Uniontown location.

“I pull a weekly computer printout of all open trials every Monday so that I can see what is available for our patients,” Harry says.

“I complete a form for every new patient and attach it to the patient’s chart so the treating physician can see which trials look promising based on the patient’s type and stage of cancer. After the doctor discusses the trial with the patient, I meet with the patient to explain the trial and walk them through the entire process. Some of our patients are candidates for their second or even third line of trials.

“If there are no trials open for a patient in the community, I’ll look to see if any are open at Hillman or Magee that the patient might be eligible for. Patients trust their physicians — so if the doctor recommends that they go to Hillman in Pittsburgh for a trial, most of them will.” Harry says that he enrolls at least one to two patients on clinical trials each month, and he has enrolled 125 patients on trials since 2005, when he began working at UPMC CancerCenter, Uniontown.

PIONEERING NEW TREATMENTS — PHASE I CLINICAL TRIALS

Phase I clinical trials are the first round of studies in which a new drug or treatment method is tested on a select group of prequalified patients. These trials usually are the first studies of a new drug’s effect on people. Although the drug has been tested in laboratory and animal studies, the side effects in people cannot always be predicted.

Phase I trials usually begin with a very small group of patients — about 15 to 80 — who are given the first dose level of the drug or agent. The patients are followed very closely and, after that dose has been determined to be safe, the next dose level will be given to the next group of patients. Dose levels are increased incrementally until the safest dose can be found. The trial also will determine the highest dose of the drug that can be given safely to people (known as the maximum tolerated dose).

All patients participating in Phase I trials must meet strict eligibility criteria, which generally means either there is no standard-of-care therapy available for the disease, or that the patient’s disease has progressed despite the used of current standardized treatment methods.

Meet one patient on a Phase I clinical trial for breast cancer on page 17.

Our focus is to offer trials to every patient when possible, regardless of their type and stage of cancer, and clinical profile. In clinical research, we follow many regulations to protect patients who choose to go on a trial.

—HOLLY GOE, VICE PRESIDENT, CLINICAL RESEARCH ADMINISTRATION

MORE PERSONALIZED CARE

Clinical trials often have significant requirements for documenting patient responses to the treatment, so they usually involve more scans, testing, and follow-up visits than the standard of care. Although clinical trials can be more time consuming for patients, many actually like the additional attention that data collection necessitates. “Because RCs represent an extra person to track dosage, side effects, and quality of life issues so closely as part of the studies, many of our patients find us to be an added concierge for their treatment — an additional set of eyes to monitor their progress,” Tammy says. “Some of our patients are on active trials that last from six months to five years; when they’re coming in at regular intervals over a long period of time, they get to know us and we get to know them, and that adds to the personalization of their care.”

Once a patient is on a trial, the RCs work closely with treatment room nurses. While the RCs coordinate the clinical trial protocols, the treatment nurses execute the protocols. They are responsible for recording the patient’s vital signs and any lab work, such as blood draws, at specific time intervals as specified in the study orders. Following the study orders is important to the researchers to ensure that they are able to capture the right data that is needed for the study. These clinical nurses not only administer the chemotherapy, but they also care for the patient’s needs during infusion, which may take from an hour to several hours, depending on the type of chemotherapy being given.

The community locations are able to offer most of the clinical trials that are available at Hillman or Magee. While the majority of clinical trials offered at community sites are Phase III trials and occasionally Phase II trials, there are a few limitations on trials that are offered at community sites. Those limitations usually are imposed by the criteria of the study, according to **Holly Goe, RN, MSN**, vice president, Clinical Research Administration. If a particular trial is only offered at Hillman, RCs at community locations are able to refer the patient there for enrollment.

“Our focus is to offer trials to every patient when possible, regardless of their type and stage of cancer, and clinical profile,” Holly says. “In clinical research, we follow many regulations to protect patients who choose to go on a trial. The Institutional Review Board — an administrative body established to protect the rights and welfare of human participants involved in research studies — is responsible to ensure that privacy is protected, confidentiality of data is maintained, and to note if the proposed research end results are beneficial and worth the risks to the participant. Within the department, all staff members are trained in ‘good clinical practice’ and how to protect the rights and ensure the safety of every patient on trial. This intense level of scrutiny is provided for patients’ safety. Additionally, patients can choose to leave a trial at any point during the trial. While the staff makes every effort to inform patients of the requirements of every study, as the patient’s condition changes or if things change within the trial over time, patients may decide they no longer want to participate in the trial. Patients can always go off the trial at any time for any reason.”

Today’s standard treatments are based on yesterday’s clinical trials and tomorrow’s treatments rely on today’s clinical trials.

Erin Eiler, RN, treatment nurse at UPMC CancerCenter at UPMC Passavant, readies a patient for chemotherapy.





Dr. Edward Chu and collaborators are studying the therapeutic effects of PHY906, a traditional Chinese herbal medicine that has been used in East Asia for thousands of years, when combined with the chemotherapy drug irinotecan.

Molecular therapy may be called “targeted therapy” or “biologic therapy,” but by any terminology, it refers to drugs or other substances that block the specific pathways that enable tumors to grow and spread.

MOLECULAR THERAPY AND DRUG DISCOVERY

The University of Pittsburgh Cancer Institute (UPCI) has invested significant effort into the discovery and implementation of new molecular therapies for the treatment of cancer. This research is conducted through UPCI’s Molecular Therapy and Drug Discovery Program (MTDDP) and the University of Pittsburgh Drug Discovery Institute (UPDDI), under the leadership of **Edward Chu, MD**, and **D. Lansing Taylor, PhD**, respectively.

The overall goal of the MTDDP is to promote collaboration among the researchers performing basic, preclinical, and clinical research and cultivate innovative approaches to drug treatment of solid tumors and hematological (blood-related) malignancies. By aligning each of the disciplines with a common purpose and scientific objective, the program aims to enhance cancer treatment by fostering a highly interactive and vertically integrated drug discovery and development program in which information moves back and forth between basic and clinical scientists.

To achieve this, members of the MTDDP carry out innovative mechanistic studies on novel agents, new targets, and novel drug delivery systems with the goals of:

- **Identifying** new anticancer agents.
- **Understanding** the mechanism(s) of action of new and existing anticancer drugs.
- **Optimizing** schedules and doses of drugs that prevent the growth or spread of cancer.
- **Developing** and conducting investigator-initiated clinical trials.

ANTICANCER DRUGS IN DEVELOPMENT

The MTDDP has a portfolio of approximately 20 anticancer drugs in various stages of development. For example, PX-866 is a potent, irreversible inhibitor of phosphatidylinositol 3-kinases (PI3K) — a family of enzymes involved in cellular functions, such as cell growth — synthesized by MTDDP member **Peter Wipf, PhD**. PX-866 has undergone target validation and dose and schedule determination, and is currently undergoing Phase II clinical evaluation. Another drug developed at UPCI is undergoing clinical trials at UPCI and other cancer centers. The drug 6-epi-dictyostatin was discovered by the MTDDP, and has undergone target identification and dose and schedule optimization studies in mice. Yet another agent, ABT-888 (veliparib), is undergoing clinical trials at UPCI and other cancer centers as a single agent and in combination with other common chemotherapy drugs.

UPCI is the lead site on a number of National Cancer Institute (NCI)-sponsored clinical trials of ABT-888, a PARP inhibitor drug that works in part by blocking the repair of DNA damage by tumor cells following chemotherapy. The Phase I group also is conducting a clinical trial with ABT-888 given as a single agent in cancers with BRCA mutations, namely certain breast and ovarian cancers. These tumors are more sensitive to PARP inhibitors and they may work without chemotherapy in this patient population. This drug is being tested in many additional tumor types in combination with other chemotherapy drugs, such as paclitaxel, temozolomide, gemcitabine, and cisplatin or radiation in several NCI-supported Phase I clinical trials at UPCI.

Dennis Curran, PhD, Billy Day, PhD, Andreas Vogt, PhD, and colleagues are developing the natural product dictyostatin, which is a microtubule-stabilizing agent that potently inhibits the growth of human

cancer cells, including paclitaxel-resistant clones. Despite the promising activities of the dictyostatins in preclinical studies, their complex chemical structure presents a major obstacle for their development into novel antineoplastic therapies. A new and highly convergent synthesis method was applied to generate two derivatives 25, 26-dihydrodictyostatin and 6-epi-25, 26-dihydrodictyostatin. Each of these agents displayed comparably potent microtubule inhibitory activity that induced growth arrest of cancer cells. These two new dictyostatins are promising candidates for scale-up synthesis and further preclinical development (*Molecular Cancer Therapeutics* 10:994-1006, 2011).

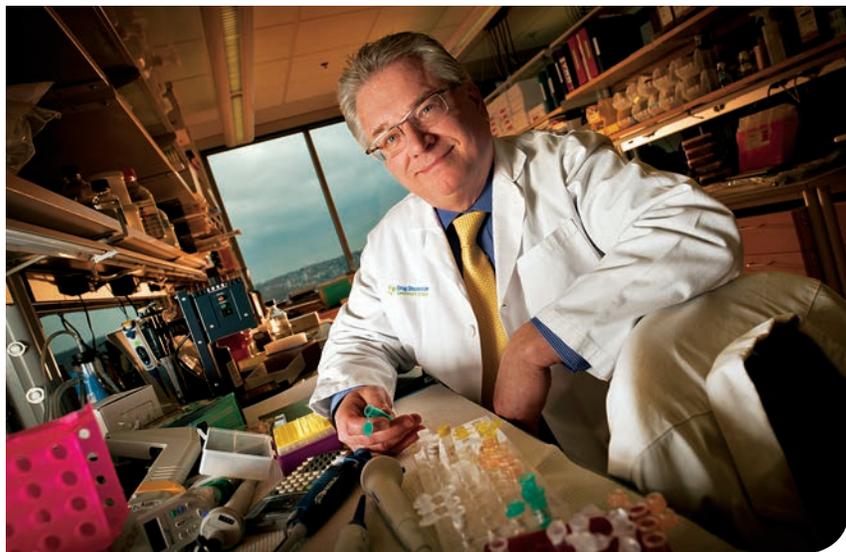
Donna Beer-Stolz, PhD, and colleagues recently identified nocodazole from a drug screening library provided by the Multiple Myeloma Research Foundation, as a potent agent to treat multiple myeloma, a cancer of the plasma cells in bone marrow. This work provides rationale for targeting the microtubular network as a new antimyeloma strategy (*Molecular Cancer Therapeutics*, 10(10): 1886-96, 2011).

The MTDDP investigators led by Dr. Chu also are testing PHY906, a traditional Chinese herbal medicine that has been used in East Asia for nearly 2,000 years, to treat diarrhea, nausea, and vomiting. Preclinical and early-stage clinical studies suggest that PHY906 can enhance the safety and quality of life in patients receiving the chemotherapy drug irinotecan, and maintain or improve its clinical activity. Dr. Chu and collaborators from the Yale Cancer Center were recently awarded an NCI grant to conduct a randomized, Phase II clinical trial in which the effects of PHY906 on the toxicity and efficacy of irinotecan will be studied in patients with metastatic colorectal cancer.

With my kind of cancer, there was nothing else for me to do. After knowing how advanced my cancer was when it came back, I was ready to try anything.

—CARRIE MARTIN, PATIENT





Dr. D. Lansing Taylor leads the University of Pittsburgh Drug Discovery Institute.

SEVERAL OTHER DRUG DISCOVERY RESEARCH PROJECTS CURRENTLY IN PROGRESS AT UPCI INCLUDE:

- **Discovery and optimization** of inhibitors of STAT3 activation for the treatment of squamous cell carcinoma of the head and neck.
- **Evaluation** of rationally-designed small molecules directed against the c-Myc oncoprotein.
- **AR-GFP** nuclear localization inhibitor screening for prostate cancer.

Preclinical testing for effectiveness, safety, and stability of a potential anticancer drug in living animal models is essential before its use in clinical trials. Supported by a highly competitive, recently renewed NCI contract, **Julie Eiseman, PhD**, and **Jan Beumer, PharmD, PhD**, have studied the pharmacokinetics (what the body does to a drug), metabolism, and activities of several compounds in preclinical development and translated these agents into early-phase clinical

trials. For example, the team has evaluated the epigenetic agent fluorodeoxycytidine and its downstream metabolites fluorodeoxyuridine, fluorouracil, fluorouridine, and tetrahydrouridine, both as single agents and in combinations in mice, nonhuman primates, and subsequently in early-phase clinical studies through the NCI Cancer Therapy Evaluation Program (CTEP). These studies have directly informed the investigation of an oral form of the two potent, cell-killing agents fluorodeoxycytidine and tetrahydrouridine, which would be more patient-friendly than intravenous administration. They also have extensively analyzed benzaldehyde dimethane sulfonate (BEN), an alkylating agent active against renal cell carcinoma and other malignancies, which is currently undergoing early-phase studies at UPCI through the NCI's CTEP. Finally, they are defining the efficacy, pharmacokinetics, and metabolism of a novel class of agents called indenoisoquinoline topoisomerase inhibitors.

The University of Pittsburgh Drug Discovery Institute, led by Dr. D. Lansing Taylor, collaborates with the UPCI MTDDP in anti-cancer drug discovery efforts. Dr. Taylor is an expert in fluorescence-based cell imaging technologies, and pioneered high-content screening (HCS) — a method now widely used in drug discovery.

In order to commercialize these technologies and make them available to the greater scientific community, Dr. Taylor created a number of life science companies prior to his arrival at the University of Pittsburgh (see sidebar below).

COMMERCIALIZING TECHNOLOGIES

Dr. D. Lansing Taylor's extensive commercial experience will help to create new opportunities at MTDDP. Life science companies created by Dr. Taylor include:

Biological Detection Systems, now part of *GE Life Sciences*, which commercialized a research imaging platform and the multicolor, cyanine, fluorescent dyes for labeling biological molecules. The first generation DNA sequencer manufactured by Amersham Biosciences was based on these dyes.

Cellomics, now part of *ThermoFisher*, which commercialized high-content screening (HCS).

Cellumen, now part of *Cyprotex*, which commercialized a platform to perform early safety testing using panels of biomarkers with organ-specific cells and bioinformatics software to predict toxicity.

Cernostics, a tissue systems biology company involved in cancer diagnostics.

MTDDP SUPPORT FACILITIES

UPCI's molecular therapies efforts are supported by two critical UPCI facilities: the Chemical Biology Facility (ChBF) and the Clinical Pharmacology Analytical Facility (CPAF).

The ChBF, led by Dr. Taylor, provides several services, including high-throughput screening (HTS) facilities for small- to large-scale screens; high-content screening (HCS) capability for primary and secondary screens; assay design, development, validation, and implementation; data management and informatics; lead characterization and optimization; access to small molecule libraries (more than 250,000 compounds); and the Ambion druggable genome siRNA library (16,560 siRNA).

The CPAF, led by Dr. Beumer, provides state-of-the-art preclinical and clinical pharmacology research facilities for UPCI. The importance of

pharmacokinetics (PK) and pharmacodynamics (PD) — or what a drug does to the body — has increased dramatically as anticancer drug discovery and development have shifted toward molecularly-targeted therapies.

The CPAF supports several UPCI disease-based programs in addition to the extensive UPCI preclinical and clinical pharmacology research activities of the MTDDP. Services include quantitation of drugs and metabolites; characterization of drug-drug interactions; PK and PD analyses of anticancer agents and/or novel combination regimens undergoing preclinical and/or clinical evaluation at UPCI; and provision of expert consultative services to UPCI investigators on the design of pharmacologic studies and drug assays, metabolism, and PK analyses.



Carrie Martin, a mother of three diagnosed with aggressive triple-negative breast cancer at age 37, enrolled on a Phase I clinical trial of ABT-888 (veliparib), a PARP inhibitor drug being evaluated at UPCI as a single agent in treating certain breast and ovarian cancers.

PATIENT PROFILE

Carrie Martin

YOUNG WOMAN ENROLLS ON CLINICAL TRIAL TO FIGHT AGGRESSIVE BREAST CANCER

Carrie Martin, of Whitehall, was a 37-year-old stay-at-home mom with three small children when she found a lump in her left breast in November 2008. Although she had not had a mammogram the previous year because she'd been pregnant, she had been getting regular mammograms for years because her mother had been diagnosed with breast cancer at age 43.

After a mammogram was read as normal, Carrie had an ultrasound and biopsy, which revealed that she not only had breast cancer, but that it had already spread to her lymph nodes. Her cancer type, triple-negative breast cancer, is known to be highly aggressive and more likely to recur and metastasize than other types of breast cancer.

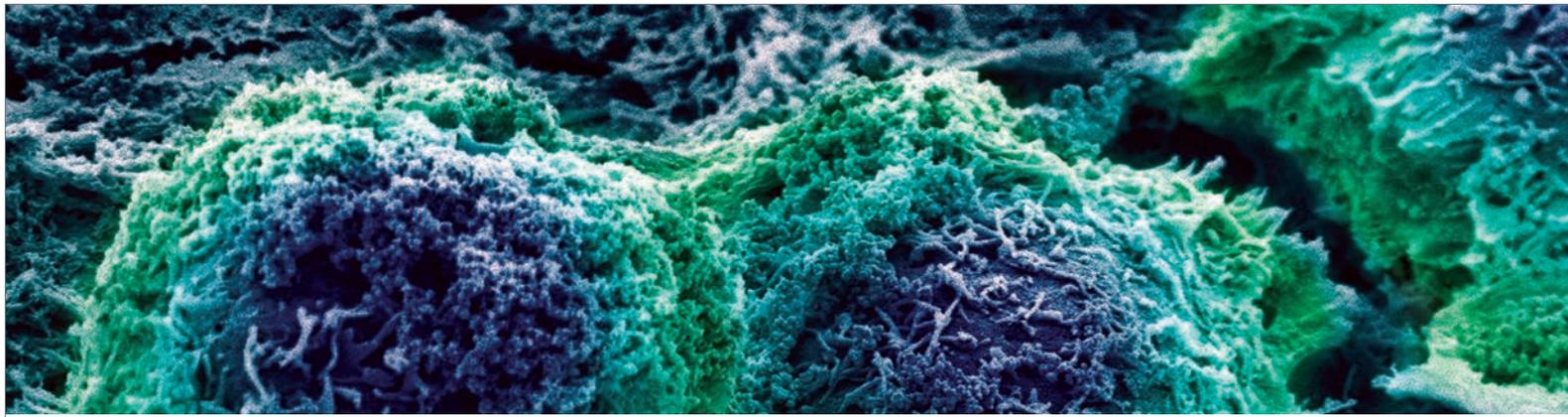
Although triple-negative breast cancer may respond well to chemotherapy, it can be difficult to treat because it does not respond well to other drugs that can be used to treat breast cancers, such as tamoxifen or Herceptin®.

Ronald Johnson, MD, her surgeon at Magee-Womens Hospital of UPMC, and **Shannon Puhalla, MD**, her breast oncologist, recommended neoadjuvant chemotherapy before surgery and she enrolled in a clinical trial of six months of chemotherapy with bevacizumab for early stage breast cancer. In July 2009, Carrie had a mastectomy of the left breast and axillary nodes, as well as a preventive mastectomy of the right breast. She learned after the surgery that she'd had a complete response to the chemotherapy and bevacizumab treatment, and after her surgical recovery the trial protocol included six more months of intravenous bevacizumab treatments.

In June 2010, at her three-month check-up, Carrie was feeling well but still had soreness in her chest above the surgical incision on her left side. A scan revealed that the cancer had come back — in both lungs and in her chest wall. At that time, Dr. Puhalla outlined her options — one of which was a Phase I clinical trial of the PARP inhibitor ABT-888, for which she was eligible.

Carrie elected to enroll on a clinical trial in which she was treated with chemotherapy drugs, carboplatin, and paclitaxel, in combination with ABT-888 for one year between July 2010 and June 2011. She had an excellent response to treatment with only minimal disease remaining. She then enrolled on another study giving ABT-888 as a single agent, which she currently continues to receive. Her side effects have been minimal and she will continue on the trial for about a year as long as there is no change in her condition.

"I've had people ask me if I feel like a guinea pig being on a Phase I trial, but I really don't," Carrie says. "With my kind of cancer, there was nothing else for me to do. After knowing how advanced my cancer was when it came back, I was ready to try anything. Dr. Puhalla is so knowledgeable — I trust her so much. I received excellent care from her and the staffs at the Clinical and Translational Research Center at Hillman Cancer Center and Magee-Womens Hospital."



Lung cancer cells used with permission from the University of Pittsburgh Center for Biologic Imaging. © 2012

Developing new drugs and techniques for treating cancer is especially important for people who have been diagnosed with cancer or will be diagnosed in the near future — but what if there were ways to prevent people from getting cancer in the first place?

UNDERSTANDING AND PREVENTING CANCER

The University of Pittsburgh Cancer Institute (UPCI) Cancer Epidemiology, Prevention, and Control Program (CEPCP) is trying to do just that. Its goals are to reduce the risk for, incidence of, and deaths from cancer, and to enhance the quality of life for cancer survivors. The CEPCP conducts epidemiologic, behavioral, social, genetic, and interventional research on the causes, prevention, and control of cancer.

The program is led by **Jian-Min Yuan, MD, PhD**, professor of epidemiology, and associate director for Cancer Control and Population Sciences. Dr. Yuan has made contributions in the area of cancer epidemiology and the role of dietary and other environmental exposures, genetic variations, and gene-environmental interaction in the causes and prevention of cancer.

BROCCOLI AND GREEN TEA MAY PREVENT CANCER

Using the databases of two large population-based prospective cohort studies involving more than 80,000 men and women in Shanghai, China, and Singapore, Dr. Yuan and his research team have made significant findings regarding diet and cancer prevention. Specifically, they found that consumption of isothiocyanates, a group of compounds present in cruciferous vegetables like broccoli, correlated with reduced lung cancer risk. The protective effect is strongest among people with certain genetic predispositions. Following

up on these novel findings, Dr. Yuan and collaborators at the University of Minnesota are conducting a randomized, double-blind Phase II clinical trial to evaluate the effectiveness of a dietary supplement containing 2-phenethyl isothiocyanates (PEITC) on lowering lung cancer risk among smokers.

Other UPCI researchers also are at the forefront of investigating the cancer chemopreventive potential of natural compounds, which are inexpensive, nontoxic, and easy to obtain.

Shivendra Singh, PhD, professor of Pharmacology and Chemical Biology, associate director of Basic Research at UPCI, and member of the CEPCP, and colleagues showed that dietary supplementation of PEITC can inhibit the development and suppress the progression of prostate and breast tumors in mice. **Thomas Kensler, PhD**, professor of Pharmacology and Chemical Biology and member of the CEPCP, and colleagues are investigating the cancer chemopreventive effects of broccoli-derived compounds (containing high concentrations of isothiocyanates) in humans. Dr. Yuan's arrival at UPCI has strengthened this important collaborative work toward the prevention of a variety of cancers.

It is believed that tea consumption originated in China approximately 5,000 years ago. Green tea has been used as both a beverage and traditional medicine in most of Asia, including China, Japan, Korea, and Singapore. Green tea contains high concentrations of polyphenols that have antioxidant and anticancer properties. Dr. Yuan and his research team conducted a series of epidemiological studies that have shown that consuming green tea or tea

UPCI members Dr. Joel Weissfeld and Dr. Marjorie Romkes conducted a study using the tumor sample bank managed by the UPCI SPORE in Head and Neck Cancer to evaluate the carcinogenic effects of tobacco. They discovered a genetic variation which may partially explain why certain people are more susceptible to cancer from smoking.

polyphenols protects against the development of breast, esophagus, stomach, and colorectal cancers. Based on these findings, Dr. Yuan and collaborators at the University of Minnesota are conducting a randomized, double-blind Phase II clinical trial to evaluate the efficacy of oral supplementation of green tea polyphenols on reduction of breast cancer risk.

PREDICTING WHO WILL OR WON'T GET CANCER

Tobacco smoking is one of the most significant causes of lung and head and neck cancers, among many others; however, it is estimated that only one in seven lifelong smokers develops and dies from lung cancer before they are 80 years old. This variation in susceptibility to smoking-related cancers is believed to depend upon the uptake and metabolism of tobacco carcinogens. Through a series of epidemiological studies in China, Dr. Yuan and his colleagues have demonstrated that elevated urinary metabolites of tobacco carcinogens can predict the risk of developing lung cancer and esophageal cancer. In Pittsburgh, **Joel Weissfeld, MD, MPH**, associate professor of Epidemiology and co-director of the CEPCP, and **William Bigbee, PhD**, professor of Pathology, both members of the CEPCP, are leading a research effort to assess whether a combination of gene and protein biomarkers improves lung cancer risk prediction in a large group of patients in the Pittsburgh Lung Screening Study (PLuSS). These studies are part of a Specialized Program of Research Excellence (SPORE) in Lung Cancer, headed by **Jill Siegfried, PhD**, professor of Pharmacology and Chemical Biology and co-leader of the UPCI Lung and Thoracic Malignancies Program.

The UPCI SPORE in Head and Neck Cancer manages an expanding tumor sample bank for translational research. Using these samples, Dr. Weissfeld and **Marjorie Romkes, PhD**, compared 203 cancer cases and 416 controls for inherited differences in genes involved in metabolizing tobacco carcinogens. They discovered that a particular genetic variation in the NAT2 gene was more prevalent in tumor samples compared to controls, which may partially explain differing susceptibilities to the cancer-causing effects of tobacco. In another study, Dr. Weissfeld, Dr. Romkes, and **Brenda Diergaarde, PhD**, showed that treatment-dependent differences in survival of head and neck cancer patients correlated with a genetic mutation in the ERCC2 gene, which is involved in DNA repair.

PROMOTING CANCER SCREENINGS

In other CEPCP activities, Dr. Weissfeld and **Robert Schoen, MD, MPH**, have led the Pittsburgh screening center for the recently completed Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial and the National Lung Screening Trial (NLST). In addition, Dr. Weissfeld and colleagues collaborated with the Association for Schools of Public Health and Centers for Disease Control and Prevention to evaluate methods for promoting cancer screening through primary care practice. They found that an enhanced office and patient management system significantly improved colorectal screening adherence among patients 50 to 79 years of age.



Dr. Jian-Min Yuan and collaborators studied the anti-cancer properties of green tea and tea polyphenols in breast, esophagus, stomach, and colorectal cancers. Their findings led to a Phase II clinical trial to evaluate the efficacy of green tea polyphenol supplements in reducing breast cancer risk.





Radiation oncologist Dr. Ryan Smith, shown with the brachytherapy equipment that enables him to place radioactive seeds with high precision into the prostate using transrectal ultrasound guidance.

UPMC CancerCenter is one of the nation's most comprehensive radiation oncology networks. Its primary site for radiation oncology and radiosurgery, the Mary Hillman Jennings Radiation Oncology Center at UPMC Shadyside in Pittsburgh, is linked to 11 community radiation oncology centers and 10 dual radiation and medical oncology centers located throughout western Pennsylvania.

ACCESS TO ADVANCED TREATMENT THROUGHOUT THE NETWORK

These 21 sites offer the most advanced imaging available to define tumors, including computerized tomography (CT), positron-emission tomography (PET), 4-dimensional CT and PET-CT, On-Board® Imager (OBI), and magnetic resonance (MR) spectroscopy.

UPMC CancerCenter provides conventional radiation therapy and total body irradiation (TBI) to treat tumors, as well as combined modality therapy, which combines radiation therapy with other treatments, such as chemotherapy or biologic response modifier therapies. UPMC CancerCenter also offers access to the latest technology — the revolutionary and versatile TrueBeam™ STx powered by Novalis® Radiosurgery system, located at the Mary Hillman Jennings Radiation Oncology Center at UPMC Shadyside, as well as the Trilogy™ linear accelerator and Synchrony™ imaging system, which adapts to the breathing movement of tumors in the lungs. UPMC CancerCenter uses these innovative systems to treat even the most complex tumors in the most difficult places to reach, with more effective, more accurate, and less toxic treatments.

Other advanced radiotherapy techniques and tools used by our radiation oncologists throughout the network are RapidArc,[®] which precisely sculpts the radiation dose to the tumor in a single 360-degree arc; image-guided radiotherapy (IGRT), which tracks a tumor through the full course of treatment as it changes shape, size, and position during therapy and adjusts therapy accordingly; intensity-modulated radiation therapy (IMRT), which allows the radiation beam to be shaped to target the tumor more precisely; gating, which opens and closes the radiation beam during treatment; CyberKnife,[®] a versatile stereotactic radiosurgery device capable of targeting tumors with submillimeter accuracy; and Gamma Knife,[®] a powerful device pioneered at UPMC in 1987, which can destroy deep-seated brain tumors once considered inoperable.

CLINICAL PATHWAYS ENSURE OPTIMAL RESULTS

Many of these advanced therapies, such as IMRT, gating, and OBI, as well as the conventional radiation therapies, are available in the community radiation oncology centers. One of the main strengths of the UPMC CancerCenter network is its ability to obtain virtually identical results whether patients are treated at Hillman Cancer Center or at any of the community locations, due to the use of Clinical Pathways — evidence-based, network-wide radiation oncology care standards developed by UPMC CancerCenter to provide uniformity across the network.

“The Clinical Pathways were developed to ensure optimal standards for oncology care

across the UPMC CancerCenter network using evidence-based, peer-reviewed radiation oncology guidelines for treating patients,” says **Dwight E. Heron, MD, FACRO**, director of radiation oncology services at UPMC CancerCenter, who spearheaded the initiation of the radiation oncology standards. Pathways also are offered for medical oncology treatments. “Clinical Pathways are updated regularly by teams of academic and community oncologists who review current literature and clinical practices to modify the Pathways, so they are always evolving at the same rate as the state of the science.”

Clinical Pathways enable individual physicians to use medical evidence and the collective knowledge base of a panel of experts to make personalized, informed recommendations about each patient’s care through a software program that integrates the Pathways into the physician’s daily work flow. “Pathways guide us to the latest standards that inform the quality of the care we offer,” says **Sanjeev Bahri, MD**, a radiation oncologist and medical director at Arnold Palmer Pavilion at Mountain View Park, a joint venture of UPMC CancerCenter and Excelsa Health. “Pathways validate what we’re doing. They give patients a level of comfort that what we’re doing is based on the latest and finest evidence and make them more confident that they’re receiving the expertise of a team of physicians, not just one physician.”

Since their development several years ago, Pathways have been used by radiation oncologists throughout the network for more than 95 percent of their treatment plans.

RADIATION ONCOLOGY BY THE NUMBERS

Through UPMC CancerCenter’s network of 21 radiation centers, patients have access to:

- 33 linear accelerators
- 35 attending physicians
- 32 physicists
- 24 dosimetrists
- 110+ therapists

The Clinical Pathways were developed to ensure optimal standards for oncology care across the UPMC CancerCenter network using evidence-based, peer-reviewed radiation oncology guidelines for treating patients with state-of-the-art techniques.

—DR. DWIGHT HERON, DIRECTOR, RADIATION SERVICES



Some patients don't realize there are clinical trials for radiation therapy, but many patients come to me looking for these trials, especially if another treatment option or trial has failed them. We try to enroll as many patients as possible on clinical trials if they are eligible.

—DR. SANJEEV BAHRI, RADIATION ONCOLOGIST

Brachytherapy seeds—smaller than a grain of rice—deliver radiation directly into the tumor. This minimally invasive, internal radiation therapy may be used to treat prostate, gynecologic, lung, and breast cancers, as well as sarcoma and other malignancies.

Clinical reasons for deviating from the Pathway — such as a patient's inability to tolerate a treatment or patient preference — are few, but can be accommodated by the interactive process the web-based, real-time Pathways platform provides.

"The Pathways are often useful in the initial decision making for offering a treatment plan to a patient," says **Ryan Smith, MD**, a radiation oncologist who sees patients mainly at UPMC St. Margaret. "The Pathways were created so that physicians can follow the standard of care supported by the literature — so patients get the best treatment that can possibly be offered."

With all the technologically advanced equipment and treatment techniques at their disposal for treating tumors, UPMC radiation oncologists find the Pathways can be particularly helpful in refining the options with certain cancers, such as prostate cancer. "Different patients can choose a number of different treatment plans for prostate cancer, and end up with the same results," explains Dr. Smith. "So we don't necessarily pick the treatment plan for prostate cancer based on outcomes — it often is based on the patient's side-effect profile, and the toxicity, invasiveness, and

time commitment of the treatment — so it really comes down to patient preference. The Pathways provide multiple choices, all of which are first-line treatments."

AUGMENTING STANDARDS OF CARE

Another unique aspect of the Clinical Pathways is the ability to augment the standard of care with therapeutic clinical trials for all stages of cancer. Often thought of only as experimental medical oncology treatments, clinical trials are also available for radiation oncology treatments and always combine the radiation oncology Pathway standard of care with an additional therapy. "Radiation oncology trials answer dosage questions, or evaluate a chemotherapy agent or immunological modulator in combination with radiation therapy," says Dr. Bahri. "Some patients don't realize there are clinical trials for radiation therapy, but many patients come to me looking for these trials, especially if another treatment option or trial has failed them. We try to enroll as many patients as possible on clinical trials if they are eligible. Clinical trials are the principal way we make major advances and improve the outcomes for patients today and tomorrow."

CLINICAL PATHWAYS

Pathways address more than 85 percent of all new cancer diagnoses, and every state and stage of the most common cancers, including:

- Breast
- Colorectal
- Esophageal
- Head and neck
- Lymphoma
- Lung
- Melanoma
- Myelodysplastic syndrome
- Myeloma
- Ovarian
- Pancreatic
- Prostate
- Recurrent tumors
- Renal cell
- Thyroid
- Uterine

SEEDS THAT SHRINK RATHER THAN GROW

One of the radiation oncology therapies UPMC CancerCenter offers for the treatment of prostate cancer is brachytherapy. Brachytherapy is a minimally invasive form of internal radiation therapy that involves the placement of radioactive metallic seeds — smaller than a grain of rice — directly into the tumor to deliver radiation. Brachytherapy can be used to treat prostate cancer, gynecologic cancers, lung cancer, breast cancer, sarcoma, and other malignancies.

For the treatment of prostate cancer, the most commonly diagnosed cancer in men, brachytherapy may be given alone or in combination with external beam radiation therapy or hormone therapy, depending on the stage of cancer. Often, the patient may receive radiation first, through daily external beam treatments for five weeks. After a short break, the patient may receive the brachytherapy implants, which deliver a high dose of radiation directly to the prostate gland and sometimes to the seminal vesicles. The seeds emit their radiation slowly over several months and, within one year, their radiation almost completely dissipates. The seeds can remain safely in place for the rest of a man's life.

The radiation oncologist performs the brachytherapy treatment using a transrectal ultrasound to visualize the prostate gland. Brachytherapy usually is done under general anesthesia or spinal anesthesia to prevent the patient from moving or experiencing discomfort, and takes only about 90 minutes to complete. The radiation oncologist places a small plastic template with tiny holes against the perineum, the area between the genitals and anus. Thin, hollow needles called catheters are inserted into the grid through the perineum and into the prostate gland. The radioactive seeds are delivered through the catheters and planted in the prostate a little less than 1/2 inch apart. Most men can leave the hospital three to four hours after the implant procedure.

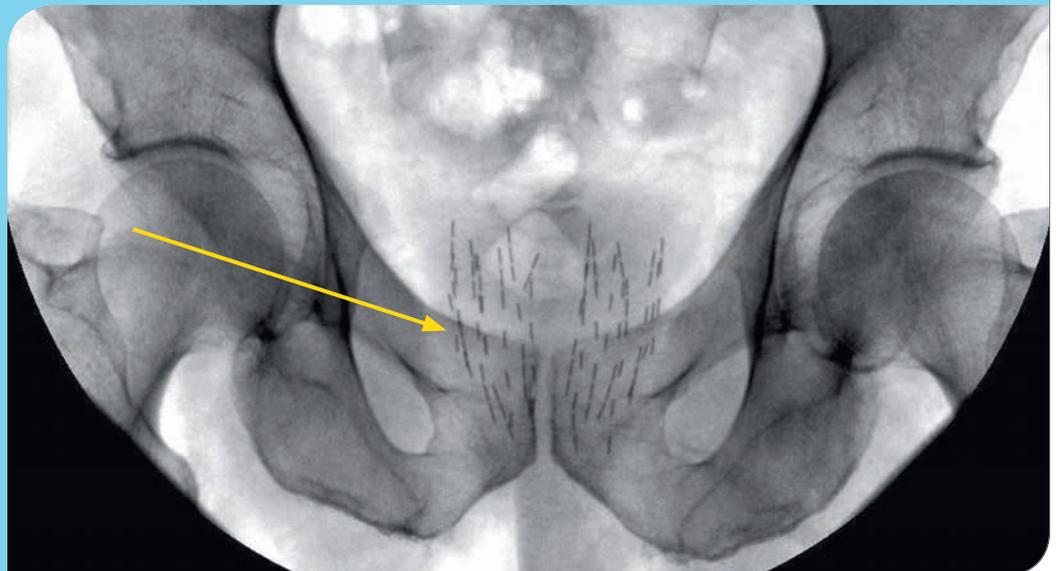
Unlike major surgery, daily radiation treatments, or external beam radiation therapy, seed implantation causes little interruption to the patient's daily activities and usually preserves continence and erectile function. Although there may be mild side effects, such as perineal soreness, an urgent or burning sensation with urination, or bowel problems, the effects usually last for only a few months to a year after the implant and decrease gradually as the seeds lose their radioactivity. The seeds present no danger to the patient's family at any point during treatment.

UPMC CANCERCENTER
RADIATION ONCOLOGY
BRACHYTHERAPY
VOLUMES*



* Fiscal Year running July 1 through June 30.

X-ray image of prostate gland with arrow showing radioactive brachytherapy seeds in place. The seeds emit radiation slowly over several months and, within a year, the radiation almost completely dissipates. The seeds can remain in place safely for the rest of the patient's life, with no danger to the people they live with.



Orthopaedic surgical oncologist
Dr. Richard McGough



The surgical oncology program at UPMC CancerCenter specializes in the surgical treatment of a wide variety of cancers, including brain, breast, colorectal, endocrine, esophageal, gynecologic, head and neck, hepatobiliary, lung, melanoma, orthopaedic, pancreatic, prostate, and soft tissue sarcoma.

EXPANDING ACCESS FOR BOTH PATIENTS AND SURGEONS

A highlight of the program this year has been the continued expansion of surgical oncology services to the northern region through the construction of three new, dedicated state-of-the-art cancer operating rooms (ORs) at UPMC Passavant in Pittsburgh's North Hills. The additional OR space has provided increased access to surgical services for patients in the northern suburbs and beyond, making travel into the city unnecessary for many procedures, and has allowed more surgeons to use the new technologies and techniques.

The new ORs also enabled the surgical oncology program to extend access to advanced surgical techniques once only available in Pittsburgh.

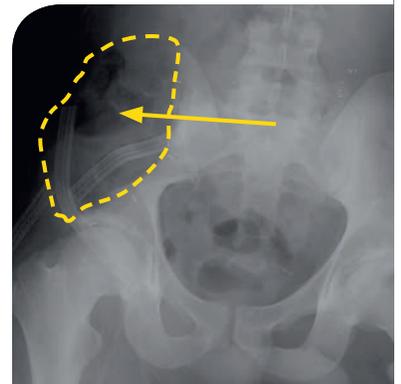
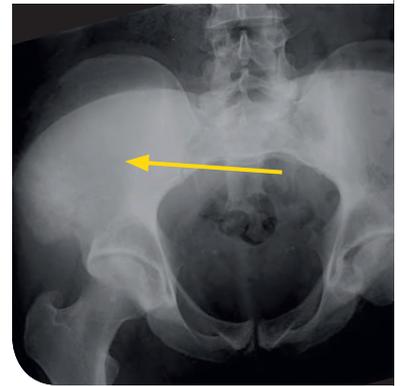
AMONG THE LATEST THERAPIES NOW BEING OFFERED IN THE NORTH HILLS ARE:

- **Robotic-assisted surgery** with the daVinci® Surgical System, a robotic platform that provides enhanced visualization and dexterity, allowing surgeons to perform complex procedures with smaller incisions

- **Hyperthermic intraperitoneal chemoperfusion (HIPEC)**, an intensive therapy using heated chemotherapy to directly treat tumors that have spread throughout the abdominal cavity and linings
- **Intraperitoneal (IP) chemotherapy** — chemotherapy medication delivered directly to the abdominal cavity organs through a catheter
- **Transarterial chemoembolization (TACE)** — a minimally invasive interventional radiology procedure that delivers chemotherapy and particles to reduce the blood supply to a tumor to stop its growth

MORE ROOM FOR COLLABORATION

The increased surgical oncology space at UPMC Passavant also has enabled increased collaboration among multidisciplinary teams of physicians who often work together to optimize the use of new equipment. An example of that teamwork is the pairing of surgical oncologists and gynecologic oncologists, who scrub in together to treat gynecologic cancers with HIPEC, or thoracic surgeons with radiation oncologists, who work together to use intra-operative computed tomography (CT) and CyberKnife® to perform ablations of lung lesions.



Above, top: Initial x-ray of pelvis with arrow showing portion of bone affected by sarcoma before surgery; above, bottom, x-ray of pelvis after surgery, showing the area where the tumor was removed and the preserved connection between the hip joint and spine.

THE NEW SURGICAL ONCOLOGY SPACE ALSO ACCELERATED THE EXPANSION OF THESE ALREADY STRONG ONCOLOGY PROGRAMS:

Gynecologic cancers, including minimally invasive surgery and photodynamic therapy

Breast cancer, through the Comprehensive Breast Center, which provides patients with access to the latest equipment — including digital mammography and MRI-guided breast biopsy — and breast cancer specialists, all in one convenient location

Liver cancer, through the Liver Cancer Center, which provides multidisciplinary clinical services and innovative treatment strategies for patients with liver tumors



Above, top: Dr. Michael Stang was among the first endocrine surgeons in the region to use the da Vinci robot to perform thyroid surgery.

Above, bottom: Dr. Umamaheswar Duvvuri is using the da Vinci robot to perform minimally invasive surgery for head and neck cancers.

Below: The dual console of the da Vinci robot allows two surgeons to operate the robot at the same time. It enables surgeons to perform minimally invasive procedures in hard-to-reach places that once required open surgeries to access.

MORE SURGICAL ONCOLOGY PROGRESS

Another advancement that has taken place over the past year has been the expanded use of current cutting-edge technology for other innovative surgical applications. For example, **Michael T. Stang, MD**, and the highly experienced team of endocrine surgeons from the Multidisciplinary Thyroid Center, were the first endocrine surgeons in the region to use the da Vinci® robot to perform thyroid surgery for removal of cancerous or suspicious thyroid nodules and lymph nodes, with low complication rates and excellent outcomes.

Historically done through a large incision in the front of the neck, thyroid surgery often resulted in a large, visible scar which many patients found cosmetically undesirable. Using the robotic assistance, surgeons now can perform the thyroid surgery with no incision in the neck — but rather a small incision under the arm and a minimally invasive endoscopic procedure. Robotic thyroid surgery gives patients an option that is cosmetically superior to scarring of the neck, with the same safety and results as traditional thyroid surgery.

BLOODLESS SURGERY

Umamaheswar Duvvuri, MD, a UPMC otolaryngologist specializing in head and neck cancer surgery, also is performing minimally invasive robotic-assisted surgery for removal of the thyroid and parathyroid glands, as well as to remove parathyroid disease that has metastasized to the chest. Using the dual console of the da Vinci robot, which allows each surgeon to work on the robot simultaneously, Dr. Duvvuri and UPMC cardiothoracic surgeon **Benny Weksler, MD**, have worked as a team to remove these tumors in the chest through a minimally invasive surgical procedure. This surgery, which once required a large, open incision with thoracotomy, and often resulted in blood loss and blood transfusions, now can be done through a very small incision in the chest, with minimal to no blood loss and a very short recovery time.

Even more dramatic is the improved outcomes for Dr. Duvvuri's patients with the use of the robot to treat cancers of the back of the throat, tonsils, and larynx — an area that is very difficult to reach. Traditional open oropharyngeal surgery requires a large external incision in the skin of the throat and jaw and a surgical break of the jawbone to gain access to a tumor in the back of the throat. The surgery requires blood transfusions, a lengthy hospital stay, a tracheotomy tube for breathing support, a feeding tube for nutrition, and a long, painful recovery period. Often, the patient is left with disfigurement and difficulty eating, speaking, and swallowing, and may need reconstructive or plastic surgery to rebuild the removed bone or tissue.

The minimally invasive approach allows the surgeon to insert the arms of the robot directly into the mouth to maneuver them precisely into the area to remove the tumors. This surgical approach offers the same margins as the traditional resection, but using the natural orifice of the mouth eliminates the need for any



incisions, decreases blood loss, reduces hospital stays from one week to one day, and shortens the recovery time from several months to one week.

Dr. Duvvuri and UPMC radiation oncologist **Gregory Kubicek, MD**, are in the initial phases of developing the first randomized clinical trial to evaluate the efficacy of robotic-assisted minimally invasive surgery in the management of patients with head and neck cancers.

SPECIALTY CARE CENTERS

For patients with challenging cancers or recurrent metastatic disease, UPCI and UPMC CancerCenter offer disease-specific multidisciplinary clinics called Specialty Care Centers (SCCs). Through the SCCs, patients see an entire team of specialists relevant to their diagnoses in a short

period of time, expediting the development and implementation of treatment plans. The SCCs may be used by referring physicians to confirm diagnoses, provide second opinions, or consult on difficult cases. Once seen through the SCCs, patients can be treated at Hillman Cancer Center or referred back to their primary oncologists for treatment.

SCCs are offered for 16 different diseases in adults, including cancers of the brain, bladder, breast, esophagus, head and neck, liver, lung, pancreas, prostate, and thyroid, as well as for hematological malignancies, melanoma and skin cancers, mesothelioma, metastatic colorectal cancer, peritoneal carcinomatosis and ovarian cancer, and sarcomas.



Above: Adam Frederick, right, with wife, Sarah, and daughter, Grace, was 26 when he was diagnosed with Ewing's sarcoma, a rare cancer that might have claimed not only his leg, but his life. Neoadjuvant chemotherapy and orthopaedic surgery spared both.

PATIENT PROFILE

Adam Frederick

COLLABORATING FOR CARE

The multidisciplinary approach to oncology care is a highly effective way to explore all available treatment options and offer optimal care for patients. Surgeons often work with medical oncologists and/or radiation oncologists to plan a patient's neoadjuvant care (chemotherapy or radiation given before a surgery to shrink the tumor) or adjuvant care (chemotherapy or radiation given to destroy any remaining microscopic cancer cells that might be present after the tumor is surgically removed, and to prevent a possible recurrence.)

Collaboration benefits patients both by ensuring that their care is comprehensive and seamless, but also in making it more convenient and easier to receive. Just ask Adam Frederick, a former all-state high school quarterback and college football player at Kent State University. In 2007, at age 26, Adam experienced pain and numbness in his lower back but attributed it to an old sports

*injury. But after weeks of physical therapy, his symptoms weren't improving. His physician ordered an MRI, which revealed a mass near his pelvis. After receiving the results, Adam made an appointment with **Richard McGough, MD**, an orthopaedic surgical oncologist at UPMC CancerCenter.*

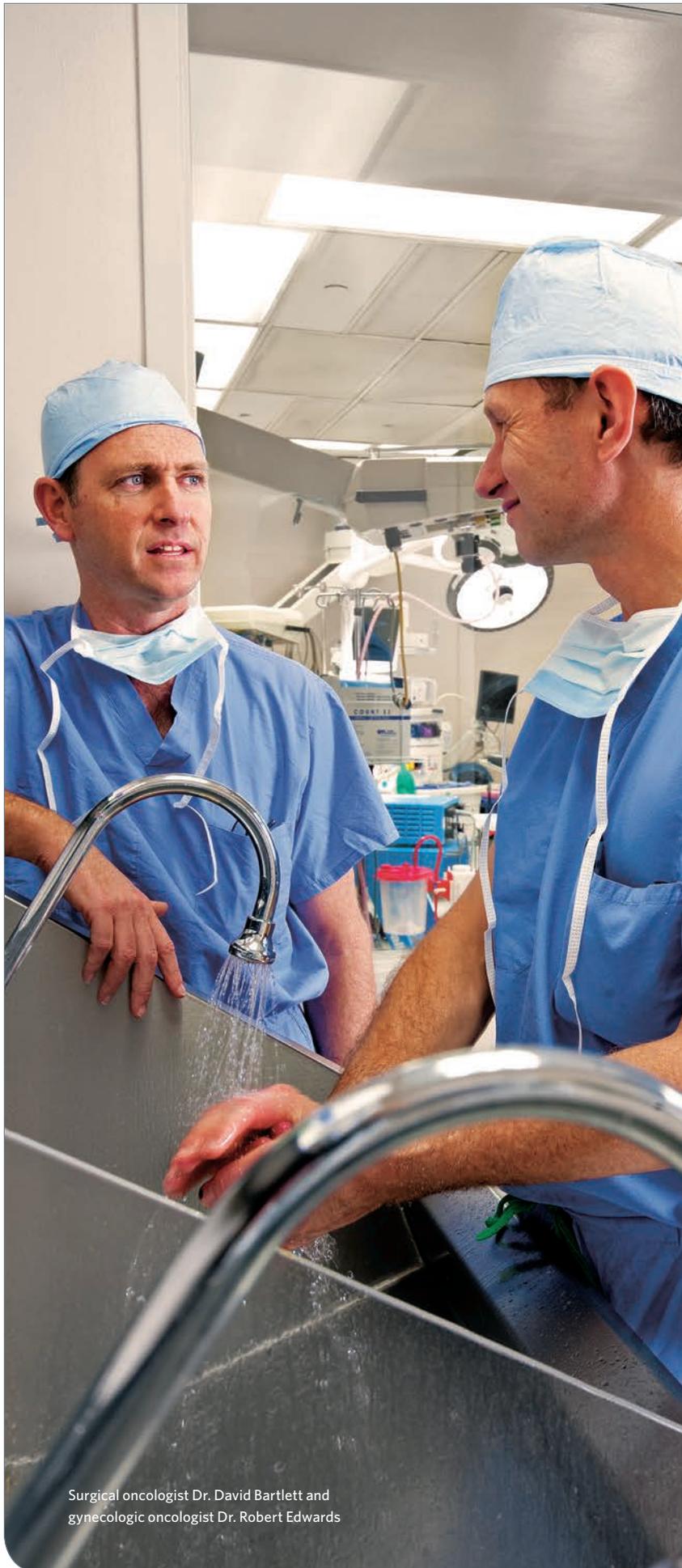
A week following the scan, Adam's pelvic bone broke while he was walking at work. After being admitted to UPMC Shadyside, he learned he had Ewing's sarcoma, a rare, aggressive, malignant tumor often seen in children and young adults.

*Dr. McGough and medical oncologist **Stanley Marks, MD**, recommended intensive neoadjuvant chemotherapy treatment, which Adam received every other week for two months at Hillman Cancer Center, under Dr. Marks' care. After chemotherapy, Adam had surgery at UPMC Shadyside to remove the rest of the tumor.*

Although Ewing's sarcoma can sometimes make amputation of a limb necessary, fortunately, Dr. McGough was able to successfully remove the tumor and save Adam's leg.

Adam was glad that the care he needed was within a short drive of his home in Gibsonia. "To have UPMC in my backyard was a huge blessing when I was diagnosed with cancer," Adam says. "When you're undergoing treatments and not feeling well, you don't want to spend four or five hours in a car."

Now three years later, Adam is in good health. He works as a financial adviser with PNC Bank, and is happily married to his wife, Sarah, whom he met through his sister while in the hospital during his year-long treatment regimen. In spring 2011, Adam and Sarah celebrated both their first wedding anniversary and the birth of their first child, Grace.



Surgical oncologist Dr. David Bartlett and gynecologic oncologist Dr. Robert Edwards

The Magee-Womens Cancer Program of UPMC CancerCenter is dedicated to the diagnosis and treatment of women's cancers — including all types of breast and gynecologic cancers — offering patients strategic and innovative approaches to treatment.

A TEAM APPROACH TO TREATING DIFFICULT ABDOMINAL CANCERS

The Magee-Womens Cancer Program of UPMC CancerCenter allows teams of specialists to identify, diagnose, and treat each patient's case individually. For breast cancer cases, factors determining the course of treatment include the stage and biological subtype of the cancer. Based on those and other factors, treatment plans can include several different therapies, including chemotherapy, hormonal therapy, radiation, surgery, and reconstructive breast surgery.

Treating gynecologic cancers can be particularly difficult and complex, as the primary treatment often requires a regimen of surgery, followed by chemotherapy. Because the optimal surgical treatment of gynecologic cancers varies from patient to patient, the Peritoneal Carcinomatosis and Ovarian Cancer Specialty Care Center allows a team made up of specialists from multiple fields to develop personalized treatment plans for each individual patient.

David Bartlett, MD, vice chairman for surgical oncology and gastrointestinal services at UPMC, works closely with **Robert Edwards, MD**, director, Ovarian Cancer Center of Excellence, co-director, Women's Cancer Research Center, and one of UPMC CancerCenter's gynecologic oncologists, on the Peritoneal Carcinomatosis and Ovarian Cancer Specialty Care Center's team of physicians, to carefully plan every patient's surgical treatment.

The Magee-Womens Cancer Program of UPMC CancerCenter has a truly multidisciplinary approach to treating women's cancers.

—DR. ROBERT EDWARDS, GYNECOLOGIC SURGICAL ONCOLOGIST

Dr. Bartlett says one of the reasons behind forming the Specialty Care Center two years ago was to streamline treatment and facilitate better communication between physicians and patients.

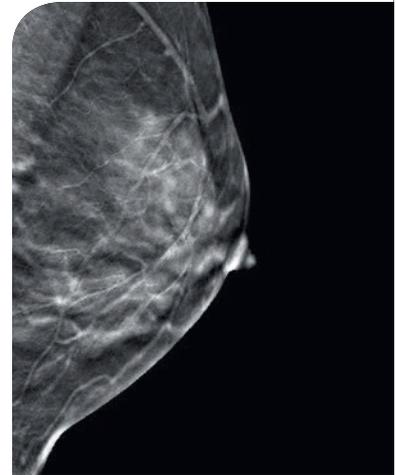
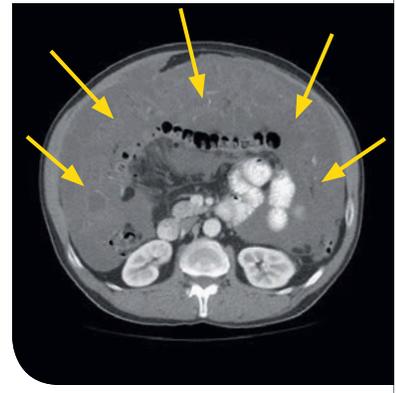
According to Dr. Bartlett, this method allows surgeons to utilize their specialties — gynecologic surgical oncologists focus on removing malignancies in the pelvis and lower abdomen, while surgical oncologists work to remove cancer from areas like the liver and diaphragm. “Working together with Dr. Edwards and other gynecologic surgical oncologists allows us to provide a more complete surgical result for the patient,” says Dr. Bartlett. “That’s the biggest way that we help patients.”

Dr. Bartlett also says that one of the main benefits of the Specialty Care Center’s structure is that it allows multiple specialists to see and talk with the patient simultaneously. This approach prevents the patient from having to set up numerous appointments and facilitates easier communication among doctors, creating a more efficient model of care and the opportunity to bring in ancillary services when necessary.

UPMC CancerCenter and UPCI physician-researchers are part of the University of Pittsburgh’s Clinical Translational Research Science Institute, which is supported by a highly regarded grant from the National Institutes of Health (NIH), to help translate science into clinical application. This effort includes the Women’s Cancer Research Center (WCRC), a collaboration between UPCI and the Magee-Womens Research Institute.

“At the WCRC, we have physicians and scientists working together to investigate women’s cancers ranging from breast and gynecologic malignancies to how lung and colorectal cancers affect women,” says Dr. Edwards.

The Peritoneal Carcinomatosis and Ovarian Cancer Specialty Care Center is just one of the many special features and services that continues to make the Magee-Womens Cancer Program one of the country’s best facilities in the diagnosis and treatment of women’s cancers.



Top: CT scan with arrows showing pseudomyxoma peritonei (PMP), a rare condition characterized by the presence of mucin-producing tumors in the abdominal cavity. There are a number of possible origins of PMP, but the most common source is appendiceal (appendix) cancer.

Bottom: Digital breast tomosynthesis (DBT) generates a 3-D image of the breast, which may improve tissue characterization, tumor visualization, and diagnostic ability, and reduce unnecessary follow-up testing when used with conventional mammography.

WOMEN'S IMAGING

Magee offers a wide range of imaging services for both men and women at nine locations. Imaging services combine top-flight technology with highly-skilled specialists who read and interpret images. High-quality images interpreted by expert radiologists offer the best chance for accurate diagnosis and treatment planning.

Among the advanced imaging techniques the experts of the Magee-Womens Breast Cancer Program may use is digital breast tomosynthesis (DBT) in conjunction with conventional mammography to provide optimal breast imaging for a clear diagnosis. Tomosynthesis uses low-energy x-rays to create a 3-D image of the breasts. While conventional mammography takes pictures of the breast from two angles — up and down, and left and right — tomosynthesis takes multiple pictures from many angles.

Neuro-oncologist Dr. Regina Jakacki and neurosurgeon Dr. Ian Pollack



Pediatric brain and spinal cord tumors are a leading cause of cancer-related deaths among children, and the management of these tumors is often very complicated.

A UNIFIED APPROACH TO TREATING THE MOST COMPLEX BRAIN TUMORS

Close collaboration between the neurosurgeons and neuro-oncologists at Children's Hospital of Pittsburgh of UPMC has streamlined the treatment of these complex tumors — and has led to more successful outcomes.

The Brain Tumor Management team is part of Children's Hospital's newly established Brain Care Institute, a multidisciplinary, comprehensive team of physicians from a variety of specialties. The institute calls upon the expertise of neurologists and neurosurgeons, as well as experts in neuro-trauma and critical care, neuro-oncology, neuroimaging, ophthalmology, otolaryngology, neurodevelopment, and behavioral health. This collaboration results in expert clinical care,

as well as the opportunity for these physicians to work together on progressive research, effective treatment strategies, and protocol development.

Each year, our internationally renowned specialists may treat more than a dozen different types of pediatric brain tumors that range from benign (non-cancerous) to aggressive forms of cancer. Unlike adult brain tumors, pediatric brain tumors can vary greatly and pose unique age-related management issues. Specialists in pediatrics, the members of the Children's Brain Care Institute team have the knowledge of the latest developments in pediatric brain tumor research, as well as of the most appropriate and effective therapies for the smallest and youngest of patients.

Depending on the diagnosis, treatment may include surgery, standard and experimental chemotherapy, biologic agents, radiation therapy, steroids, anti-seizure medications, ventriculoperitoneal shunts, or third ventriculostomies.



ADVANCED SURGICAL APPROACHES

When a surgical approach is recommended, members of the Division of Pediatric Neurosurgery can offer a range of treatment options. These complex, delicate procedures require the coordinated efforts of a team of experts from different disciplines who work together to help each child get the best care possible before, during, and after surgery. Our Neurosurgery team includes some of the world’s leading pediatric brain tumor specialists and researchers, assisted by highly trained nurses and staff. Many have pioneered breakthrough treatments and neurosurgical techniques, and continue to make innovative strides in pediatric neurosurgery.

Our Pediatric Intensive Care Unit (PICU) provides full intensive care services following neurosurgery for patients ranging in age from newborn to young adults. Within the PICU, our dedicated Pediatric Neurocritical Care Service is among the best in the world. This service was the first of its kind in the nation — and Children’s is still one of a select few hospitals to offer this type of specialized service. Unlike other programs at large, academic children’s hospitals

that rely on consulting physicians who provide temporary care, clinicians at our Pediatric Neurocritical Care Service become the patient’s physician of record during the child’s entire stay in the PICU, ensuring both excellence and consistency in care.

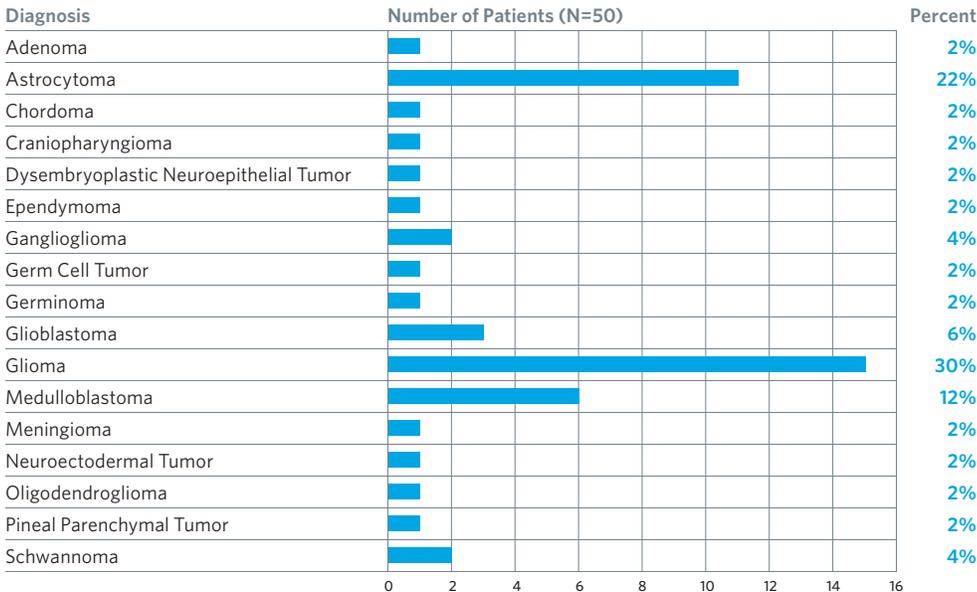
THE ART OF NEURO-ONCOLOGY

Sometimes surgical resection is all that is needed if the brain tumor can be completely removed. But when surgery is not an option due to the location of the tumor, or when only a portion of the tumor can be removed surgically, treating the remaining tumor is complicated. Although radiation often is used without hesitation to treat many brain tumors in adults, that is not the case with brain tumors in children. The dose level of radiation needed to destroy the tumors often has devastating effects on a developing child’s cognitive function, particularly in children under age three. Although chemotherapy alone is an option in treating some slow-growing brain cancers, and may be the only option in very young children, it seldom has a curative effect, and is, in many cases, only used to “buy time” until a child is as old as possible before he or she needs to receive radiation.

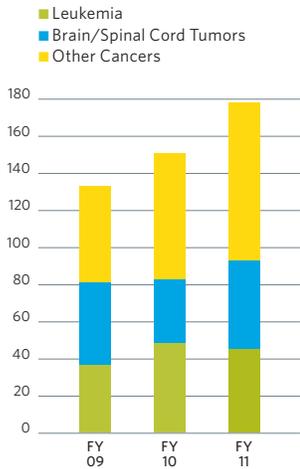
The crux of what we do in pediatric oncology is maximize the child’s chance of becoming cancer-free while preserving their ability to function independently and participate in society as an adult in the same way they would have if they hadn’t had a brain tumor.

—DR. REGINA JAKACKI, PEDIATRIC NEURO-ONCOLOGIST

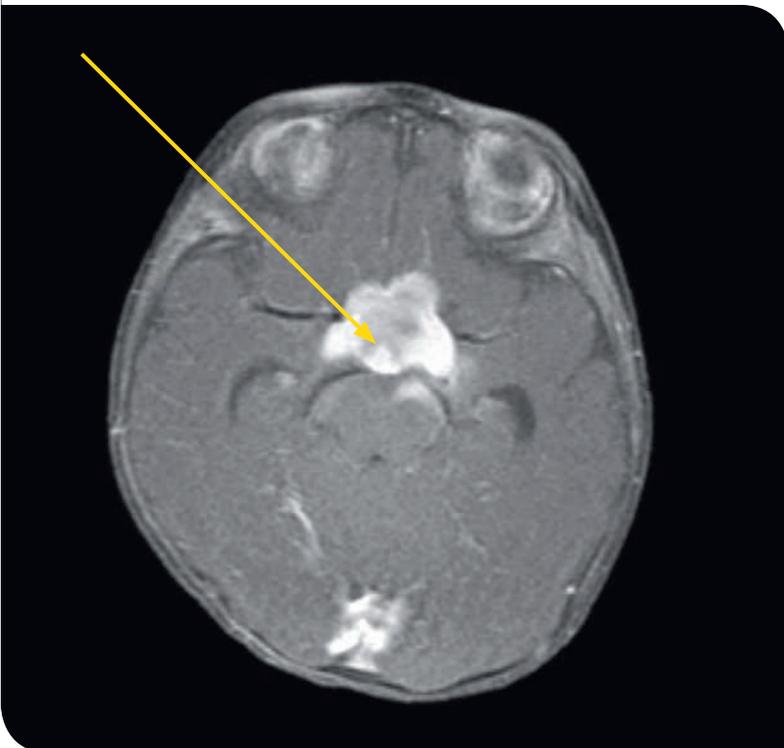
CHILDREN’S HOSPITAL BRAIN/SPINAL CORD PATIENTS (Fiscal Year 2011)



CHILDREN'S HOSPITAL NEW CANCER PATIENTS



Scan with arrow showing tumor involving the main visual center deep in the brain behind the eyes of a pediatric patient.



For children with malignant brain tumors, who do not have the luxury of time, balancing chemotherapy and radiation therapy is even more critical — and heart-wrenching. Sometimes parents are faced with the agonizing decision between having a good chance of completely destroying their child's tumor with radiation that will permanently disable their child in the process or trying aggressive chemotherapy that will not disable their child, but has a much lower chance of saving their child's life.

"Each case is tremendously complex, and that is why we personalize every treatment for each individual patient and family," says **Regina Jakacki, MD**, director of Children's Hospital's Pediatric Neuro-Oncology Program. "The vast majority of tumors, especially malignant tumors, require radiation in order to be completely destroyed, but we know that radiation to certain parts of the brain or to the entire brain will result in significant neurocognitive impairment. Depending on the type and location of the tumor and age of the child, some families find the risk of

permanent damage to their child's brain from radiation to be too high, so they may choose treatment with repeated regimens of conventional chemotherapy or even experimental chemotherapy for as long as possible — sometimes for years — until the need for radiation cannot be delayed or avoided any longer.

"The crux of what we do in pediatric oncology is maximize the child's chance of becoming cancer-free while preserving their ability to function independently and participate in society as an adult in the same way they would have if they hadn't had a brain tumor," she says. "At Children's, a major advantage is our access to experimental chemotherapy agents and biologic agents that only a few centers have, as well as our expert knowledge of which agents to use and how to use them to maximize the chance of patients having a productive future after their treatment."

When radiation therapy is used to treat pediatric patients with brain tumors, the Pediatric Radiation Oncology Department works closely with the neuro-oncologist to provide specialized treatment plans using the latest radiation therapy techniques, tailored to the specific needs of children and teenagers.

TEAMING UP TO OFFER COMPLETE CARE

Led by **Ian Pollack, MD**, chief of Pediatric Neurosurgery at Children's and co-leader of the Brain Tumor Program of the University of Pittsburgh Cancer Institute (UPCI), and Dr. Jakacki, a pediatric neuro-oncologist, the UPMC Brain Tumor Program has particular strengths in detecting, diagnosing, and treating children with even the most complex pediatric brain and spinal cord tumors.

As part of the Children's Hospital Neuro-Oncology Tumor Board, the Brain Tumor team meets regularly with specialists from multiple disciplines — including staff from

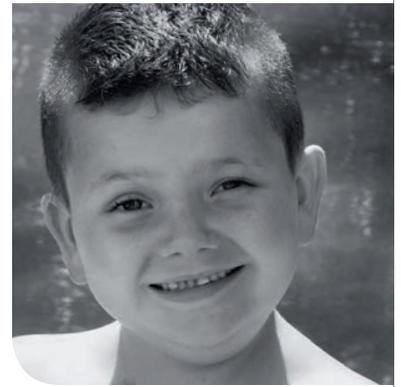
pediatric neurosurgery, neuro-oncology, radiation oncology, neurology, and pediatric neuroimaging — to discuss all treatment options. The comprehensive Neuro-Oncology Tumor Board discusses each patient’s situation, considers all treatment options, and develops a treatment plan to share with parents so they can make an informed decision about their child’s care.

Our team also includes a wide range of experienced pediatric physicians from such support specialties as behavioral health, otolaryngology (ENT), genetics, ophthalmology, and physical medicine and rehabilitation. Experienced nurses, audiologists, and speech/language pathologists augment the team.

ADVANCED NEUROIMAGING

The Pediatric Neuroimaging Section within Children’s Department of Pediatric Radiology is a leader in the comprehensive and innovative imaging of the brains and spinal cords of infants and children. Pediatric radiologists, with a subspecialty in brain imaging, provide evaluation using the most innovative imaging and diagnostic equipment, and are active in pioneering new procedures that can detect even the smallest brain abnormalities in children of all ages — even those in utero.

The first step in providing the right treatment is making the right diagnosis the first time. When children are very young or very sick, they’re often unable to tell doctors how they’re feeling.



Zachary Henry, 7, has been treated with a series of chemotherapy agents throughout his life since his diagnosis with optic glioma at four months of age. The chemotherapy is staving off the need to use radiation therapy for as long as possible.

PATIENT PROFILE

Zachary Henry

QUIET COURAGE AND PERSEVERANCE NEEDED IN TREATING CHILDHOOD BRAIN TUMORS

Heidi Henry, of Franklin, Pa., is a mom who lives in the moment and tries not to think too far ahead. That is because her son, Zachary, the youngest of her three children, has been on a series of different chemotherapy drugs for most of his seven years in an effort to delay the need for radiation therapy as long as possible. Zachary was diagnosed with a tumor behind his eyes when he was only four months old.

“Zachary’s left eye was protruding, so we asked about it at his four-month check-up,” Heidi recalls. “Our pediatrician did an exam of his eye and sent us to Children’s for a CT scan.” The CT scan was followed by an MRI, which revealed an extensive optic glioma not only on Zachary’s optic nerves, but extending through the chiasm to the hypothalamus deep within his brain. Due to the size and location of the tumor, surgery was not an option. Upon their son’s diagnosis, Heidi and her husband, Gary, met with Children’s neuro-oncologist Dr. Regina Jakacki. She explained that the only option for treatment at this point was chemotherapy drugs to kill dividing cells, since radiation therapy — high

energy x-rays aimed at the tumor — would so severely damage his brain at his age that he would be unlikely to survive. Zachary was started on chemotherapy without delay. Zachary had a central venous line placed, though which his chemotherapy treatments were infused every week and later every other week throughout the next year. He tolerated the chemotherapy fairly well, but Heidi says it was hard to figure out what was bothering him when he cried — whether it was just typical baby fussiness or discomfort from the tumor and hydrocephalus (pressure from fluid buildup in the brain) that accompanied it.

That first round of chemotherapy has been followed by multiple regimens of different types of chemo drugs, always in an attempt to delay the need for radiation therapy. As Zach has gotten older, the effects of radiation therapy would not be quite so devastating, but would still result in significant learning disabilities. “After a while on one drug, the tumor figures out what we’re doing and finds a way to grow again,” Heidi says. “So when one chemo drug stops working, we move on to the next.”

Since his diagnosis, Zachary has been on chemotherapy for all but a seven-month period when he was around four years old. His current therapy is in the form of two separate pills that Heidi mixes into his drinks. Zachary really doesn’t understand that he’s on chemotherapy. “He just knows that his brain is broken,” Heidi says. “Every three months, he gets a scan to see how the tumor is doing. Sometimes he understands his brain is getting better, and then sometimes it isn’t.”

Despite a complete vision loss in his left eye and decreased vision in his right eye, Zachary is doing well. He is in first grade at the local elementary school; he has an aide in the classroom who helps him with his work and a vision specialist who is teaching him Braille. He makes frequent visits to an ophthalmologist to evaluate his vision and has quarterly scans at Children’s and regular check-ups with Dr. Jakacki, for whom Heidi has nothing but the highest praise. But most importantly, he remains a personable, outgoing little boy in a busy family of five.

GLIOMA VACCINES: TRANSLATING ADULT VACCINES INTO CHILDREN'S VACCINES

Malignant gliomas are among the most common and deadly childhood brain tumors. Over the past decade, researchers at the University of Pittsburgh Cancer Institute (UPCI), under the direction of **Hideho Okada, MD, PhD**, have gained significant preclinical and clinical experience with immunotherapy for adult gliomas (*J Clinical Oncology*, 29:330-6, 2011). Published studies from UPCI show substantial similarities between pediatric and adult gliomas in their expression of glioma-associated antigens (GAAs) (*J Neurooncol*. 88:245-50, 2008). Dr. Okada and colleagues Dr. Ian Pollack and Dr. Regina Jakacki have developed a GAA-based vaccine cocktail, combined with an immunoadjuvant (poly-ICLC) to further boost immune response, and are conducting a clinical trial with this vaccine on children with gliomas.

Gliomas arise from glial cells, which are the supportive tissue of the brain. There are several types of gliomas, categorized by where they are found and the type of cell that gave rise to the tumor, including astrocytomas, brain stem gliomas, ependymomas, and visual pathway gliomas.

Dr. Jakacki and Dr. Pollack are collaborating on this study with Dr. Okada to use the preclinical and clinical experience with immunotherapy for adult gliomas that researchers in the UPMC Brain Tumor Program have gained over the last decade. In this pediatric study, they are extending these insights to the treatment of childhood gliomas based on their recently published observations that there are substantial similarities between these tumors and normal brain tissue in their expression of GAAs.

A vaccine made from small proteins specific to gliomas is given in combination with an experimental drug called poly-ICLC, which boosts the immune system, in an attempt to induce an immune response. Both are given to patients by injection at three-week intervals for 24 weeks. Responding patients may continue receiving vaccines every six weeks for up to two years. Physical examinations, blood testing, and MRI scans are performed periodically to assess the vaccine's effectiveness.

The study is specifically evaluating the vaccine's efficacy and safety in treating patients with newly diagnosed brainstem gliomas who have received radiation therapy, who have not had chemotherapy after radiation therapy. The clinical study and biological correlative analyses represent the first application of this multi-peptide epitope vaccine-based strategy in pediatric patients with gliomas.

Pediatric experts at Children's Hospital understand these needs and are skilled at using the latest technology — combined with special distraction techniques designed to put kids at ease and reduce or eliminate the need for sedation — to capture the most accurate images, from which neuroimaging specialists can identify a full spectrum of common or complex conditions.

CUTTING-EDGE RESEARCH

Access to the newest treatment strategies and most promising drugs available at only a select number of pediatric centers around the country is an important component of Children's Brain Tumor Program. Patients may be eligible for treatment through one of the many innovative clinical trials offered through the Pediatric Neuro-Oncology Program. The program is a long-time member of the Children's Oncology Group (COG) and the Pediatric Brain Tumor Consortium (PBTC), a select group of pediatric hospitals that is committed to identifying and evaluating novel treatments and furthering the progress of pediatric neuro-oncology care.

Children's is one of the leading sites in the United States for pediatric cancer clinical studies. Specifically, Children's Neuro-Oncology Program has received significant funding from the National Cancer Institute (NCI), the National Institute for Neurological Disorders and Stroke, the National Brain Tumor Society, and the Children's Brain Tumor Foundation. These funds are used to take research from the lab to clinical trials as quickly as possible — to benefit as many children as possible. A collaborative working and information-sharing relationship with the University of Pittsburgh Cancer Institute (UPCI), the region's only NCI-designated Comprehensive Cancer Center, augments this translational research effort.

Currently, some of Children's research initiatives include developing therapies to interrupt pathways in the brain that drive tumor growth and creating a vaccine to treat gliomas, some of the most resistant and aggressive of childhood brain tumors.

Established cancer therapies — such as surgery, chemotherapy, and radiation therapy — are often effective in reducing tumor mass in patients, but seldom eliminate remaining cancer cells or prevent the disease from recurring. Toward that end, physician-researchers have attempted to use patients' own immune systems to identify and destroy persisting cancer cells.

CANCER VACCINES

Although the immunologic effectiveness of new cancer vaccines continues to increase, and their ability to delay cancer progression seems promising, overall effectiveness of the currently available therapeutic cancer vaccines still trails the effectiveness of preventive vaccination against infectious agents.

The University of Pittsburgh Cancer Institute (UPCI) has a robust Cancer Immunology Program (CIP), and many investigators are involved in the research and development of

more effective and specific cancer vaccines. Dendritic cells (DCs) are immune cells specialized in initiating immune responses. When combined with a tumor antigen, DCs have been shown to induce tumor rejection.

Pawel Kalinski, MD, PhD; Hideho Okada, MD, PhD; David Bartlett, MD; John Kirkwood, MD; and Larisa Geskin, MD, have developed a third generation of DC vaccines, alpha-type-1-polarized DC (α DC1). These vaccines are currently being clinically tested at UPCI in patients with glioma, melanoma, lymphoma, colon, and prostate cancers. The preliminary results from these studies are promising.



Jamie Clouser, 31, has been receiving UPCI's glioma vaccine every three months and has responded well; his tumor has shown partial but significant shrinkage.

PATIENT PROFILE

Jamie Clouser

GLIOMA VACCINE WORKING WELL FOR LAW STUDENT

When Jamie Clouser was diagnosed with malignant brain stem glioma in early 2007, his symptoms weren't yet severe, but doctors in his hometown of New York City did not recommend surgery due to the location of the tumor. So in 2008, when his symptoms worsened, Jamie traveled to Arizona for a partial resection, which was followed by months of chemotherapy and radiation therapy back at home.

*Weakened from his intense chemo and radiation therapy regimen, he was on a slow path of recovery throughout 2009, when his parents' online research unearthed a glioma vaccine trial being conducted by **Hideho Okada, MD, PhD,** at the University of Pittsburgh Cancer Institute (UPCI).*

"I was just starting to feel better after finishing up my chemo and radiation treatments, which really knocks you out," Jamie recalls. "I just wanted to be done with therapy and really wasn't looking

for anything else to try when my parents found Dr. Okada's immunotherapy study, but I figured it couldn't hurt."

Dr. Okada leads the study of the first-ever cancer vaccine developed for low-grade gliomas, a slow-growing type of brain cancer that is at high-risk for transforming into more aggressive high-grade gliomas, such as glioblastoma multiforme. The vaccine targets specific brain tumor proteins which, given in combination with an immune system booster, could slow, stop, or even reverse the growth of glioma cells in patients.

The eligibility requirements for the protocol required recurrence in the patient's tumor. Although Jamie was feeling better, there was a radiologic sign of tumor recurrence and clinical evidence, including double-vision and nystagmus, which made him eligible for the study.

After meeting with Dr. Okada and researching the vaccine, at the end of 2009 Jamie began immunotherapy treatment with the glioma vaccine, traveling to Pittsburgh for injections once every two weeks for a few months, tapering back to once a month, then once every three months over two years.

"Within days of receiving the first vaccine, I showed remarkable improvement," Jamie says. "Within a month, I was really feeling good." Now, more than two years after the start of his immunotherapy treatment, he continues to receive vaccines every three months, and is feeling better than ever. His tumor size, which had remained stable for a year and a half, has now shown partial but significant shrinkage.

His first career in marketing was a bit derailed by his diagnosis and treatment, so Jamie felt the time was right to switch career paths and, at age 31, now is in law school at Fordham University.



Medical oncologist and melanoma expert Dr. John Kirkwood

For example, progression-free survival increased to at least 12 months compared with the expected three to four months (*J Clinical Oncology* 29:330-336, 2011) in recurrent high-grade glioma patients treated with this vaccine by Dr. Okada, and several patients demonstrated tumor shrinkage or tumor rejection. The clinical data and preclinical results reported by Dr. Kalinski, Dr. Okada, and colleagues show that α DC1s are particularly effective when combined with interferons, prostanoid blockers, and TLR-ligands, the factors that enable “conditioning” tumor microenvironments for effective immune attack. This progress led to the design of follow-up combination treatments involving vaccines and tumor-conditioning regimens. Two such trials — one for patients with colorectal cancer, led by **Amer Zureikat, MD**, and the other for ovarian cancer, led by **Robert Edwards, MD** — are planned for 2012.

There is convincing clinical evidence that tumor antigens, such as the epidermal growth factor receptor (EGFR)-specific monoclonal antibody (mAb) cetuximab, act as effective therapy for advanced head and neck squamous cell carcinoma (SCCHN); however, not all patients respond to cetuximab, and clinical responses are not correlated with the level of EGFR expression on tumor cells. Thus, there is a need to understand why clinical responses vary among patients, in order to identify patients who are most likely to respond to cetuximab therapy.

In contrast to EGFR tyrosine kinase inhibitors, the antitumor activity of cetuximab may benefit from its interactions with the host’s immune system. **Robert Ferris, MD, PhD, FACS**; **Soldano Ferrone, MD, PhD**; **Theresa Whiteside, PhD**; **Michael Gibson, MD**, and colleagues are studying whether the antitumor activity of cetuximab is influenced by its ability to trigger an EGFR-specific cellular immune response and by the escape mechanisms SCCHN cells utilize to avoid immune recognition and destruction. This ongoing R01-funded study also is part of the Specialized Program of Research Excellence (SPORE) grant

from the National Cancer Institute (NCI). Preliminary results show activation of natural killer (NK) cells by the therapeutic monoclonal antibody and interaction of DC and NK in stimulating the adaptive immune response (*Immunological Research 50:248-54, 2011*).

VACCINES TO TREAT ADVANCED MELANOMA

Immunotherapy has emerged as an effective treatment with enduring impact for patients with metastatic melanoma. One experimental approach utilizes U.S. Food and Drug Administration (FDA)-approved therapy with the cytokine IL-2, which has uniquely been coupled with anti-angiogenic agent VEGF trap for treatment of patients with advanced melanoma.

A second approach has been to block one of the immune checkpoints or damping mechanisms with an antibody that inhibits

immunoregulation through the cell surface molecule, cytotoxic T lymphocyte-associated 4 (CTLA-4), which plays a critical role in regulating immune response. Ipilimumab, an anti-CTLA-4 antibody, is designed to block the activity of CTLA-4, and activate or release the damping of the immune system against cancer. In early 2011, this antibody was approved by the FDA for treatment of inoperable melanoma; however, it has been associated with severe toxicities that appear to be the result of the release of the immune system. **John Kirkwood, MD, Ahmad Tarhini, MD**, and colleagues developed novel combinations of ipilimumab and interferon-alpha, an immunotherapy that this team previously pioneered through FDA approval for therapy of operable melanoma. They are studying the combination of the two drugs toward development of new, more effective therapies for operable and inoperable melanoma patients.



Dr. Hideho Okada, top, and Dr. Pawel Kalinski, bottom, and their team have developed third-generation dendritic cell vaccines that are currently being tested at UPCI.

SEQUENCING GENOMES FOR A BETTER UNDERSTANDING OF HEAD AND NECK CANCER

Head and neck squamous cell carcinoma is the sixth most common non-skin cancer in the world, with more than 500,000 new cases diagnosed each year, and is frequently lethal. Smokers, drinkers, and people infected with human papillomavirus (HPV) have the highest risk of developing head and neck cancer. The survival rate of 50 percent has improved minimally over the past 40 years, yet there was little understanding of the spectrum of mutations in these tumors, which impaired the development of more effective therapies.

To uncover the profile of mutation in head and neck cancer, **Jennifer R. Grandis, MD, FACS**, leader of UPMC CancerCenter's Head and Neck Cancer Program, partnered with Levi A. Garraway, MD, PhD, of the

Dana-Farber Cancer Institute and Harvard Medical School, on a study of 74 pairs of tumor and normal tissue samples from the University of Pittsburgh's collection. The two served as senior authors of a paper in *Science*, which confirmed genetic abnormalities previously suspected in head and neck cancer, including defects in the tumor-suppressor gene known as p53.

The team also found mutations in the NOTCH family of genes, which control how cells differentiate into other kinds of cells, mature, stop dividing, and ultimately die. In head and neck cancer, the scientists saw mutations that most likely turn NOTCH1 off, blocking differentiation and trapping cells in a proliferative, pro-cancer state. Such a maturation arrest may cause the cells to become stuck in an earlier stage

where damage from smoking, alcohol, or even p53 mutations can destabilize the genome. The NOTCH1 inactivating mutation in head and neck cancer was surprising because in other cancers, such as leukemia, too much NOTCH signaling led to cancer. Further studies will be needed to define the role of NOTCH mutations in the diagnosis, prognosis, and treatment of head and neck cancers.

The team also confirmed the role of HPV infection, thought to be transmitted by oral sex, in head and neck cancer, particularly oropharyngeal cancer. The study revealed that HPV-positive tumors carried fewer mutations than HPV-negative tumors. Patients with HPV-positive head and neck cancers tend to fare better than patients whose cancers are not caused by the virus.



Above, left to right: Architectural renderings of patient reception area, stem cell treatment room, and patient waiting area of the new Mario Lemieux Center for Blood Cancers, which is currently under construction at Hillman Cancer Center.

Leukemia, myelodysplastic syndromes (MDS), lymphoma, and multiple myeloma are cancers that affect the bone marrow, blood, and the immune system. There are approximately one million Americans living with some form of blood cancer and, of these, approximately 60,000 will die each year from their disease. An estimated 150,000 such cancers were diagnosed in the United States in 2010, accounting for approximately 10 percent of all new cancer diagnoses.

HEMATOLOGICAL MALIGNANCIES

In western Pennsylvania, approximately 2,000 new cases of blood cancers are diagnosed each year, and approximately 70 percent of patients with these cancers are cared for within the UPMC CancerCenter network.

Advances in medical science and care have led to significantly improved treatments, prolonged life spans, and improved quality of life for many people with blood cancers. Despite these advances, many blood cancers remain incurable. A large number of current therapies are highly toxic and expensive, and require prolonged treatments at medical centers far from patients' homes and families.

To address these obstacles, the University of Pittsburgh Cancer Institute (UPCI) and UPMC CancerCenter have designed and developed the Mario Lemieux Center for Blood Cancers, a 24,000-square-foot outpatient treatment facility which will be located on the fourth floor of Hillman Cancer Center. The new facility is being funded by a five-year, \$100 million capital campaign kick-started by a \$20 million gift from The Hillman Foundation and Henry L. Hillman Foundation, and capped by a \$3 million gift from the Mario Lemieux Foundation in late 2010.

The Mario Lemieux Center for Blood Cancers will operate 12 hours a day, seven days a week, and will be staffed by a multidisciplinary team of physicians, nurses, and other UPCI/UPMC CancerCenter employees. For patients and families, the new center will offer complex treatments for hematological malignancies on an outpatient basis, improve quality of life and access to care, provide greater access to clinical trials, and reduce length of hospital stays, which can help lower health care costs. The new clinical space will provide more flexibility and new treatments in this specialty using the latest information management technologies critical to the upcoming era of personalized medicine.

Treatments for blood cancers may include chemotherapy, biological therapy, radiation therapy, and stem cell transplantation (also called bone marrow transplantation or BMT), or a combination of these therapies.

ONE OPTION: STEM CELL TRANSPLANTATION

Stem cell transplantation can be an effective treatment for patients with advanced or recurrent blood cancers. Stem cells are immature blood cells that are removed from the blood or bone marrow of the patient or a

donor which are frozen and stored. High doses of chemotherapy and/or radiation therapy are needed to kill existing bone marrow that is producing the cancerous cells, followed by the transplant. The infused stem cells replace the blood-forming cells destroyed by the cancer treatment by growing into and restoring the body's blood cells.

The Stem Cell Transplantation Program of UPMC CancerCenter is committed to developing and improving stem cell transplantation (SCT) therapies for adults and children with blood and bone cancers, as well as other diseases. As one of the largest regional providers of stem cell transplantation services in western Pennsylvania, this accredited program offers tailored treatment on an outpatient or inpatient basis. Program leaders work closely with experts in the Leukemia and Lymphoma Program of UPMC CancerCenter, and perform approximately 130 transplants annually.

THE STEM CELL TRANSPLANTATION PROGRAM AT UPMC CANCERCENTER OFFERS A COMPLETE AND COMPREHENSIVE ARRAY OF SCT SERVICES, INCLUDING:

- **Allogeneic transplant** — Physicians collect and transplant stem cells from a donor who matches the recipients' cells.
- **Autologous transplant** — Stem cells are harvested from the patient prior to other cancer treatments, purged of abnormal cells, and transplanted into the patient.
- **Syngeneic transplant** — Similar to an allogeneic transplant, however, the donor cells are collected from the patient's identical twin.

UPMC CancerCenter's program participates in the International Bone Marrow Registry and the Autologous Blood and Marrow Transplant Registry, providing patients with the greatest opportunity to find a donor "match" if needed. The program is an approved transplant center

by the National Cancer Institute's Eastern Cooperative Oncology Group (ECOG), a national multi-institutional organization that coordinates and facilitates cancer-related clinical trials. Through ECOG, the program can offer cancer patients participation in innovative clinical trials of promising new transplant approaches to treat the disease.

RESEARCH IN CANCERS OF THE BLOOD

UPCI investigators are engaged in basic, clinical, and translational research aimed at understanding the molecular development of blood diseases, their progression, and their response to treatment. The program is broadly divided into four major research areas: myeloid malignancies, lymphoid malignancies, multiple myeloma, and stem cell transplantation.

The extensive scientific resources and expertise at UPCI have enabled the program to build research strengths in areas relevant to its overall goals, including signaling pathways involved in normal and cancerous formation of blood cells, stem cell division and differentiation, the role of the marrow microenvironment in blood cancers, immunobiology of stem cell transplantation, and development of targeted agents for the treatment of blood cancers.

Among those investigators conducting cutting-edge research in blood diseases is **Deborah Galson, PhD**, and her colleagues, who have determined the molecular mechanism of action of two thalidomide compounds that are highly effective in multiple myeloma treatment (*Blood 117:5157-65, 2011*).

BLOOD DISEASE RESEARCH

UPCI's overall scientific goals in blood disease research are to:

- Increase our understanding of the molecular and cellular biology of normal and leukemic stem cell formation, and the impact of the molecules and compounds in bone marrow on normal and malignant cell formation.
- Uncover the molecular basis of blood cancers and their resistance to therapy.
- Identify and validate clinically relevant biomarkers of disease.
- Use this information to develop novel, preventive, diagnostic, and therapeutic strategies for treating blood cancers.



Dr. Peter Ellis, a medical oncologist and deputy director of clinical services at UPMC CancerCenter, is the physician leader responsible for medication error and medication risk mitigation reporting. He works with nursing, executive, and front-line staff in actively seeking opportunities to improve patient safety, decrease risk, and review chemotherapy administration practices.

At UPMC CancerCenter, patients are at the heart of everything we do. Ensuring the quality of the health care and safety of patients is of utmost importance.

QUALITY INITIATIVES AND PATIENT SAFETY

In an effort to measure and assess clinical operations, we voluntarily elected to undergo review and certification of each of our medical oncology facilities through the Quality Oncology Practice Initiative (QOPI®) of the American Society of Clinical Oncology (ASCO). UPMC CancerCenter is the largest network in the United States, both in number of sites and geographic area, to apply for QOPI certification.

QOPI promotes excellence in cancer care by helping oncology practices create a culture of self-examination and improvement by standardizing, monitoring, and assessing their measureable outcomes. Developed by world-renowned, practicing oncologists and quality experts, QOPI enables practices to compare themselves to their peers on a variety of core measures using clinical guidelines and published standards of such organizations as:

- National Initiative on Cancer Care Quality (NICCQ)
- American Society for Clinical Oncology (ASCO)
- National Comprehensive Cancer Network (NCCN) Quality Measures
- American Society for Radiology and Oncology (ASTRO)
- American Medical Association's Physician Consortium for Performance Improvement® (AMA PCPI) Oncology Measures
- Oncology Nursing Society (ONS)

For UPMC CancerCenter, the QOPI certification provides measurable quality improvement goals, learning opportunities, and feedback. For patients and insurers, it provides meaningful indicators that UPMC CancerCenter is achieving the highest quality cancer care.

MEASURING OUR PROGRESS

The certification process began with our application for certification in 2009, and an initial retrospective abstraction of 400 patient charts from across the network in fall 2010. The detailed abstraction reviewed chemotherapy administration for 72 different disease-specific safety standards to determine if patients received the recommended standard of care. The abstraction looked at staffing, charting, informed consent practices, chemotherapy orders, drug preparation, chemotherapy administration, and patient monitoring and assessment. The information was sent to QOPI and analyzed. Feedback from the reviewer enabled UPMC CancerCenter to revise policies and procedures. A second abstraction was done in spring 2011 and submitted to QOPI, comparing the results between the two chart abstractions to determine if the improvements were successful.

The next step in the certification process was a three-day on-site visit by the QOPI certification evaluator in December 2011. An oncology nurse reviewer with more than 30 years of experience visited five of the UPMC CancerCenter network sites chosen at random, and reviewed clinical practice at each site. The evaluator interviewed and shadowed nursing staff and assessed daily clinical operations of chemotherapy administration using the 17 ONS safety standards, including such criteria as policies and procedures, hand hygiene adherence, patient identification, pharmacy safety measures, and the chemotherapy mixture process. The evaluator recommended some small changes to improve efficiency that the administrative team was able to make immediately.

We not only mark ourselves against nationally accepted oncology standards, but we take proactive steps to safeguard both our practices and our patients.

—DR. PETER ELLIS,
MEDICAL ONCOLOGIST



The Gumberg Family Resource Center, located at Hillman Cancer Center, is the hub for patient education at UPMC CancerCenter.

Following the on-site visits, UPMC CancerCenter administration received a full report of findings and recommendations, and had one year to implement the suggested changes across the entire network.

“The QOPI Certification process is evidence of UPMC CancerCenter’s commitment to quality,” says **Peter Ellis, MD**, a medical oncologist and Deputy Director, Clinical Services. “It confirms that we not only mark ourselves against nationally accepted oncology standards that are reliable and credible, but that we also take proactive steps to incorporate standards and processes that safeguard both our practices and our patients.”

QUALITY INITIATIVES

QOPI certification is only one of the ways UPMC CancerCenter is working to improve the quality of the care we provide. New quality assurance (QA) programs are being developed and initiated on an ongoing basis, with the goal of improving patient experiences and outcomes.

Among the many initiatives we are undertaking are two programs, one which focuses on

increasing efficiency and decreasing patient wait times, and another which highlights our commitment to guide patients through the continuum of care.

- **Our recent conversion to hospital-based clinics enabled UPMC CancerCenter to add on-site chemotherapy pharmacists** throughout our network sites. These pharmacists review each patient’s lab results and chemotherapy orders to ensure that dosing is accurate, and then scan orders electronically to another pharmacist in a remote location, who reviews and confirms the order independently prior to mixing. This double-check pharmacy process adds an extra level of safety to the administration of chemotherapy for patients, further evidence of our absolute commitment to quality and patient safety.
- **Through increased collaboration** with the Institute for Pain and Palliative Care, and the recent addition of a LiveWell Survivorship Clinic, patient care is coordinated from the very first visit through the completion of cancer treatment.

MULTIPLE LAYERS OF PATIENT SAFETY

The chemotherapy team of UPMC CancerCenter at UPMC St. Margaret illustrates the chain of safety precautions used at our hospital-based sites. At far left, on-site pharmacist **Molly McAleer, PharmD**, reviews the chemotherapy order submitted for each patient and checks their lab results to ensure the dosage is accurate. She then scans the order electronically to another pharmacist at a remote location for verification. Once confirmed by the remote pharmacist, the order is checked again by pharmacy technician **Joshellen Tolbert, CPht**, middle, before she mixes the medication. The chemotherapy is checked yet again by treatment nurse **Amanda Spagnolo, RN, BSN**, far right, prior to administering it to the patient.



VALUE-ADDED SERVICES

With the patient experience in mind, UPMC CancerCenter also has taken steps to improve patient comfort and well-being by developing a new tool that enables clinical nurses and ancillary staff to determine and document which supportive resources each individual patient might need. Although not reimbursable, these valuable additions to the medical services UPMC CancerCenter offers are important to the overall patient experience.

SUPPORTIVE SERVICES INCLUDE:

- **Nutrition information:** Patients may schedule an appointment to meet with a dietitian with special training in the nutritional needs of cancer patients and survivors.
- **Financial counseling:** Coordinating insurance and paying for cancer treatments can be a challenge. Our specially-trained financial counselors can help guide patients and their families through this process.
- **Social workers:** Our social workers can help patients apply for medical assistance or other programs, such as transportation

assistance and links to our community partners, that will facilitate the patient’s successful completion of treatment.

- **Patient education:** The Gumberg Family Resource Center, the hub for patient education at UPMC CancerCenter, is the central repository for cancer education in the region. Our patient navigators and nurse educators are happy to provide information to patients and their families about cancer diagnosis, treatment, side effect management, available support groups, and vital services provided in conjunction with our numerous community partners. UPMC CancerCenter also offers patients an online initial treatment tool that outlines what to expect during visits, and offers opportunities to provide feedback.

The QOPI Certification process is evidence of UPMC CancerCenter’s commitment to quality.

YOUR CARE. OUR COMMITMENT.

These and other initiatives are part of UPMC CancerCenter’s commitment to providing patient-centered, individualized, safe, and convenient clinical care for each and every patient, each and every time they visit.





Dr. Lyn Robertson, left, associate director of Cancer Outreach at UPCI, and Lora Ann Bray, of the University of Pittsburgh Center for Health Equity, visit Bat's Barbershop in East Liberty to enlist the help of barber Kevin "Bat" Andrews in encouraging customers like Rich Williams to be screened for colorectal cancer.

In 2011, the National Cancer Institute (NCI) renewed the University of Pittsburgh Cancer Institute's (UPCI's) status as a Comprehensive Cancer Center (CCC), the highest distinction it grants.

COMMUNITY OUTREACH

The CCC designation brings national and international recognition of UPCI as a center of excellence in basic and clinical research, prevention and control programs, and population sciences, as well as a vital part of the region for cancer education and outreach.

Community education and outreach at UPCI and UPMC CancerCenter come in two distinct and important forms: donated services and supplies in support of community agencies and organizations, and a formal program of cancer education and outreach services.

COMMUNITY EVENT SUPPORT

Each of the individual sites within the UPMC CancerCenter network is proactive in building and maintaining close working relationships with its local community agencies and partners with them on many events and activities throughout the year. Support for these activities and events may come in the form of donated staff hours, supplies, materials, meeting sites, and program underwriting.

Among the many groups with which UPCI and UPMC CancerCenter partners are Susan G. Komen for the Cure®, the National Ovarian Cancer Coalition, the American Cancer Society, the Glimmer of Hope Foundation, the Young Women's Breast Cancer Awareness Foundation, and the Leukemia and Lymphoma Society.

Each year, UPMC CancerCenter employees participate in local health fairs, benefit activities, screenings, and presentations at a variety of sites, including malls, workplaces, charitable runs/walks, and other cancer-related events.

VOLUNTEER SERVICES

In addition, UPMC CancerCenter's Volunteer and Community Services Program, led by **Lisa Huntley**, director, works to improve the quality of life for patients and their families during their visits to UPMC CancerCenter, and to enhance the efforts of the medical and research staff. In 2011, roughly 600 volunteers — many of whom are cancer survivors themselves — donated nearly 50,000 total hours through the program.

HIGHLIGHTS OF THE YEAR'S EVENTS WERE COLLABORATIVE PROJECTS WITH:

- **The Greater Pittsburgh Unit of the American Cancer Society**, which raised more than \$42,000 for research, education, service, and rehabilitation for cancer patients and their families. Daffodil Day sales at 100 departments within UPMC provided more than 2,800 Gifts of Hope daffodil bouquets to patients throughout UPMC.
- **Gilda's Club**, a cancer clubhouse offering free support for anyone living with cancer, which provided on-site activities for patients at Gilda's Club, and an outreach effort for oncology inpatients at UPMC Shadyside.
- **University of Pittsburgh School of Pharmacy**, which hosted 30 students for learning experiences in the clinical setting.
- **University of Pittsburgh Cancer Institute Summer Academy program**, an eight-week program which provided faculty mentors for 20 high school students interested in careers in cancer care and research.
- **Other educational programs that focus on teen workforce development**, including School2Career and Goodwill Industries, to give teens first-time work experience after school and in the summer.

20 YEARS OF SUPPORT

UPCI and UPMC CancerCenter will celebrate the 20th year of their **African-American Cancer Support Group** in 2012. The group meets monthly and includes about 150 male and female cancer survivors of all ages. The support group was formed to meet the unique cancer information and education needs of minorities in an effort to provide health equity to these underserved populations.

MAKING A DIFFERENCE

Lyn Robertson, DrPH, RN, MSN, is passionate about her work, and it shows. As associate director of Cancer Outreach at UPCI, she has seen the effects of community outreach first hand. "I've taught people how to make small changes in their lives and they've come back to tell me about them," she says. "They, in turn, become the best examples for their friends and families in making healthier lifestyle choices."

Dr. Robertson and her team of two outreach coordinators have established relationships in minority communities by working with local community centers, businesses, YMCAs/YWCAs, libraries, food banks, support organizations, and shelters. The team works to connect with residents, gain their trust, and identify their health care needs, while promoting positive lifestyle choices for exercise, smoking, drinking, drugs, sun and skin care, and cancer screenings. This effort is particularly important among minorities who may already be underserved by health care or insurance providers, and who also may have higher risk factors for certain chronic diseases. "Our main goal is to remove any barriers to care that might exist," Dr. Robertson says. "Sometimes that means we have to be creative in how we reach people."

Among the innovative approaches her team has tried is using local beauty academies as proponents for breast self-exams (BSEs). The team provides printed materials and a breast model that have been donated so students can simulate a BSE and feel for the various-sized tiny lumps located inside the breast model. Through the beauty academies, her team was able to reach 150 beauticians-in-training to teach them how to do their own BSEs, and they have begun to promote the importance of BSEs among their friends, family members, and clients.

The team also has reached out to African-American men by going to local barbershops in urban communities to educate them on their risks of colorectal cancer and provide screenings. If screenings indicate a follow-up colonoscopy, Dr. Robertson works with each client individually based on his needs.

CANCER OUTREACH

2011 by the numbers:

Children reached by Healthy Choices for Students program:

- During the school year: 7,280 in 8 counties.
- During the summer: 1,309 in Allegheny and Washington counties.
- School districts where the program was presented: 19.

Adults reached:

- 13,500 through 120 education and one-on-one counseling events and 28 community screening events.
- 7 percent of adults participated in an on-site screening.
- 92 percent of those screened were African-Americans.

New sites: 21

Individuals screened: 379

CANCER EDUCATION AND OUTREACH

UPCI and UPMC CancerCenter have a long-standing commitment to provide all patients, regardless of race, ethnicity, age, or socio-economic status, with quality cancer care and early access to new and innovative treatments both at Hillman Cancer Center and throughout UPMC hospitals and UPMC CancerCenter network locations.

UPCI provides community outreach programs to educate the public about cancer and to identify ways to reduce cancer risk by increasing public awareness about primary prevention; reducing exposure to cancer risk factors; educating about the importance of early detection through mammography, pap smears, colonoscopy, prostate and skin cancer screenings; and informing the public about the importance of clinical trials.

OUR COMMITMENT TO HEALTH EQUITY

UPCI has a special commitment to enhancing cancer care in underserved communities and focuses its efforts based on the demographics of our regional population. Our underserved populations include African-Americans, the uninsured/underinsured, elderly, homeless, individuals residing in rural communities or transitional living centers, and the mentally or physically challenged.

For example, UPCI Cancer Outreach collaborated with the African-American Cancer Care Partnership (AACCP) to provide free cancer screenings, with the goal of reducing mortality from cancer in minority and underserved populations. UPCI Cancer Outreach holds free community-based cancer screening programs in underserved areas and at Hillman Cancer Center. These services include prostate screening (PSA) and, when private facilities are available, digital rectal exam (DRE), breast, and cervical screenings.

Most of these screening events are done in collaboration with community partners, which strengthens relationships and ensures better compliance with follow-up recommendations. Screenings also are provided to area firefighters, police officers, and other city and county employees who do not already access screening services.

In addition to regular screenings, UPCI and various community partners collaborate on event-related activities, such as a Father's Day prostate screening program in collaboration with the Obediah Cole Foundation and several local churches in African-American neighborhoods. Screening clinics are always coupled with one-on-one education and strictly adhere to screening guidelines as published by national groups such as the U.S. Preventive Services Task Force, using academic experts from UPCI and UPMC for guidance and support.

Outreach may be as simple as helping a senior fill out a form to access benefits, or as complex as teaching a group of women about the benefits of mammograms and breast self-examination (BSE), scheduling their mammograms, and helping to set up transportation to and obtain vouchers for the mammograms.

UPCI Cancer Outreach also has cultivated a three-year relationship with Healthcare for the Homeless, providing education, screening, follow-up, and client navigation in local homeless shelters, soup kitchens, and transitional living centers. Over the past year, approximately 450 men and women in 11 facilities have participated in these efforts, and compliance to recommended screening follow-up services has remained at roughly 95 percent. UPCI Cancer Outreach provides navigation services to identify barriers to follow-up and to develop plans with these clients to make sure that services are provided. Clients who may require ongoing care and/or support are referred to the Patient Navigation Program at UPMC CancerCenter.

CANCER CARE GOES GLOBAL

In 2006, following the successful integrated model established in western Pennsylvania, UPMC CancerCenter opened its doors abroad with its first international cancer center, UPMC Whitfield Cancer Centre in Waterford, Ireland. International expansion came again just one year later when UPMC CancerCenter took on the management of Beacon Hospital Cancer Centre in Dublin.

UPMC CancerCenter continues to meet the needs of international patients with its newest endeavor, the management of an advanced Radiotherapy and Radiosurgery Center of Excellence at San Pietro Hospital in Rome, Italy. The center, set to open in summer 2012, will offer stereotactic radiosurgery via the Novalis powered by TrueBeam™ STx system, developed by Varian Medical Systems and BrainLab, Inc., the same state-of-the-art platform operating in Mary Hillman Jennings Radiation Oncology Center at UPMC Shadyside in Pittsburgh. Varian's TrueBeam is one of the most advanced linear accelerators in the world, and the Radiotherapy and Radiosurgery Center of Excellence will house the only one in Rome.

A NEW LEVEL OF RADIATION TREATMENT

Stereotactic radiosurgery (SRS) is a highly specialized, effective form of radiation therapy that combines the principles of 3-D target localization (also called stereotaxy) with multiple intersecting radiation beams to precisely treat tumors in difficult or hard-to-reach areas, including the brain, lungs, spine, head and neck, prostate, pancreas, liver, and gynecologic cavities.

"Stereotactic radiosurgery via the TrueBeam platform enables us to precisely target and eradicate tumors that otherwise may have been untreatable," says **Dwight E. Heron, MD, FACRO**, director, radiation oncology services, UPMC CancerCenter. "Bringing this level of radiosurgery to the region will improve the treatment of these cancers, increase the quality of care, and improve patient access."

Patients also will benefit from real-time telemedicine, enabling them to receive high-quality care without having to travel far distances. Telemedicine uses technology to electronically exchange medical information and provide medical services to patients from a distance. Patients in Rome will be able to videoconference with health care providers in western Pennsylvania, have their images transmitted for interpretation by another physician, and have their vital signs monitored remotely.

The center will benefit cancer patients in Rome by fulfilling an unmet need for advanced radiotherapy treatment options, as patients currently travel to other regions for this type of treatment. The center also will set the stage for additional opportunities in Rome as it promotes UPMC's recognition among the international scientific and academic community.

As with all UPMC CancerCenter network sites in the United States and abroad, patients at the Radiotherapy and Radiosurgery Center of Excellence at San Pietro Hospital will receive the same individualized, high-quality care and treatment.

Right, the revolutionary and versatile Novalis powered by TrueBeam STx system can be used for all forms of advanced external-beam radiation therapy and radiosurgery. The TrueBeam linear accelerator at San Pietro Hospital will be the only one of its kind in Rome.

Far right, the bridge of Victor Emmanuel II over the Tiber River, with St. Peter's Basilica in background, Rome.





Dr. Rodney Wegner, right, radiation oncology resident, uses UPMC's electronic health record (EHR) system to access patient data from the exam room. EHRs help physicians make data collection a part of patient care, rather than simply a record of it, which creates efficiencies and provides direct opportunities to improve care.

Hand-held and wireless technologies, such as smartphones and tablet computers, are becoming more and more prevalent in our day-to-day lives and, as such, are changing the way we think about cancer prevention, screening, diagnosis, treatment, and survivorship care.

EHRs AND PHRs: ENHANCING CONSUMER HEALTH INFORMATICS TO SUPPORT PEOPLE AFFECTED BY CANCER

Ellen Beckjord, PhD, MPH, a member of the Biobehavioral Medicine in Oncology Program at the University of Pittsburgh Cancer Institute (UPCI), is leading research efforts to determine how to leverage mobile devices and health information technology (HIT) to improve cancer prevention, cancer care, and the lives of people affected by cancer.

Consumer health informatics is the study of HIT applications that have direct implications for how patients experience health care. Two consumer health informatics applications that Dr. Beckjord has studied in her research, funded by LIVESTRONG® (the Lance Armstrong Foundation), are electronic health records (EHRs), electronic medical records used by health care providers, and personal health records (PHRs), electronic repositories of medical information used by health care consumers.

Dr. Beckjord and LIVESTRONG surveyed more than 8,000 people, more than 3,000 of whom had personal histories of cancer, about their needs and preferences related to EHRs and PHRs. More than 70 percent of those who took the survey reported that it was "very important" to them to be able to access their own medical

information electronically, and over half “strongly agreed” that medical researchers should be able to acquire their de-identified health information for the purposes of research.

Dr. Beckjord first reported these results at the 2011 American Society of Clinical Oncology annual meeting and admits that she and her colleagues were surprised by these results. “We’ve known for a long time that large percentages of people affected by cancer are online, looking for information and resources,” she said. “But we didn’t anticipate that so many would attach a strong value to being able to access their own medical information electronically, or that more than half would want to be so-called ‘information donors,’ and be willing to share their own medical information to support research.”

In this same study, Dr. Beckjord and LIVESTRONG asked people what they would expect and want from an EHR or a PHR. In results she published in 2011 in *The Journal of Oncology Practice*, the preferences of people affected by cancer were clear: More than 70 percent of respondents “strongly agreed” that EHRs should be secure and confidential; that EHRs should make information-sharing between health care providers and patients easier and more convenient; and that EHRs should improve care coordination for patients who have multiple health care providers — the norm for patients during and after cancer treatment.

In January 2012, Dr. Beckjord presented additional results from the study at a conference on systems sciences. “The conference has a relatively new track focused on consumer health informatics, and I’m thrilled to have had the chance to share the voices of people affected by cancer at the meeting.” Her presentation highlighted new data on PHR needs and preferences. Specifically, more than 60 percent of people affected by cancer want a secure

and confidential PHR that helps them keep track of medical information, allows them to see their medical information in the same way that their doctors do, and lets them efficiently store all of their medical information in one place.

Dr. Beckjord says that she is excited about the timing of this research, and about expanding on it in planned research at UPCI and UPMC CancerCenter. “Consumer health informatics and HIT are all about innovation,” she says, “and we are at the forefront of innovation in ways to harness electronic platforms to improve health. It’s a fantastic setting to be in for this kind of research, and I’m grateful for the support and enthusiasm of the UPCI Biobehavioral Medicine in Oncology Program as I develop new projects in this area.”

Beyond using research to inject the patient voice into the design of EHRs and PHRs, Dr. Beckjord is interested in applying consumer health informatics and mobile devices (“mHealth”) into other areas of cancer prevention and care, including use of mobile devices, like smartphones. The goal is to help people make behavior changes to decrease cancer risk (for example, to quit smoking), or to help cancer survivors monitor their own symptoms in less burdensome ways, supporting earlier identification of problems and fostering more meaningful patient-provider communication.

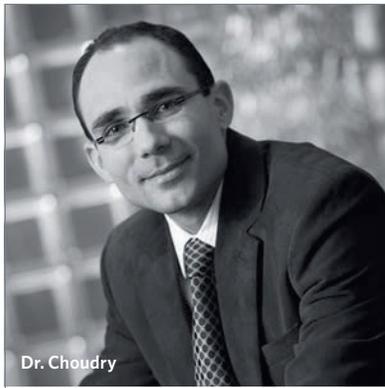
Dr. Beckjord thinks that patients will be interested in participating in this kind of research. “More than 80 percent of respondents in the LIVESTRONG survey stated that they believe health care will improve as HIT plays a larger role in care delivery,” she says. “Not every problem in cancer has a technological solution, but we’re only beginning to understand how HIT can improve the lives of people affected by cancer. We owe it to everyone who is treated at UPCI and UPMC CancerCenter to do our best to find out how.”

We didn’t anticipate that more than half of the people affected by cancer would want to be so-called ‘information donors,’ and be willing to share their own medical information to support research.

—DR. ELLEN BECKJORD,
ASSISTANT PROFESSOR

Dr. Ellen Beckjord’s study with LIVESTRONG found that more than 70 percent of survey respondents felt it was “very important” to them to be able to access their own medical information electronically.





Dr. Choudry



Dr. Holder-Murray



Dr. Holtzman



Dr. McAuliffe

UPMC CancerCenter and UPCI actively recruit young talent, and a new crop of some of the country's brightest surgeons, physicians, and scientists joins our ranks each year. These are some of the up-and-coming young professionals who have joined us or who have advanced in their careers recently.

Wendie Berg, MD, PhD, FACR
Radiologic Imaging, Magee-Womens Hospital of UPMC

Dr. Wendie Berg joined the Department of Radiology and University of Pittsburgh School of Medicine as a professor in March 2011 and practices breast imaging at Magee-Womens Hospital of UPMC. Dr. Berg, an influential imaging expert whose research has created new avenues for breast cancer screening and diagnosis, was widely sought after but joined UPMC after considering many institutions across the country.

Dr. Berg led a major 21-center trial, sponsored by the Avon Foundation and the National Cancer Institute (NCI), demonstrating that screening breast ultrasound detects more invasive breast cancers than mammography, and can improve detection of early invasive breast cancer when added to mammography. The first-year results were published in *JAMA* in 2008. While MRI was even more sensitive in detecting cancers and should be recommended for women at high risk, the combination of mammography and ultrasound was quite effective in women with dense breast tissue.

Dr. Berg is a leader of national and international efforts to make women aware of their breast density, which may mask cancers on mammography. In addition to helping implement screening ultrasound and MRI, Dr. Berg also will evaluate molecular breast imaging and will assist a team that is evaluating the role of tomosynthesis in improving breast cancer screening.

Kara Bernstein, PhD
Molecular and Cellular Cancer Biology Program, UPCI

Kara Bernstein, PhD, is an assistant professor at the University of Pittsburgh School of Medicine in the Department of Microbiology and Molecular Genetics. She recently was awarded the first Director's Distinguished Scholar Award from PNC Foundation and the University of Pittsburgh Cancer Institute (UPCI). She seeks a better understanding of the biological processes related to cancer, with a focus on how double-strand breaks in DNA are repaired. Understanding this process will advance understanding of tumor formation and could lead to the development of new cancer treatments.

Dr. Bernstein received an undergraduate degree from Bryn Mawr College and a doctorate from Yale University, where she studied cell cycle regulation of the SSU processome. She completed an NIH-supported postdoctoral fellowship at Columbia University, where her research focused on the role of Sgs1, a yeast Werner/Bloom homolog, in DNA repair.

M. Haroon Choudry, MD
Surgical Oncology, UPMC CancerCenter

Dr. M. Haroon Choudry is a surgical oncologist at UPMC CancerCenter and an assistant professor of surgery at the University of Pittsburgh School of Medicine. Dr. Choudry's areas of interest include gastrointestinal malignancies, pancreatico-biliary malignancies, and peritoneal surface malignancies.

Board-certified in general surgery, he received his medical degree from Aga Khan University Medical School in Karachi, Pakistan. Dr. Choudry completed both a residency in general surgery and a research fellowship in surgery and physiology at the Milton S. Hershey Medical Center in Hershey, Pa. Most recently, Dr. Choudry completed a clinical fellowship in surgical oncology at UPMC. He has authored more than 20 scholarly publications, including peer-reviewed articles, abstracts, and book chapters.

Jennifer Holder-Murray, MD
Surgical Oncology, UPMC CancerCenter

Dr. Jennifer Holder-Murray specializes in the surgical treatment of benign and malignant diseases of the lower gastrointestinal tract. Her special emphasis includes minimally invasive techniques for cancer,

inflammatory bowel disease, transanal endoscopic microsurgery, and sacral nerve stimulation for fecal incontinence.

Dr. Holder-Murray completed her general surgery residency at the University of Chicago, and a colon and rectal surgery fellowship at the Mayo Clinic. She earned her medical degree from the University of Nevada School of Medicine.

Matthew Holtzman, MD
Surgical Oncology, UPMC CancerCenter

Dr. Matthew Holtzman is a surgical oncologist specializing in the treatment of colorectal, liver, pancreatic, and GI cancers, as well as melanoma and sarcoma. In addition to traditional surgery, he specializes in isolated perfusion chemotherapy (IPC), a special method of concentrated chemotherapy. Dr. Holtzman's research interests include the treatment of recurrent cancers, and using drugs to prevent melanoma recurrence.

Dr. Holtzman received his medical degree from the State University of New York Health Science Center at Brooklyn, where he graduated magna cum laude. He completed his residency at Boston University's department of surgery, where he received the university's Critical Care Resident Award. Dr. Holtzman joined UPMC in 2004.

Priscilla McAuliffe, MD, PhD
Surgical Oncology, UPMC CancerCenter

Dr. Priscilla McAuliffe specializes in premenopausal breast cancer, breast conservation therapy, locally advanced breast cancer, and high-risk breast disease. Her research interests include chemoresistance and targeted therapeutic strategies for breast cancer.

Dr. McAuliffe earned a medical degree from Cornell University, completed a residency in general surgery at the University of Florida, and received fellowship training in surgical oncology at The University of Texas MD Anderson Cancer Center. She has authored more than 30 papers, presentations, abstracts, and book chapters.

David Medich, MD
Surgical Oncology, UPMC CancerCenter

Dr. David Medich is the chief of the Division of Colon and Rectal Surgery at UPMC. Dr. Medich completed his general surgery training at UPMC and colon and rectal surgery training at the Cleveland Clinic. He specializes in the surgical

care of patients with rectal cancer and ulcerative colitis, with expertise in sphincter-preserving procedures. His other areas of expertise include the surgical care of patients with Crohn's disease, diverticulitis, familial adenomatous polyposis, and benign diseases of the colon and rectum.

Maddie Sharma, MD
Radiation Oncology, UPMC CancerCenter

Dr. Maddie Sharma is a radiation oncologist with UPMC CancerCenter. Dr. Sharma has a special interest in the treatment of breast cancer.

Dr. Sharma earned a medical degree from Tufts University School of Medicine in Boston, completed a radiation oncology residency at Rush-Presbyterian St. Luke's Medical Center in Chicago, and received fellowship training in radiation oncology at the Medical College of Wisconsin in Milwaukee.

Mark A. Socinski, MD
Medical Oncology, UPMC CancerCenter

Dr. Mark A. Socinski is professor of medicine and cardiothoracic surgery at the University of Pittsburgh School of Medicine. He is the director of the Lung Cancer Section of the Division of Hematology-Oncology at the University of Pittsburgh, co-director of the UPMC Lung Cancer Center of Excellence, and a co-leader of the UPCI Lung and Thoracic Malignancies Program. Dr. Socinski specializes in thoracic malignancies, including small cell and non-small cell lung cancers and mesothelioma.

Dr. Socinski is board-certified in internal medicine and medical oncology. He earned undergraduate and medical degrees at the University of Vermont in Burlington. He completed a residency in internal medicine at Harvard Medical School Beth Israel Hospital in Boston, and a fellowship in medical oncology at Dana-Farber Cancer Institute in Boston.

G. (Josie) van Londen, MD, MS
Medical Oncology, UPMC CancerCenter

Dr. G. (Josie) van Londen, a medical oncologist and geriatrician, is director of the Women's Cancer LiveWell Survivorship Center at Magee-Womens Hospital of UPMC, and director of the Cancer LiveWell Survivorship Program at Hillman Cancer

Center. Her research interests focus on topics relevant to survivors, especially assessing and managing adverse effects of adjuvant endocrine therapy in older cancer survivors.

Dr. van Londen is board-certified in internal medicine, medical oncology, and geriatric medicine. She received a medical degree at the University of Utrecht in the Netherlands, completed a residency in internal medicine at UPMC, and fellowships in hematology and oncology and geriatric medicine at the University of Pittsburgh School of Medicine.

Liza C. Villaruz, MD
Medical Oncology, UPMC CancerCenter

Dr. Liza C. Villaruz is a hematologist and oncologist specializing in lung cancer and thoracic malignancies. Board-certified in internal medicine, Dr. Villaruz earned her medical degree at the University of Maryland School of Medicine in Baltimore. She completed a residency in internal medicine at UPMC and a fellowship in hematology and oncology at the University of Pittsburgh School of Medicine. Dr. Villaruz is a member of professional organizations, including the American Society of Hematology and the American Society of Clinical Oncology.

Nathan A. Yates, PhD
Analytical Chemistry, UPCI

Dr. Nathan A. Yates joined UPCI and the University of Pittsburgh to establish a state-of-the-art Biomedical Mass Spectrometry Center in the Schools of the Health Sciences. This center will support basic research and advance mass spectrometry-based tests toward clinical use. Dr. Yates was previously scientific director in the Department of Exploratory and Translational Science at Merck & Co., Inc.

His extensive applications of mass spectrometry in pharmaceutical research have helped define the field of quantitative proteomics and advanced new technologies for the detection, diagnosis, and treatment of disease. Dr. Yates received his bachelor's degree in chemistry from Allegheny College, his doctorate in analytical chemistry from the University of Florida, and completed a postdoctoral fellowship at the University of Virginia.

Jian-Min Yuan, MD, PhD
Cancer Epidemiology, Prevention, and Control, UPCI

Dr. Jian-Min Yuan is associate director for cancer control and population sciences, and the leader of the Cancer Epidemiology, Prevention, and Control Program at UPCI. He is a professor of epidemiology at the University of Pittsburgh Graduate School of Public Health.

He earned his medical and public health degrees from Shanghai Medical University in China and a doctorate in epidemiology from the University of Southern California. Dr. Yuan is recognized for his contributions in cancer epidemiology and the roles of dietary and environmental exposures, genetic variations, and gene-environmental interaction in causing and preventing lung, liver, colorectal, breast, bladder, and urinary cancers. Dr. Yuan has authored more than 120 publications in peer-reviewed journals.

Amer Zureikat, MD
Surgical Oncology, UPMC CancerCenter

Dr. Amer Zureikat specializes in the surgical treatment of complex gastrointestinal malignancies, focusing on minimally invasive treatments for all types of gastrointestinal cancers. Dr. Zureikat is a principal investigator in several clinical trials focusing on immunotherapy in the treatment of patients with metastatic colorectal cancer.

Board-certified in general surgery, Dr. Zureikat received his medical degree from the Royal College of Surgeons in Dublin, Ireland. He completed a residency in general surgery at the University of Chicago Medical Center, and a fellowship in surgical oncology at the University of Pittsburgh School of Medicine. He is a member of the Society of Surgical Oncology, the American College of Surgeons, and the Association of Academic Surgeons. Dr. Zureikat joined UPMC in 2010.



Dr. Sharma



Dr. van Londen



Dr. Villaruz

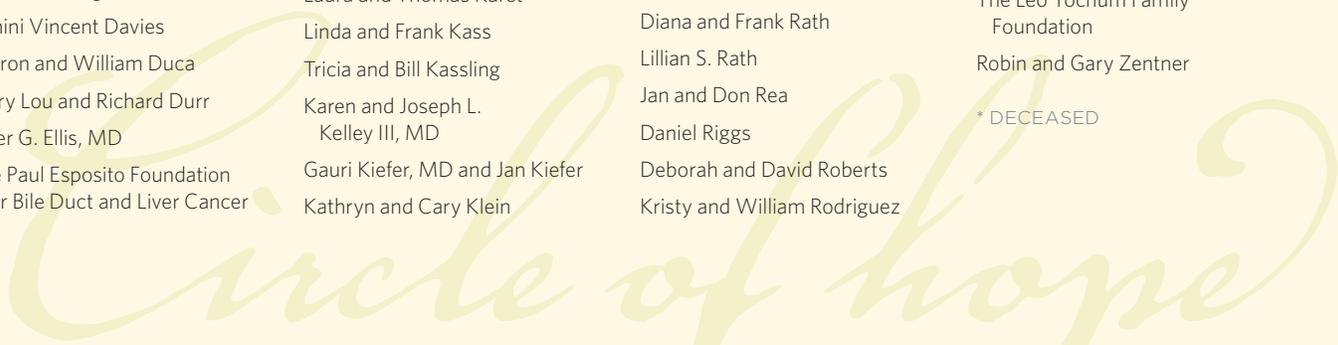


Dr. Zureikat

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★ HILLMAN CANCER CENTER
Mary Hillman Jennings Radiation Oncology Center

▲ RADIATION ONCOLOGY CENTERS

- 1 UPMC/Jameson Cancer Center
- 2 UPMC/HVHS Cancer Center at Heritage Valley Beaver
- 3 UPMC/HVHS Cancer Center at UPMC West
- 4 UPMC/St. Clair Hospital Cancer Center
- 5 Radiation Oncology Center at Jefferson Regional Medical Center
- 6 UPMC and The Washington Hospital Cancer Center
- 7 Robert E. Eberly Pavilion

■ MEDICAL ONCOLOGY CENTERS

- 8 UPMC CancerCenter, New Castle
- 9 UPMC CancerCenter, Beaver
- 10 UPMC CancerCenter, Steubenville
- 11 UPMC CancerCenter, Sewickley Medical Oncology
- 12 UPMC CancerCenter, Upper St.Clair
- 13 UPMC CancerCenter, Jefferson
- 14 UPMC CancerCenter, Washington
- 15 Arnold Palmer Pavilion at Oakbrook Commons
- 16 Arnold Palmer Pavilion at Mt. Pleasant
- 17 UPMC CancerCenter, Uniontown
- 18 UPMC CancerCenter, Windber
- 19 UPMC CancerCenter at UPMC Mercy
- 20 UPMC CancerCenter, Indiana
- 21 UPMC CancerCenter, Greenville
- 22 UPMC CancerCenter, 400 Oxford Drive

● DUAL CENTERS (RADIATION AND MEDICAL ONCOLOGY)

- 23 UPMC CancerCenter at UPMC Horizon
- 24 The Regional Cancer Center, Erie
- 25 UPMC CancerCenter at UPMC Passavant
- 26 UPMC CancerCenter, Natrona Heights
- 27 UPMC CancerCenter at UPMC McKeesport
- 28 Arnold Palmer Pavilion at Mountain View Medical Park
- 29 John P. Murtha Regional Cancer Center
- 30 UPMC CancerCenter at UPMC St. Margaret
- 31 UPMC CancerCenter at Magee-Womens Hospital of UPMC
- 32 UPMC CancerCenter at UPMC Northwest

▼ INTERNATIONAL

- 33 UPMC Beacon Hospital, Dublin, Ireland
- 34 UPMC Whitfield Cancer Centre, Waterford, Ireland
- 35 UPMC San Pietro FBF Advanced Radiotherapy Center, Rome, Italy

