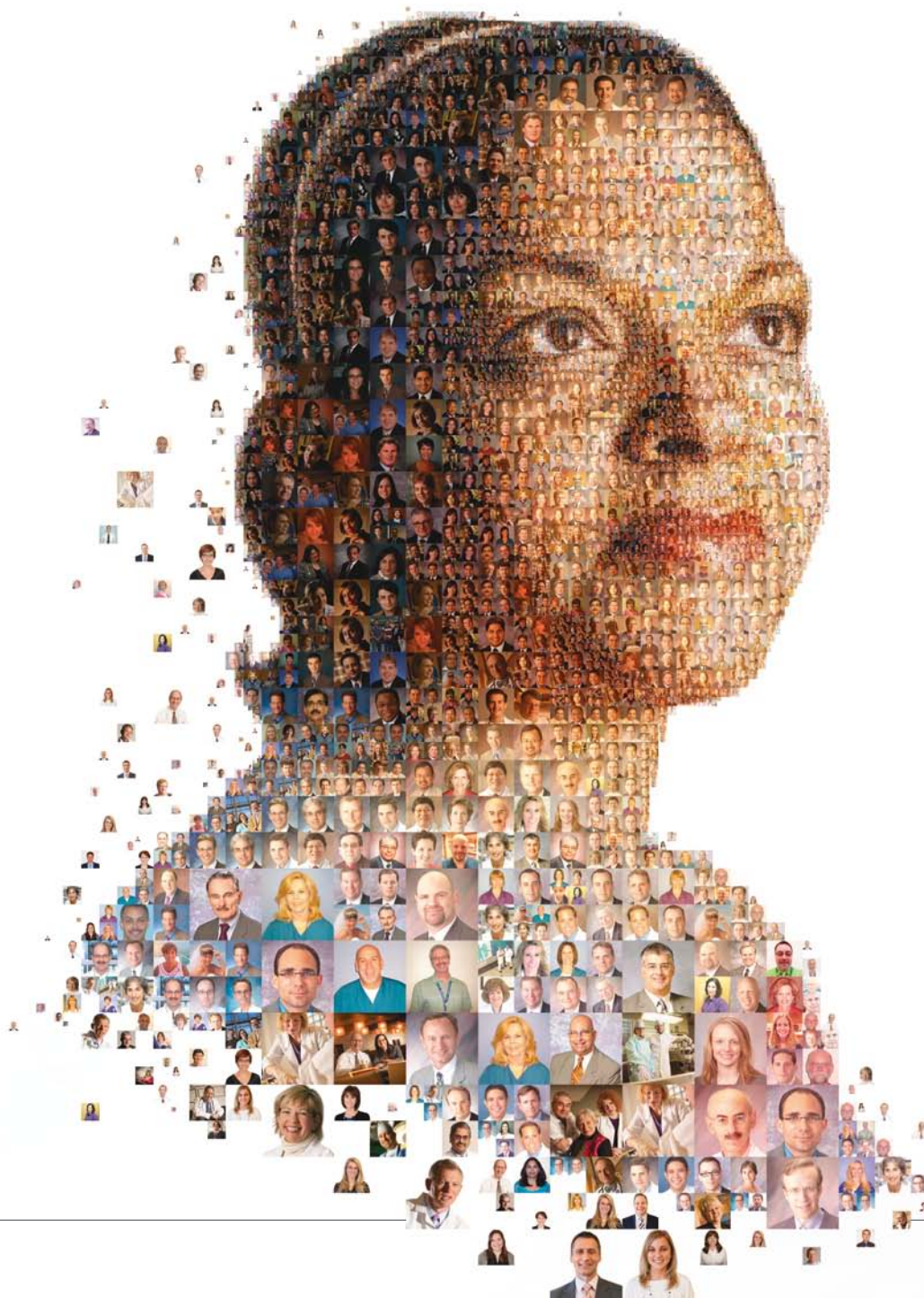



2012

For one, we are many. For many, we are one.

UPMC CancerCenter

Partner with University of Pittsburgh Cancer Institute



A close-up photograph of a woman with dark hair and bangs, smiling warmly. She is wearing a teal sweater and a colorful, multi-colored striped scarf. She is holding a yellow mug in her right hand and looking down at a newspaper or magazine in her left hand. The background is softly blurred, showing a warm, indoor setting.

“Faith, fight, family, and friends — if you recognize and do those things in that order, I truly believe your chances are much greater at beating cancer.”

For one, we are many. For many, we are one.

The cover of our 2012 Annual Report highlights the MANY physicians, researchers, administrators, and staff who contribute to our mission to provide each patient with comprehensive oncology services and programs through UPMC CancerCenter, and who work tirelessly to translate effective cancer treatments to clinical care through the University of Pittsburgh Cancer Institute.



Meet our cover model, Margo Brown.

Margo was initially diagnosed with breast cancer at UPMC CancerCenter in 2001 at age 34, following the removal of what was thought to be a cyst on her breast. “Behind the cyst was a very small tumor that had attached itself to my chest wall — it was cancer,” says Margo. Margo’s surgeon, **John A. McKeating, MD**, referred her to **Stanley M. Marks, MD**, medical oncologist, who recommended an aggressive treatment plan that included four rounds of chemotherapy at UPMC Shadyside, followed by radiation at Magee-Womens Hospital of UPMC. Margo’s radiation therapy was administered by **Dwight E. Heron, MD, FACRO, FACR**. Margo’s cancer was in remission for seven years until a very small tumor was detected during a routine mammogram in 2008. Margo again underwent aggressive chemotherapy at Hillman Cancer Center and ultimately decided to undergo a double mastectomy, performed by **Gretchen M. Ahrendt, MD**, with reconstruction performed by **Michael Gimbel, MD**. With her cancer in remission, Margo enjoys talking with other women about her experiences with cancer and sharing her philosophy for overcoming the disease. “Faith, fight, family, and friends — if you recognize and do those things in that order, I truly believe your chances are much greater at beating cancer,” says Margo.

Margo is a flight attendant and lives in Penn Hills, a suburb of Pittsburgh, with her husband, Rev. Dr. Eric Brown. In 2011, with the help of her church family, Margo coordinated an outreach project that raised \$3,500 for the Pittsburgh Affiliate of **Susan G. Komen for the Cure®**. The money ultimately provided mammograms for 35 women who were unable to afford them. She is excited to continue this effort moving forward.

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The mosaic on our cover is symbolic of the unity and partnership that is UPMC CancerCenter. Comprising more than 400 photos of our physicians, researchers, caregivers, and staff, it represents the way all of us work together to benefit our patients.

For one, we are many. For many, we are one.

We introduced these powerful words in our 2011 Annual Report when we rolled out our new UPMC CancerCenter brand. They epitomize the unification of our UPMC and University of Pittsburgh Cancer Institute (UPCI) oncology activities — from medical and radiation services to surgical services, from research and specialty areas of expertise to education — all offered across one of the nation's largest networks of cancer treatment centers.

The year 2012 marked the 10th anniversary of our move to the Shadyside campus, located just a few miles from the heart of downtown Pittsburgh. The move to this campus allowed us to bring together the research and clinical aspects of our program under one roof in what has become the nucleus of our network of cancer centers — Hillman Cancer Center.

At Hillman, basic researchers collaborate with physician-researchers and clinicians to rapidly advance the most promising laboratory studies into novel clinical trials, providing patients with early access to new and innovative treatments. This approach has yielded many success stories and we are exceptionally proud to highlight some of them from the past year.

Physician accomplishments

In 2012, **Patrick S. Moore, MD, MPH**, and **Yuan Chang, MD**, were elected to the National Academy of Sciences, a high honor bestowed on only 105 scientists around the world. They led the team that identified the virus that causes Merkel cell carcinoma and isolated a protein that allows tumor survival. These findings led to identification of a drug that hinders the effect of that protein and could lead to a therapy for this deadly skin cancer. A national clinical trial to test this approach will start this year — truly an example of bench-to-bedside research.

We are pleased that head and neck cancer specialist **Jennifer R. Grandis, MD, FACS**, was elected to the Institute of Medicine. This prestigious organization serves as the health arm of the National Academy of Sciences and seeks answers to the nation's most pressing questions about health and health care.

Two of our neurosurgery leaders, **Ian F. Pollack, MD**, and **Robert M. Friedlander, MD**, were elected to the Association of American Physicians, an honorary society for physicians that dates back to the 1880s.

And we were proud to learn that The Alliance for Cancer Gene Therapy (ACGT) named UPMC surgical oncologist **Herbert Zeh III, MD, FACS**, as its 2012 ACGT Investigator. The award comes with a \$500,000 grant that will allow him to continue his promising research focused on gene therapy for pancreatic cancer.

In Pediatrics, **A. Kim Ritchey, MD**, vice chair of Clinical Affairs at Children's Hospital of Pittsburgh of UPMC, was elected president of the American Society of Pediatric Hematology/

Oncology (ASPHO), and we welcomed **Linda McCallister-Lucas, MD, PhD**, as chief of the Division of Hematology-Oncology in the Department of Pediatrics.

Clinical highlights

In December, we were delighted to open the Mario Lemieux Center for Blood Cancers, a beautiful patient-centered outpatient facility equipped with the latest technology to provide state-of-the-art therapy and access to clinical trials for patients with leukemia, myeloma, and lymphoma. The 24,000-square-foot facility will serve about 25,000 patients a year and caps off the build-out of Hillman Cancer Center.

We began the implementation of an oncology-based electronic medical record (EMR) system. This innovative EMR will eventually connect all of our network locations, optimize our record-keeping capabilities, and enhance our patient care experience. We also opened our newest medical oncology center at UPMC Passavant-Cranberry, in one of Pittsburgh’s fastest growing suburbs located north of the city.

UPMC CancerCenter’s radiation oncology program also achieved a significant milestone when it became the largest radiation oncology system in the United States to receive accreditation by the American College of Radiation Oncology (ACRO).

Our women’s cancer program introduced radioactive seed localization technology for breast surgery at Magee-Womens Hospital of UPMC and several other UPMC outpatient surgery sites. This technology replaces wire localization procedures and is being evaluated for its impact on improved outcomes.

We also participated in a national clinical trial for sentinel mapping for vulvar cancer. The traditional treatment of vulvar cancer has involved removal of the lymph nodes in the lower abdominal region and often results in high complication rates. Sentinel mapping can help identify which patients can be treated without surgery.

Internationally, our oncology operations celebrated two milestone achievements:

- We opened the Advanced Radiosurgery Center of Excellence at San Pietro FBF Hospital in Rome, Italy, offering patients targeted high-dose radiation to treat the most challenging tumors.
- UPMC CancerCenter was selected by Nazarbayev University in Kazakhstan to conduct a feasibility study on the development of a national oncology treatment and research center in that country. UPMC is assessing the types of oncology services needed in Kazakhstan and the possibility of developing a national cancer center in the capital city of Astana.

Anticipating success

Celebrating accomplishments like these offers us the opportunity to pause, if only for a moment, to reflect on what a truly amazing year it was. That reflection, however, is exceeded by our anticipation of a new year that will bring many more successes. We look forward to scientific triumphs that will lead to better care and perhaps, one day, bring us closer to the eventual eradication of this disease that has afflicted so many of our family members and friends.

Behind every one of our patients is the collective expertise and compassion of nearly 2,500 UPMC CancerCenter and UPCI staff members. We are proud to represent them in bringing you this report.

Sincerely,

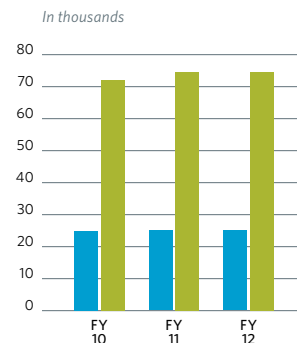


Nancy E. Davidson, MD
Director

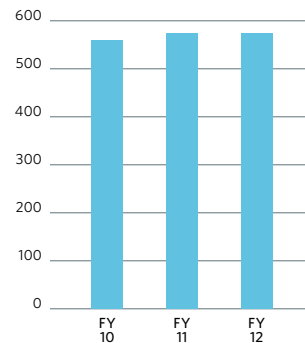


Stanley M. Marks, MD
Chairman

UPMC CANCERCENTER PATIENT VISITS*
■ New Patients
■ Unique Patients Receiving Services/Treatment



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

Diagnosis: Destiny

For ONE young man, osteosarcoma meant an eight-year odyssey through surgery, chemotherapy, remission, recurrence, and the eventual amputation of his right leg. But it also meant a passionate career commitment and a 23-year relationship with the orthopaedic oncologist who healed and later mentored him as he became an orthopaedic oncologist himself.

Rare cancer ignites a passion for a cure

When UPMC orthopaedic surgical oncologist **Kurt Weiss, MD**, reassures parents of young patients with osteosarcoma that the disease is treatable and their child has good odds of surviving this rare disease, they have reason to believe him — because in 1989, at the age of 15, Dr. Weiss himself was diagnosed with osteosarcoma in the tibia, or shinbone, of his right leg.

A high school athlete and marching band musician, Dr. Weiss had endured months of pain that wouldn't go away, despite regular doses of ibuprofen. His mother insisted they see a sports medicine specialist who, after reviewing the x-rays, referred him to UPMC orthopaedic oncologist **Mark Goodman, MD**, the very next day.

Dr. Goodman diagnosed a textbook case of osteosarcoma and broke the news to the Weiss family. "Dr. Goodman told my parents that, if the cancer hadn't spread to my lungs, I would have a 65 percent chance of being alive in five years," Dr. Weiss explains.

Dr. Weiss underwent an initial 10-week round of chemotherapy to shrink the tumor, then surgery to remove it and a bone grafting procedure to repair the damage to his tibia. A few weeks later, he underwent another surgery to remove the tumors that had spread to his lungs. "When metastases were found in my lungs, Dr. Goodman moved my odds to about 25 percent," he remembers.

About that same time, his leg incision separated and became infected. That was the start of a six-year ordeal of complications and chronic infections that accompanied the bone graft and resulted in numerous surgeries in an effort to save his leg. Only a few months later, Dr. Weiss received a **Make-A-Wish®** Foundation trip to the Orange Bowl, where he played a new tenor sax with the Notre Dame marching band.

But shortly afterward, the cancer returned to his lungs. Dr. Weiss underwent resection surgery to remove the tumors from his lungs, and his odds of survival were considered poor. His parents made burial arrangements and planned a funeral Mass. Weeks later, Dr. Weiss's sister, Gretchen, read an article in her local paper about a doctor in Houston, Texas, who was offering an experimental chemotherapy for patients with osteosarcoma that was not responsive to conventional chemotherapy. Because of his lung recurrence, he became eligible to participate in a Phase 2 clinical trial of a chemotherapy known as MTP-PE, which was being investigated as a single agent by Eugenie Kleinerman, MD, at M.D. Anderson Cancer Center in Houston.



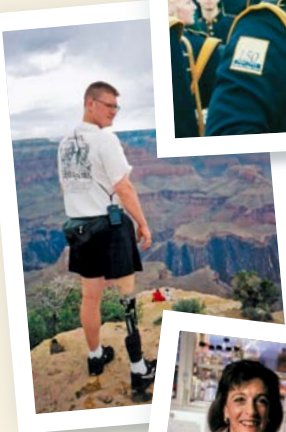
Above: Kurt Weiss following allograft surgery to save his leg, summer 1989; senior year of college with Notre Dame marching band, 1996; with Dr. Mark Goodman, left, his orthopaedic oncologist, mentor, and now, colleague.

Opposite: Dr. Kurt Weiss with his wife, Laura, and children, Connor and Annaliese.

M A N Y
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Diagnosis: Destiny



From top: Kurt with parents Joanne and Frank, and sister, Gretchen, on a family outing just before Kurt's diagnosis, spring 1989; Joanne and Frank with Kurt while he received treatment in Texas, summer 1990; Kurt as president of the Notre Dame marching band, 1995; trip to the Grand Canyon following his amputation, summer 1998; with Dr. Eugenie Kleinerman as a research assistant, summer 1999.

His treatment was initiated in Houston, and, because of Children's Hospital of Pittsburgh of UPMC's participation in the organization now known as the Children's Oncology Group (COG), Dr. Weiss was able to transfer his care and continue his treatments in Pittsburgh, under the supervision of pediatric oncologist **Michael Wollman, MD**. After six months of treatment in the clinical trial, his response was considered successful, and he has been in remission ever since.

Unfortunately, the repair surgery on his leg was not as successful, and a supportive metal plate in his leg broke a few months later, requiring several additional surgeries and treatment for severe infections. Yet he continued to defy the odds when, the next year, he was able to fulfill one of his earliest dreams — attending the University of Notre Dame. But just weeks into the first semester of his freshman year, his leg repair came apart and became so infected that he was forced to leave school and undergo several more operations to repair the bone.

He was eventually able to return to college but, not long afterward, his leg became infected yet again and, after 20 major surgeries trying to save his leg, Dr. Weiss made the decision to undergo an amputation above the knee. Although a difficult and permanent decision, the amputation ironically made his final year at Notre Dame his most mobile, because of his prosthesis, and enjoyable, because he was no longer in pain or worried about future surgeries. He marched in the Notre Dame marching band for the full football season and, the following May, graduated from Notre Dame.

The following year, he began attending Jefferson Medical College in Philadelphia. The next summer, Dr. Weiss was given an opportunity to do research at M.D. Anderson, where he worked alongside Dr. Kleinerman, the very physician who had developed the experimental chemotherapy drug that had saved his life. Also that year, he married his wife, Laura.

He then took a year off from medical school to participate in the Howard Hughes Medical Research Scholars Program at the National Institutes of Health (NIH), under the tutelage of Lee Helman, MD, one of the world's premier pediatric bone cancer investigators. At that point, he made the decision to dedicate a significant portion of his time to basic scientific research on bone cancer.

After earning his medical degree, he matriculated to the University of Pittsburgh for an orthopaedic surgery residency, which included one year in the lab of **Johnny Huard, PhD**, professor at the University of Pittsburgh and Henry J. Mankin Endowed Chair in Orthopaedic Surgery Research. While working in the Huard lab, Dr. Weiss began his own research and, using cell lines he was given by Dr. Helman at the NIH, he and Dr. Huard published a paper that same year, marking the beginning of the osteosarcoma basic science research program at UPMC.

Following his residency at UPMC, Dr. Weiss was offered a fellowship in musculoskeletal oncology at the University of Toronto. He returned to Pittsburgh in 2010 to work with his former surgeon and mentor, Dr. Goodman, and **Richard McGough, MD**, chief of orthopaedic oncology at UPMC. He has been married for almost 13 years and is the father of Connor, 12, and Annaliese, 8.

Although delivering the news of an osteosarcoma diagnosis is always difficult, Dr. Weiss often relates his personal success story and reminds parents that osteosarcoma is both treatable and curable. "I tell them that I know it's a tough situation, but they can get through it," he says. It doesn't hurt that he is living proof that not only can patients with osteosarcoma go on to live normal lives, but they can fulfill their dreams, as well.

Collaborative osteosarcoma program fights aggressive, rare bone cancer from all angles

Successfully treating the aggressive, yet rare, disease of osteosarcoma, or cancer of the bone and connective tissues, takes a combination of physicians from multiple disciplines. Although a surgical approach is typically the best option to remove the tumor, chemotherapy to shrink tumors prior to surgery and to eliminate any remaining cancer cells after surgery can be highly effective and help provide a better surgical outcome.

Fighting osteosarcoma is a team sport, according to orthopaedic surgical oncologist **Kurt Weiss, MD**. “It takes a team of orthopaedic surgeons, thoracic surgeons, surgical oncologists, medical oncologists, radiation oncologists, pathologists, and radiologists working together to provide the right combination of treatments with the right timing to yield the best patient outcomes.”

At UPMC, sarcoma patients usually enter care in the network by referral to UPMC’s surgical oncologists or through the Sarcoma Specialty Care Center (SCC), a program just for sarcomas that offers streamlined, efficient care by a multidisciplinary team of specialists. Either entry point provides access to a multidisciplinary tumor board that meets weekly to discuss and examine patients, and arrive at a consensus treatment plan that patients can begin right away. This coordinated approach allows UPMC CancerCenter, partner with University of Pittsburgh Cancer Institute (UPCI), to offer novel, intensive, and cutting-edge cancer treatments and therapies.

Sarcoma is treated surgically by the team of Dr. Weiss, **Mark Goodman, MD**, and

Richard McGough, MD, chief of orthopaedic oncology. A surgical oncology team, led by **David Bartlett, MD**, **Matthew Holtzman, MD**, **Herbert Zeh, MD**, and **James Pingpank, MD**, also participates in the management of soft tissue sarcomas. In 2007, medical oncologist **Hussein Tawbi, MD, PhD**, was recruited to establish a medical oncology program for sarcoma at UPMC CancerCenter that would enable close collaboration among the multidisciplinary team. Dr. Tawbi completed a sarcoma fellowship with sarcoma pioneer Larry Baker, MD, at the University of Michigan.

Soon after, UPCI became affiliated with the Sarcoma Alliance for Research and Collaboration (SARC), an organization dedicated to the development and support of research for the prevention, treatment, and cure of sarcoma. Within one year, UPCI had several of its own clinical trials open and accruing patients, and was participating in several additional cooperative trials with other cancer centers. In only five years, UPCI has become one of the top centers internationally for the number of sarcoma patients enrolled in clinical trials.

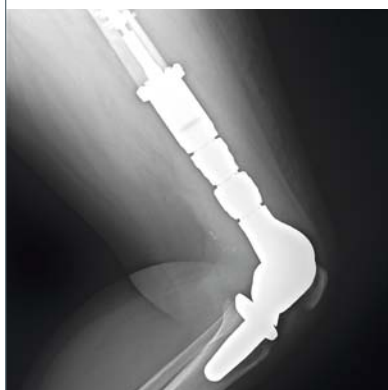
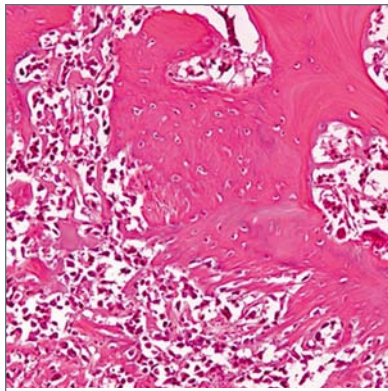


Dr. Hussein Tawbi is a medical oncologist specializing in the treatment of sarcoma at UPMC CancerCenter’s Sarcoma Specialty Care Center.

“Fighting sarcoma is a team sport. It takes a team of orthopaedic surgeons, thoracic surgeons, surgical oncologists, medical oncologists, radiation oncologists, pathologists, and radiologists working together.”

—DR. KURT WEISS

BONE CANCER



Above, top: Osteosarcoma literally means “bone-growing cancer,” but that bone growth is disordered, destructive, and malignant. This histology slide shows osteosarcoma cells both making new bone and destroying the normal, healthy bone.

Middle: This preoperative MRI scan shows a large osteosarcoma destroying the posterior femur (thigh bone) and invading the surrounding tissues of a patient diagnosed at age 16.

Bottom: After radical removal of the cancerous bone and surrounding tissues, Dr. Weiss replaced the patient’s knee joint and missing bone with a large “megaprosthesis.” Following postoperative chemotherapy, the patient was able to return to school and walks without pain or a limp.

“Our surgeons see close to 600 sarcoma patients every year, and I see about 150 of them,” says Dr. Tawbi. “Of those 150 patients, half have metastatic disease and are treated through the Sarcoma SCC. In addition, we are able to enroll roughly 25 patients a year in one of our six or seven active clinical trials that are accruing at any given time. When you consider how rare sarcoma is to begin with, those accrual volumes are very good.”

And outcomes are improving all the time. “We see patients with bone and soft-tissue sarcomas every single day, hundreds of patients every year, even though these cancers are rare — because patients are referred to UPMC from all over.” This volume, combined with excellent patient care and capability to conduct research, makes our sarcoma program among the best in the country.

One distinct advantage of seeing so many sarcoma patients has been the program’s ability to quickly build a tissue bank that can be used for research. Initially using the tissue banking resources established by UPMC CancerCenter’s melanoma program, Drs. Tawbi, Weiss, and the multidisciplinary team were able to get the sarcoma tissue bank up and running quickly. “Every sarcoma tumor removed by a surgeon at UPMC with patient consent is contributed to the sarcoma tissue bank,” says Dr. Tawbi. “This research resource is an absolutely invaluable component of any translational or clinical research program, and our tissue bank continues to grow steadily.”

“Sarcoma is a tough disease,” says Dr. Weiss. “The only good thing about it is that it is predictable — we know where it likes to go, and that’s to the lungs. We also know, historically, that more than 80 percent of people have metastatic tumor cells moving throughout their bodies at the time they’re diagnosed. The addition of chemotherapy has changed the survival rate from about 10 percent in the 1960s and 1970s to about

65 percent survival now, but it hasn’t really improved for about 30 years. So the survival rate from osteosarcoma for the kids I diagnose now is about the same as it was for me when I was diagnosed in 1989, and that’s what we’re out to change.”

There are no agents that specifically target the metastatic process for osteosarcoma, because chemotherapy targets replicating cells indiscriminately. “Nobody dies from the tumor in their arm or leg, and we can almost always save the limb where the tumor originates,” says Dr. Weiss. “But we need more intelligent ways to fight the metastatic disease, which is what I’m working on.”

Dr. Weiss’ research aims to find out how metastatic cancer cells differ from regular cancer cells and why some make that journey from the original tumor to the lungs. By figuring that out, he hopes to interrupt or stop that process. The difference between metastatic cancer cells and regular cancer cells is part of the reason why chemotherapy agents that target lung cancer do not work on metastatic cancer of the lung, which is chemoresistant.

And the tumor bank is central to his research. “The sarcoma registry and tumor bank are important initiatives,” he adds. “As soon as a surgeon removes a sarcoma in the operating room, we’ll get a sample of that tumor to start a cell line. We have all the patients’ clinical data to be able to compare patients who did well with patients who did poorly. By looking at the difference between their cells, we hope to understand the biology behind why one cell spread and another did not.”

Because osteosarcoma is so rare, only a handful of medical centers worldwide are involved in sarcoma research. UPCI, because of its existing research infrastructure, is able to conduct this research, fueled by Dr. Weiss’ passion and the support from his department head.

Radiation oncology and osteosarcoma

YEARS AGO, TREATMENT OPTIONS FOR OSTEOSARCOMA WERE LIMITED AND CONSISTED OF AMPUTATING THE LIMB WITH THE TUMOR.

Thankfully, there are now many more treatment modalities for patients with osteosarcoma — and research has shown that a multidisciplinary approach, consisting of surgical oncology, radiation oncology, and medical oncology, can positively affect patient outcomes.

“Today, we do less aggressive, ‘limb-sparing’ surgeries in conjunction with more intensive, multidisciplinary therapies in an attempt to preserve function,” says **Dwight E. Heron, MD, FACRO, FACR**, director of radiation services at UPMC CancerCenter. “Often we can use chemoradiotherapy as a neoadjuvant therapy to shrink the tumor and make it more resectable, so that when the surgery is performed, limb preservation may be realized.”

But patients with osteosarcoma almost invariably have pain; in fact, it is usually persistent pain that drives patients to their doctors in the first place when they get their initial diagnoses. “Radiation can be used for pain control, both as part of the therapeutic process — for cure — or as palliation for recurrent cancer in other bones or at end of life, because it is a very potent, but very localized, effective treatment,” explains Dr. Heron. “Radiation can reduce pain and eliminate the need to keep patients on large doses of narcotics that make them feel groggy and negatively impact their quality of life.”

UPMC is constantly pushing the boundaries with clinical trials and trying to understand this rare cancer and develop multidisciplinary ways to treat it. Often these trials draw from clinical research that was done over the past 10 to 20 years, much of which has come from the pediatric arena, since the disease is more prevalent in children and young adults.



Dr. Dwight Heron often recommends radiation to treat pain caused by osteosarcoma.

RACING FOR A CURE

Often, fundraising efforts start at the grassroots level, and that is especially true for the **Pittsburgh Cure Sarcoma 5K Run and Walk**.

What began in 2008 with a small informational gathering organized by **Anette Duensing, MD**, a UPCI pathologist and researcher, grew within two years into the Pittsburgh Cure Sarcoma (PCS) Committee, made up of former patients and family members. The committee's first major fundraising event, a 5K run/walk, was held in summer 2010 and raised \$50,000; their second event in 2012 more than doubled that amount and attracted more than 1,500 runners.

Hussein Tawbi, MD, PhD, head of UPMC CancerCenter's Sarcoma Specialty Care Center, serves on the PCS Committee, and is appreciative, not only of the work done by the committee, but also the money they raise, which helps fund sarcoma research, both locally at UPCI and nationally through the Sarcoma Foundation of America (SFA).

Dr. Tawbi's own research projects are supported by the proceeds of the event. He is currently working toward a clinical trial that will introduce novel epigenetic agents with chemotherapy in hopes of making sarcoma less resistant to chemotherapy.

CLINICAL TRIAL FOR OSTEOSARCOMA

Children's Hospital of Pittsburgh of UPMC has an actively accruing clinical trial specifically focused on patients with osteosarcoma. This Phase 3 trial is being conducted in conjunction with the Children's Oncology Group (COG) for children ages 5 and up who have resectable, histologically confirmed, high-grade osteosarcomas, including second malignancies. "The trial is studying the effectiveness of chemotherapy followed by surgery and two different combinations of chemotherapy regimens — with or without PEG-interferon alfa-2b — to compare how well they work in offering durable remission and possible cure," says **Yatin M. Vyas, MD**, the institutional principal investigator on the trial. "The idea is to see if adding a biological agent, such as interferon, augments cure rates, or not." Participants enrolled in the study will undergo chemotherapy using the standard anticancer regimen for two months, followed by surgery and assessment of their response. Participants will then be separated into two groups — those who had good response and those who had poor response — and each group will be randomly assigned to further chemotherapy using standard or experimental regimens. Results will be compared to see whether the experimental regimen is better than, equal to, or worse than the currently accepted regimen based on effectiveness, side effects, and hospital lengths of stay.

UPCI building strong bone and mineral research program

Bone-related research has always been a strength of the University of Pittsburgh Cancer Institute (UPCI). **Deborah L.**

Galson, PhD, assistant professor of medicine at the University of Pittsburgh and member of the UPCI Molecular and Cellular Cancer Biology Program, recognized that strength and helped form the collaborative Pittsburgh Center for Bone and Mineral Research (PCBMR).

A molecular biologist whose expertise lies in osteoclast differentiation, Paget's disease, and multiple myeloma, Dr. Galson is pioneering efforts to unite researchers at the University of Pittsburgh, Carnegie Mellon University, and Duquesne University who have interest in all aspects of bone biology.

The PCBMR is expected to:

- Help investigators locate resources around Pittsburgh, including state-of-the-art instrumentation and methodology for conducting bone-related research.
- Develop fruitful collaborations.
- Serve as a resource for researchers who find their work moving unexpectedly into the field of bone biology.
- Showcase the extensive bone-related research that is being conducted in Pittsburgh.

The PCBMR sponsors a monthly seminar series that features lectures by both internal and external experts in the field of bone and mineral research, covering a diverse array of topics, including bone development and remodeling, bone cancers and bone metastases, and immune-related bone issues, such as arthritis and inflammation, among many others.

SARCOMA WARNING SIGNS

Bone sarcoma is a very rare disease — roughly one in 500,000 children receives a sarcoma diagnosis — that typically causes pain in the limbs, particularly the legs. Because many youngsters complain of "growing pains" in their legs, how do you know when bone pain is a part of normal growth and when it should be checked out by a doctor?

"Osteosarcoma, or cancer of the bones, usually occurs during periods of rapid growth — mainly adolescence — when the child is past the typical growing pain years," says **Michael Wollman, MD**, pediatric oncologist at Children's Hospital of Pittsburgh of UPMC. "About 75 percent of osteosarcomas present in the long bones above or below the knee. Ewing sarcoma, another form of bone sarcoma, can present anywhere — but the hip, the spine, and the long bones are common sites."

Parents should seek a doctor's advice if their child has any pain that:

- Is persistent in one place.
- Does not respond to ibuprofen or acetaminophen.
- Wakes a child up during the night.
- Causes a limp, difficulty walking, or change in gait.
- Includes swelling at the site.
- Is present with fever or other systemic symptoms.

Because teenagers often are more private with their bodies, parents should ask about and monitor any persistent pain of which their child may complain.

Aposense clinical trial improving predictive abilities of imaging

For years, doctors have been able to image apoptosis, or programmed cell death, in “dead” tissue that has been removed from a patient and stained for visualization. But how would doctors change their patients’ treatment plans if they could visualize apoptosis in vivo — in the living tissue of a live patient?

Dwight E. Heron, MD, FACRO, FACR, director of radiation services at UPMC CancerCenter, recently served as a principal investigator on a clinical trial of Aposense®, an experimental small-molecule tracer that makes it possible to image apoptosis in living patients, in real time. UPMC CancerCenter, partner with University of Pittsburgh Cancer Institute (UPCI), served as the lead institution working with Aposense Ltd. to evaluate the use of this tracer to measure changes in apoptotic levels before and after treatment, and recently presented the interim results of one study at the annual meeting of the American Society for Radiation Oncology (ASTRO).

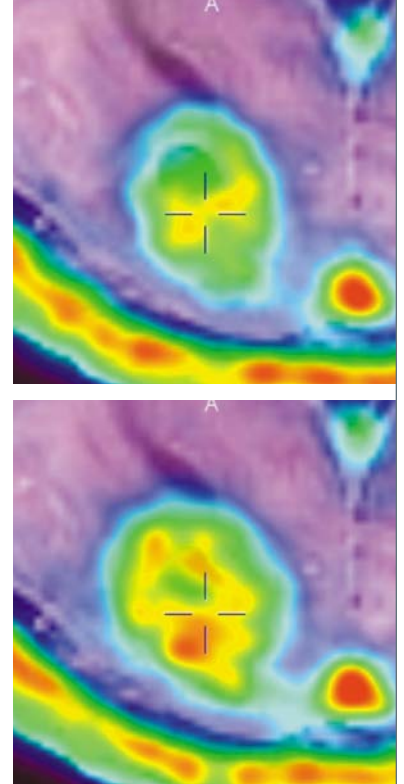
The study used Aposense to image patients with metastatic brain tumors who had been treated with stereotactic radiosurgery (SRS). As part of the study, each patient received a PET-CT scan using the Aposense tracer before undergoing SRS to determine a baseline level of apoptotic activity. The PET-CT scan was repeated 24 hours after SRS and compared to the first MRI three months after treatment. The premise was that the change in apoptotic levels between the pre-SRS and post-SRS images would predict the patient’s response to intervention. The study found that, within 24 hours, the change in apoptotic index revealed on the second PET-CT using the Aposense tracer predicted the patient’s

response to treatment with the same accuracy as an MRI performed at three months post-intervention.

“This advance knowledge gives physicians information about how well the patient is going to respond to the treatment right away, rather than three months down the road,” says Dr. Heron. “That shortened time-to-knowledge offers unique and interesting opportunities, not only for the patients who are going to respond well, because we know they’re going to do fine, but more importantly for the patients who don’t respond as well to SRS. We can then intervene in a way that would make a difference in outcome — such as adding another course of radiosurgery or chemotherapy or some other treatment — with the benefit of time on our side.”

A similar study is actively enrolling patients with head and neck and lung cancers and preliminary results seem promising. Results are expected to be published within the next year.

These studies represent the future of cancer care, which is moving away from an anatomic approach toward a more molecular assessment of tumor profiles and response. Because the images reveal what is happening in the tumor functionally at the cellular level, physicians may be able to tell whether patients are responding to intervention and can provide more targeted approaches for patients earlier if the intervention isn’t working.



Before, top, and after: MRI PET-CT study demonstrating increase in apoptotic signal (yellow area) in the index tumor with 24^h after SRS treatment.

Understanding brain cancer and developing novel treatments

Gliomas are tumors in the brain that arise from glial cells, the supportive glue-like tissue that helps to keep neurons in place and functioning. Malignant gliomas are among the most common and deadly brain tumors. There are several types of gliomas, characterized 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.

Glioblastoma multiforme (GBM), also known as grade IV (severe) astrocytoma, is the most aggressive malignant primary brain tumor in adults and has the worst prognosis of any central nervous system malignancy, with the exception of the brainstem gliomas, which can begin as low-grade tumors and evolve into GBM. Despite multimodality treatment — including surgical resection to remove as much of the tumor as possible, concurrent or sequential chemotherapy and radiation therapy, antiangiogenic therapy, and stereotactic radiosurgery — prognosis is extremely poor, and the disease is almost always fatal.

The University of Pittsburgh Cancer Institute (UPCI) has initiated a number of research projects devoted to a daunting task — increasing the understanding of gliomas so that novel treatment for these malignant brain cancers can be developed.

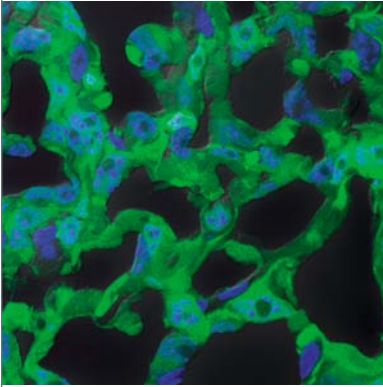
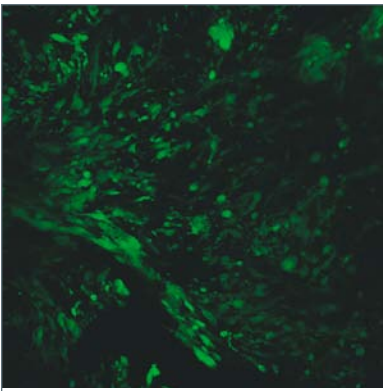
Nduka M. Amankulor, MD, recently joined UPCI and UPMC CancerCenter and the Department of Neurological Surgery as an assistant professor. In addition to his clinical practice, Dr. Amankulor is a cancer biologist whose research focuses on the tumor microenvironment, which contains normal, non-neoplastic cells that may contribute to tumor growth and maintenance. Within platelet-derived growth factor (PDGF)-driven

murine gliomas, tumor-associated astrocytes (TAAs) make up a large component of the tumor microenvironment. Dr. Amankulor and his colleagues identified unique gene expression patterns between populations of TAAs and suggested potential roles for stromal astrocytes within the glioma microenvironment. They showed that certain stromal astrocytes in the tumor microenvironment express a GBM-specific gene signature and that the majority of these stromal astrocyte genes can predict survival in humans with GBM.

Hideho Okada, MD, PhD, is a professor in the departments of Neurological Surgery, Surgery, and Immunology, as well as co-leader of the UPCI Brain Tumor Program.

Dr. Okada's lab was the first to identify and fully characterize cytotoxic T-lymphocyte (CTL) epitopes for gliomas. His seminal discovery of CTL epitopes in glioma-associated antigens and work on the mechanisms underlying the adjuvant effects of the experimental drug poly-ICLC enabled Dr. Okada to launch novel glioma vaccine trials in combination with poly-ICLC as adjuvant therapy. The first of these — a Phase 1 study for recurrent high-grade glioma — has already yielded evidence of the vaccine's safety and ability to evoke relevant immunological responses, as well as preliminary, but promising, clinical responses, such as a case of complete remission of GBM.

Recently, Dr. Okada has been working to launch clinical trials for glioma patients using a novel personalized medicine approach to immunotherapy. This Phase 1-2 study will be part of a larger collaborative effort by the nine-center Glioma Actively Personalized Vaccine Consortium (GAPVAC), which comprises eight European centers and the University of Pittsburgh. Dr. Okada and his collaborators will try to transform the treatment of glioma



Above, top: Interferons are important mediators of immune response against cancer. This slide shows the cells producing interferons, expressing green-fluorescence signals, in genetically engineered mice.

Middle: Close up of genetically engineered mouse glioma tissues, showing many interferon-producing cells.

Bottom: Dr. Hideho Okada is advancing glioma treatment options by launching novel clinical trials for glioma patients.

“Radiosurgery can be used with neoadjuvant chemotherapy to shrink tumors in patients who were considered unresectable, rendering them surgical candidates and positively affecting their odds for survival.”

—DR. DWIGHT HERON

by developing a novel method for generating a glioma vaccine customized to each patient based on the genetic pattern of his or her tumor. Each patient’s tumor tissue will be analyzed for peptides that are overexpressed or mutated. Next-generation exome sequencing and a novel method for predicting immunogenic peptides (peptidomics) will be integrated to assess each patient’s specific mutated peptides. The European Union has

funded this research at the eight European sites; Dr. Okada was able to obtain generous funding from Voices Against Brain Cancer, the Musella Foundation for Brain Tumor Research and Information, and Gray Matters Brain Cancer Foundation, making UPCI the only site in North America to participate and enroll patients.

CyberKnife® is a highly versatile stereotactic radiosurgery device capable of targeting tumors throughout the body with millimeter accuracy.

UPMC’S RADIOSURGICAL EXPERIENCE GOES GLOBAL

For more than 30 years, UPMC has been known as a pioneer in stereotactic radiosurgery (SRS), “bloodless” surgery that enables the treatment of tumors deep within the brain and spinal cord. Three years ago, UPMC attained the milestone of treating its 10,000th patient using the Gamma Knife®.

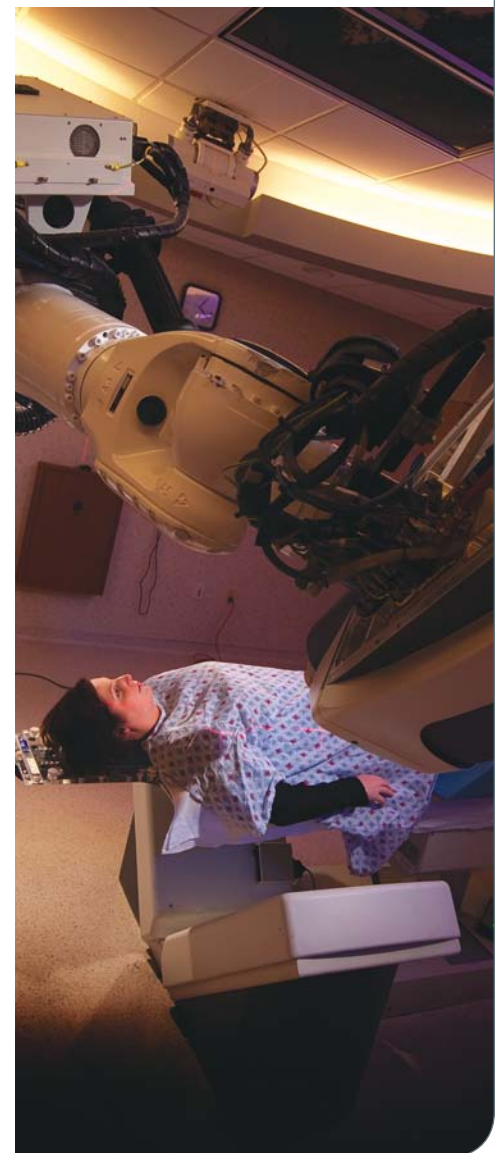
Now, through the close collaboration of radiation oncologists, neurosurgeons, and medical physicists, UPMC is approaching a new radiosurgical milestone of treating its 12,000th patient using the Gamma Knife — yet countless more patients have been helped throughout the world by the sharing of UPMC’s radiosurgery experience.

According to **Dwight E. Heron, MD, FACRO, FACR**, director of radiation services, UPMC CancerCenter regularly hosts physicians from around the world to be trained on these devices. These physicians then return to their own countries to implement successful radiosurgery programs, affecting thousands more people worldwide.

The concept of radiosurgery began in Pittsburgh in 1987 when the Gamma Knife was first used here, and has evolved into the newer technologies that make up UPMC CancerCenter’s SRS program, among them the CyberKnife®. UPMC was one of the first centers in the world to use the CyberKnife and, in the last two years, its Mary Hillman Jennings Radiation Oncology Center at UPMC Shadyside was recognized as the top site in the United States and fourth in the world for total procedures done using the device.

Two additional cutting-edge devices — the Trilogy™ linear accelerator and our newest acquisition, the Novalis® powered by TrueBeam™ STx system, a novel radiosurgical device — complete UPMC’s radiosurgical offerings and have been used over the past decade to treat nearly 18,000 patients.

“These devices use the same principal of applying a highly focused radiosurgical beam to treat the most challenging cancers, such as head and neck, liver, and pancreatic cancers,” says Dr. Heron. “In addition, radiosurgery can be used with neoadjuvant chemotherapy to shrink tumors in patients who were considered unresectable, rendering them surgical candidates and positively affecting their odds for survival.”



One sister's mission

Her MANY followers (5,000) know her as Steelegurl, the blogger and football fan dedicated to all things Steelers n'at. To her family and friends, she's Lahne, whose love for the Pittsburgh Steelers turned into a side job, and whose love for her younger brother turned into a mission.

Steelegurl's blog raises funds for cancer research

Lahne Mattas grew up in a close-knit family in Altoona, Pa., with her parents, grandparents, and brother Brian. Everyone in her family loves the Pittsburgh Steelers. "People say they 'bleed black and gold' and that would be true for everyone in my family," says Lahne, whose love for the black and gold stayed with her through college and a career in public relations and marketing.

In 2008, after her friend joked that she should create a Steelers blog, she purchased the URL Steelegurl.com and has since had booming success, even catching the eye of the NFL. "Women fans have been a target market for the NFL," says Lahne. "I've been lucky to have the opportunity to attend the NFL Draft a few times and Media Day at Super Bowl XLV when the Steelers played Green Bay in 2011."

In 2011, Lahne's priorities shifted when she learned her brother Brian had developed oral cancer. "Brian didn't have the typical risk factors associated with this type of cancer, such as smoking and drinking," says Lahne. "It was a shock to the family." Brian had surgery in November 2011 to remove the tumor, but a scan in February 2012 showed that the cancer had recurred. He underwent a second surgery, followed by chemotherapy and radiation.

"It's so hard to watch a loved one go through cancer treatment and know there's nothing you can do to take away the pain," she says. "Cancer really makes you feel helpless. That's when I realized I could help others through my blog and social networking."

Lahne was put in touch with **Robert L. Ferris, MD, PhD**, chief of the Division of Head and Neck Surgery; professor of otolaryngology, immunology, and radiation oncology; and associate director of translational research and co-leader, Cancer Immunology Program, UPCI. According to Dr. Ferris, the majority of oral cancers are associated with tobacco and alcohol, but in recent years, the oncology community has learned that the human papillomavirus (HPV) has also been associated with causing cancer of the oropharynx, which is the middle part of the throat, including the soft palate, the base of the tongue, and the tonsils. Still, in up to 30 percent of cases, patients have no known risk factors, as was the case with Brian. Yet, he succumbed to his cancer in January 2013.

Dr. Ferris currently is investigating a vaccine that would inhibit HPV from initiating cancer development. Although Brian's cancer wasn't associated with the virus, Lahne felt it was important to support his research. "While Dr. Ferris' work did not help my brother directly, we're looking to help Dr. Ferris prevent HPV-positive patients from getting cancer so no other family has to go through this," says Lahne.

\$10 FOR 10K

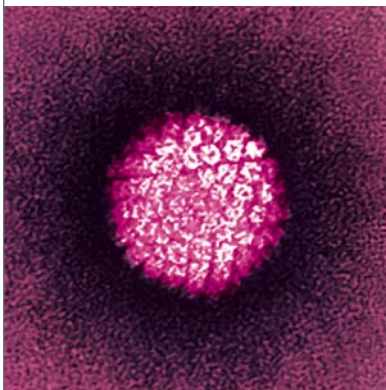
Lahne has called upon her blog friends and community to step up and donate to Dr. Ferris' research in a campaign called \$10 for 10K. "If every one of my followers donated \$10, we would easily reach our goal of \$10,000," she says.

"Lahne's effort to educate the public about this type of oral cancer is just as important as funding the research to prevent it," says Dr. Ferris. "Her campaign will help drive UPMC CancerCenter and UPCI efforts to curb HPV-associated oral cancers."



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Awareness is key to early diagnosis of HPV-related head and neck cancers



Above, top: Recruited in 2012, Dr. Julie Bauman specializes in head and neck cancer and thyroid cancer, as well as pioneering novel clinical trials.

Bottom: The human papillomavirus has been shown to cause cancer of the oropharynx.

Tobacco and alcohol have long been identified as risk factors for developing many types of cancers, including head and neck cancers. In the last decade, however, researchers have determined that the human papillomavirus (HPV), a common cause of cervical cancer, also plays a large role in causing cancer of the oropharynx. Head and neck cancer experts at UPMC CancerCenter and the University of Pittsburgh Cancer Institute (UPCI) are actively pursuing preventive therapies and targeted treatment for patients with HPV-associated head and neck cancers.

Not everyone infected with HPV will develop cancer, according to **Jonas T. Johnson, MD, FACS**, the Dr. Eugene Myers Professor and chairman of otolaryngology. In 2011, UPMC CancerCenter treated 645 patients with head and neck tumors, 64 of which were HPV-positive. “Most HPVs are innocuous,” says Dr. Johnson. “Unfortunately, some people will be exposed to the oncogenic subtypes, but won’t be diagnosed with a cancer until 15 to 20 years later, when the HPV mutates and the cancer exposes itself as an ulcer on the back of the tongue or tonsils, the most common sites for HPV-positive head and neck cancers.”

Dr. Johnson meets weekly with other head and neck specialists from radiation oncology, medical oncology, immunology, and radiology in a multidisciplinary forum called the Head and

Neck Cancer Specialty Care Center (SCC), to discuss new patient cases, develop treatment plans, and evaluate existing patients’ treatment plans. This multidisciplinary approach to oncology care is a highly effective way to explore all available treatment options and offer optimal care for patients. One of Dr. Johnson’s colleagues in the meeting is **Dwight E. Heron, MD, FACRO, FACR**, director of radiation services at UPMC CancerCenter.

“HPV has revolutionized how we think about head and neck cancers and is challenging us to rethink our conventional assumptions about these tumors,” says Dr. Heron. Within the last five years, it’s been determined that HPV-positive head and neck cancers respond better to standard treatment than head and neck cancers caused by other risk factors, such as smoking.

ONE OF THE NATION’S TOP CLINICAL RESEARCHERS COMES TO PITTSBURGH

UPMC CancerCenter and UPCI have added to their already experienced group of head and neck cancer specialists with the recruitment of **Julie Bauman, MD, MPH**. Dr. Bauman is a medical oncologist, assistant professor of medicine, director of the Head and Neck Cancer Section and Thyroid Cancer Section in the Division of Hematology-Oncology, and co-director of the UPMC Head and Neck Cancer Center of Excellence. She specializes in the treatment of head and neck cancer and thyroid cancer. Since coming on board, Dr. Bauman has developed three clinical trials intended to bring cutting-edge laboratory findings into the care of head and neck cancer patients. In 2011, she was honored with the NCI Cancer Clinical Investigator Team Leadership Award.

"Knowing that a patient's tumor is HPV-positive, we can adjust the patient's treatment plan to de-intensify therapies, which may reduce treatment-related side effects, and achieve the same result — remission," says Dr. Heron.

James Ohr, DO, medical oncologist, UPMC CancerCenter, and assistant professor of medicine, also attends the weekly meetings and says early detection of HPV-positive head and neck cancers is as important as in any other cancer, but notes the lack of education surrounding HPV-associated head and neck cancers is a problem. "We have done such a good job at educating the public on the cancer dangers of tobacco that many people will ignore symptoms — such as a prolonged tongue or mouth ulcer, a hoarse voice, or difficulty swallowing — because they're unaware that HPV can lead to head and neck cancers," says Dr. Ohr. "Educating

patients and dentists to perform oral cancer evaluations is important."

Multidisciplinary care

Designated nurse coordinators for the Head and Neck Cancer SCC will schedule a patient to see a member from each specialty, oftentimes on the same day, or within a few days of each other. Afterward, the patient's options are weighed during the meetings and a final treatment plan is developed, based on input from all specialties. Clinical trial options also are considered for patients who might benefit from them.

"I can't speak highly enough about the benefits of the multidisciplinary approach in treating HPV-positive head and neck cancers," says Dr. Heron. "Our team works well together in developing ideas and sharing resources. We have tremendous talent focused on making the therapies we deliver kinder, gentler, and more effective."

HPV is a group of up to 150 viruses that are spread through sexual contact. According to the National Cancer Institute (NCI), half of sexually active people are infected with one or more HPV types at some point in their lives — making HPV the most common sexually transmitted disease.

Dr. James Ohr, left, and Dr. Jonas Johnson meet weekly with head and neck cancer colleagues to discuss and review treatment options for current patients.



New program provides personalized care for patients with virus-associated cancers

For patients who present with virus-associated cancers, such as human papillomavirus (HPV)-positive head and neck cancers, a new research-based collaborative effort between UPMC and the University of Pittsburgh Cancer Institute (UPCI) has been formed to improve personalized treatment options. The Translational Microenvironment/Viral Oncology Program was founded and is directed by **Robert Ferris, MD, PhD, FACS**, chief of the Division of Head and Neck Surgery; professor of otolaryngology, immunology, and radiation oncology; associate director for translational research; and co-leader, Cancer Immunology Program, UPCI.

According to Dr. Ferris, the program aims to enhance and accelerate a cancer patient's own body response to virus-associated cancer by understanding how cancer cells interact with their microenvironment, including immune, inflammatory, and patient-specific factors that regulate the development, progression, and response to cancer treatment, such as chemotherapy.

The program will examine why some people develop a virus-associated cancer, such as HPV-positive head and neck cancer, while others exposed to the same virus do not. Utilizing molecular findings from laboratory research in this specific subset of cancer cells, program investigators are teaming up to develop targeted, virus-specific therapeutic interventions and methods for immunoprevention, such as a vaccine that would provide an opportunity to intervene and prevent the virus from initiating cancer development.



UPCI SPORE in head and neck cancers

Since 2002, the University of Pittsburgh Cancer Institute (UPCI) has received continuous funding from the National Cancer Institute (NCI) for a Specialized Program of Research Excellence (SPORE) in Head and Neck Cancers. Led by **Jennifer Rubin Grandis, MD, FACS**, principal investigator, pictured above, and **Jonas T. Johnson, MD**, co-principal investigator, the SPORE uses an interdisciplinary approach to meet its objective, which is to improve the detection and treatment of head and neck cancers by carrying out projects with co-investigators in basic, applied, and clinical science.

The long-term goal of the SPORE is to conduct clinical studies using research results from the translational research projects that will serve as the basis for improving the outcome of patients diagnosed with head and neck cancer. SPORE investigators work together and interact with other SPORE investigators from across the country to improve the outcome of patients with head and neck cancers.

UPCI Head and Neck SPORE investigators recently validated a novel method of inhibiting the signal transducer and activator of transcription (STAT3), which is involved in uncontrolled cell growth, or cancer. This new method also may be used to inhibit other cancer-causing proteins. EGFR-expressing head and neck tumors typically result in poor survival. Furthermore, the presence of a modified EGFR protein is an independent predictor of a poor outcome.

High copy number of the TMEM16A gene occurs in several malignancies. Recently, UPCI Head and Neck Cancer SPORE researchers discovered a function of TMEM16A in tumor development. They also developed a small-molecule inhibitor of the protein. Future investigations will explore the clinical application of the TMEM16A inhibitor.

"While the clinical treatments available to HPV-positive head and neck cancer patients — such as surgery, chemotherapy, and radiation — are helpful for patients with advanced disease, we have an opportunity to intervene and prevent the virus from promoting development into cancer by enhancing antiviral immunity, monitoring for recurrent disease, and developing better screening methods," says Dr. Ferris. "That is our goal with the program."

Emphasis within the program is placed on establishing productive scientific collaborations between researchers and clinicians so that research observations can be quickly developed into novel therapeutic targets and established in clinical trials.

Program laboratories will be located in the newly designed Center for Innovative Sciences (CIS) building that is scheduled to open in 2016 on the UPMC Shadyside campus, adjacent to Hillman Cancer Center.



Dr. Robert Ferris and investigators at the Translational Microenvironment/Viral Oncology Program are committed to improving personalized treatment options for patients with virus-associated cancers.

MIKE BERDAR: HEALING FROM HEAD AND NECK CANCER

Following a lingering bronchitis infection in late 2011, Mike Berdar of West Mifflin, Pa., noticed that his left lymph node was enlarged. At his wife's urging and his family's insistence, Mike found himself in the office of **Jonas T. Johnson, MD, FACS**, the Dr. Eugene Myers Professor and chairman of otolaryngology.

After examining Mike, Dr. Johnson noticed an abnormality on his tonsil, and suggested a tonsillectomy, or surgical removal of both his tonsils. Dr. Johnson sent the tonsil tissue for biopsy, which confirmed squamous cell carcinoma, related to exposure to the human papillomavirus (HPV). Dr. Johnson also determined that Mike's enlarged neck was a result of the cancer spreading from his tonsils.

"I had never heard of this type of cancer," says Mike. "But I prayed with my family and kept my faith that I would get through this."

Within the last decade, the oncology community has studied the link between HPV and oropharynx cancer, which is cancer that arises on the middle part of the throat, including the soft palate, the base of the tongue,

or the tonsils, and the public is now being educated that HPV, in addition to smoking and tobacco use, may be a risk factor for developing this type of cancer.

Three weeks following his procedure, Mike began his cancer treatment regimen, which included eight rounds of chemotherapy and 35 radiation treatments. "The radiation treatments, for me, were the hardest part of my treatment," says Mike. "Because the radiation was directed at my mouth, I developed extremely painful blisters and swollen lips. I couldn't eat because swallowing hurt so bad."

Prior to his treatment, Mike was surgically fitted with a feeding tube, which allowed him to take in liquid protein and calories during his treatment. "The feeding tube was really a blessing," says Mike. "After the first two radiation treatments, I lost my taste buds, salivary glands, and I developed dry mouth, which made it difficult to swallow. Soon, it became too painful to swallow, so the feeding tube was really important."

Due to the tonsillectomy and the radiation treatments, Mike ultimately lost 50 pounds, but through the support of his wife, Joan, he was able to have the feeding tube removed only a few weeks after his treatment. "My doctors were very impressed with how I was eating and maintaining my weight," says Mike. "My wife saw that I followed their instructions to the letter so that I could get back to healthy as soon as possible."

Today, Mike's cancer is in remission and according to Dr. Johnson, he has a good prognosis. "I'm so thankful for my dedicated doctors who knew just what to do, for my wife and my family who never left my side, and for my faith in the Lord," says Mike.



UPCI preclinical imaging suite expands research capabilities

“The preclinical PET-CT imaging suite will offer UPCI researchers the opportunity to noninvasively investigate the expression of a plethora of tumor-related proteins, as well as other hallmarks of cancer and metastasis, such as oxygen deprivation, tumor blood vessel formation, and glucose or fatty acid metabolism. These preclinical studies can be directly translated into humans.”

—DR. CAROLYN ANDERSON

Advancing research that will enable targeted, personalized cancer therapies requires the integration of information from many imaging modalities. The University of Pittsburgh Cancer Institute’s (UPCI’s) In Vivo Imaging Facility (IVIF) provides unique state-of-the-art resources for both clinical and preclinical research, including ultrahigh-field magnetic resonance imaging (MRI), positron emission tomography-computed tomography (PET-CT), simultaneous MRI-PET, and optical (bioluminescence and fluorescence) and ultrasound imaging. The goals of the IVIF are to facilitate protocol development for cancer detection, diagnosis, and staging; provide methods for clinical assessment of early therapeutic response; and provide preclinical assessment of biomarker expression throughout cancer treatment.

In September 2012, renovation of the multi-modality preclinical imaging suite at Hillman Cancer Center was completed, providing investigators access to a Siemens Inveon® small animal PET-CT scanner. Directed by **Carolyn Anderson, PhD**, professor of radiology, University of Pittsburgh School of Medicine, the new preclinical PET-CT and adjacent radiochemistry laboratory enable noninvasive small animal imaging of molecular targets, and represent a highly valuable tool for studying cancer biology and determining cancer therapy effectiveness. In addition, this new technology facilitates translational research aimed at improving clinical PET-CT imaging methods for cancer patients.

K. Ty Bae, MD, PhD, professor and chairman of radiology, played a key role in bringing this innovative technology to UPCI. “We are so excited to have one of the best preclinical

imaging facilities in the country in our backyard,” says Dr. Bae. “This new facility will promote and reinvigorate collaborations between imaging researchers and oncology investigators to lead to new discoveries and advance science.”

In addition to PET, CT, and PET-CT imaging services, the preclinical PET-CT imaging suite is working to develop and produce new radioactive tracer molecules that can be used in research studies to track distribution and pharmacokinetics of drugs and other molecules of interest. For example, one ongoing project is examining how diet affects glucose metabolism in tumor-bearing mice by tracking the FDA-approved glucose mimic, ¹⁸F-labeled 2 deoxyglucose (FDG), through PET-CT imaging.

Expert facility staff offers consultation services to investigators to discuss specific research objectives and the appropriate PET imaging protocol to employ. Consultations include guidance in experimental design, development, validations, and implementation of methodology and the interpretation of imaging data.

These PET-CT services complement the extensive imaging capabilities offered through the preclinical MRI, optical, and ultrasound instrumentation of the IVIF that is housed nearby.

State-of-the-art preclinical MRI technology

Comprehensive, economical, and state-of-the-art preclinical MRI services enable real-time analyses of physiological, cellular, and molecular processes, as well as responses to medical interventions and treatments. MRI methodologies aid investigators in their



cancer-related research by enabling the measurement of tumor volume, monitoring of drug pharmacokinetics, and tracking of cell division and movement, among many other applications. In addition, the instrumentation and expertise of the IVIF provides cancer researchers with the opportunity to examine tumor protein levels, tumor metabolism, and “hallmarks of cancer,” such as tumor blood vessel formation, metastasis, and evasion of programmed cell death.

The Hillman Cancer Center preclinical imaging suite houses a 7T translational small animal MRI system, a Bruker 7T ClinScan®. The instrument uses the same user interface as the human clinical systems housed in the Magnetic Resonance Research Center (MRRC) at the University of Pittsburgh, facilitating the clinical translation of new preclinical discoveries, such as cancer imaging biomarkers and techniques, to clinical studies in patients.

This instrument was purchased in part with a grant from the National Institutes of Health

(NIH) and was made possible with additional foundation donations to UPCI. “We thank those generous individuals and foundations who donate to UPCI and make life-saving research possible,” says **Nancy E. Davidson, MD**, director of UPCI and UPMC CancerCenter. “In a time of reduced government spending and budgets, contributions from individuals and foundations make our work possible.”

Optical and ultrasound imaging capabilities

The UPCI small animal optical and ultrasound imaging services of the IVIF provide expertise and equipment that enable researchers to quickly, easily, and inexpensively answer technical cancer-related questions in animal models. The imaging suite is equipped with several versatile instruments, including an IVIS® 200 bioluminescence and fluorescence imaging system (Perkin Elmer), an FMT2500 fluorescence tomographic imaging device (Perkin Elmer), a Lumina XR system with bioluminescence, fluorescence, and x-ray

Dr. Carolyn Anderson and her colleagues at the UPCI In Vivo Imaging Facility provide state-of-the-art imaging capabilities to advance physician-researchers’ understanding of cancer and how to treat it.

THE PITTSBURGH FOUNDATION ENDOWS CHAIR AT UPCI

The Pittsburgh Foundation has made a leadership gift of \$1 million to the University of Pittsburgh Cancer Institute (UPCI) to establish **The Pittsburgh Foundation Endowed Chair in Innovative Cancer Research**, which will support critical and innovative cancer research at UPCI. This major partnership is a demonstration of The Pittsburgh Foundation's deep commitment to Pittsburgh and its mission to build a better community by investing philanthropic resources to meet critical community needs.

Endowed chairs serve as cornerstones of established academic institutions, and last in perpetuity. Researchers and physicians who hold the chairs use the annual interest on the investment to fund research programs and teaching. Funds are used in conjunction with other available funding to reach even higher levels of achievement. The chairs have national and international visibility, making them important in efforts to recruit and retain world-class leaders.

UPCI development officers are working to raise \$1 million in additional donations to match The Pittsburgh Foundation's commitment and fully fund the endowed chair. For more information or to support this initiative, please call 412-623-4700.

IMAGING

imaging capabilities (Perkin Elmer), and a Visual Sonics Vevo[®] 770 small animal ultrasound. These tools facilitate numerous cancer-relevant experimental applications, including three-dimensional reconstructions of tumors in living animals; rapid and sequential measurements of tumor growth, progression and spread, and response to therapy relapse; determination of trafficking, biodistribution, and persistence of cell-based immunotherapies, stem cells, and gene-based therapies; monitoring of host immune-cell responses; targeted delivery of genes to tumors; profiling of gene-expression patterns

or enzymatic activity; and determination of tumor vasculature and blood flow prior to and after therapeutic intervention.

Optical and Ultrasound Imaging Director **Stephen Thorne, PhD**, assistant professor of surgery, is available to assist investigators in defining the best research model and imaging modality to achieve their experimental goals. "The implementation of state-of-the-art optical imaging techniques to cancer research has provided the opportunity to study the disease in a more realistic context and so has advanced our understanding of cancer and how to treat it," says Dr. Thorne.

New center brings mass spectrometry to the masses

The Biomedical Mass Spectrometry Center is a campus-wide shared facility that brings together University of Pittsburgh Cancer

Institute (UPCI) and University of Pittsburgh Office of Research Health Sciences staff and resources to advance the application of mass spectrometry in basic and translational research. The center is located on the ninth floor of Biomedical Science Tower 3 in Pittsburgh's Oakland neighborhood.

Research teams from the UPCI Cancer Biomarkers Facility and the University of Pittsburgh Genomics and Proteomics Core Laboratory are collaborating to ensure that university students and investigators working across disciplines will be able to apply new and rapidly advancing technologies to expand our basic understanding of biology and offer new ways to measure health and disease.

The center houses 11 modern instruments, including three hybrid Orbitrap[®] Fourier transform mass spectrometers that enable state-of-the-art structural characterization and quantification of biologically relevant proteins. The center also is available to

researchers who require staff assistance with their experiments, as well as researchers who prefer to take a "hands on" approach and collect their own data.

Led by **Nathan Yates, PhD**, associate professor of cell biology and physiology and co-director of the UPCI Cancer Biomarkers Facility, the center collaborates with UPCI disease-specific research programs in biomarker discovery and translational efforts. Dr. Yates is an expert in mass spectrometry analysis, and pioneered differential mass spectrometry (dMS) — a method that is widely used in the pharmaceutical industry. A unique feature of the shared facility is its interaction with industrial and academic research groups that are actively advancing technology. Through these collaborations, the center can access new instruments and technologies as they are developed and integrate these capabilities into research projects and proposals.

The center will soon be offering seminars and hands-on workshops to introduce new users to a variety of proteomics methods.

A dedication: the Mario Lemieux Center for Blood Cancers

No detail was overlooked in the design of the Mario Lemieux Center for Blood Cancers. Housed on the fourth floor of Hillman Cancer Center, the center offers a comfortable, healing environment that provides ease of care for clinical staff, patients, and families.

The center opened its doors to patients in January 2013. This new clinical space accommodates patients' needs for flexibility and incorporates the latest information management technologies essential for personalized medicine. The center was funded, in part, by grants from the Mario Lemieux Foundation, The Hillman Foundation, and The Henry L. Hillman Foundation.

Easing care for complex diseases

The center offers convenient access to a range of new outpatient treatment options and therapies in a tranquil environment. The unique space is technology-centered, providing "edutainment" for all visitors, including Web-based interactive activities and access to television shows, movies, and news. Open 12 hours a day, seven days a week, the center offers treatment and care planning for patients with cancers of the blood, bone marrow, and lymph nodes, such as leukemia, lymphoma, and multiple myeloma. These cancers can be treated with a variety of care plans, as outlined by the physician, adjusted to fit the personal needs of the patient and their family.

Treatment options include:

- Chemotherapy
- Biological therapy
- Cord blood transplantation
- Stem cell transplantation
- Radiation therapy

The center is UPMC CancerCenter's home for providing stem cell transplants. This treatment option can be effective in treating advanced or recurrent blood cancers, such as leukemia and lymphoma. Historically, the Stem Cell Transplantation Program of UPMC CancerCenter has been one of the largest providers of stem cell transplantation services in western Pennsylvania. With the new facility, the program now offers tailored treatment on an outpatient or inpatient basis, works closely with experts in the Leukemia and Lymphoma Program of UPMC CancerCenter, and is expected to perform approximately 150 stem cell transplants annually.

The center also will house research initiatives aimed at preventing and curing blood cancers.

Top: Nathalie and Mario Lemieux with Elsie Hillman

Middle: Ribbon cutting, from left, John Innocenti, president, UPMC Presbyterian Shadyside, Nancy Davidson, MD, director, UPCI and UPMC CancerCenter, Tom Grealish, president, Mario Lemieux Foundation, Mario Lemieux, and Stanley Marks, MD, chairman, UPMC CancerCenter.

Bottom: Tom Grealish, Nancy Angus, executive director, Mario Lemieux Foundation, and Dr. Nancy Davidson.



TREATING THE WHOLE PERSON

The Mario Lemieux Center for Blood Cancers goes beyond the clinical needs of treating blood cancers to look at each person's holistic needs. To help patients and families prepare for and manage treatment, recovery, and life after blood cancer, the center offers a full range of supportive care, including nutritional, psychological, and pain management services. These specialized services, coupled with coordinated treatment plans, highlight the range of needs of those facing a blood cancer diagnosis.

Experts come together to treat complex GI cancers



Dr. Herbert Zeh is the chief of the Division of GI Surgical Oncology, which has a particular strength in treating large complex abdominal tumors and tumors that have spread to the peritoneal cavity.

“The Division of GI Surgical Oncology boasts a high level of focused expertise, which allows for the use of specialized and individualized techniques that are appropriate for our patients.”

—DR. HERBERT ZEH

The human gastrointestinal (GI) tract comprises all the organs between the esophagus and rectum. Measuring up to 20 feet long, these organs collectively are responsible for the digestive process. GI cancers are diagnosed in nearly 250,000 people each year, according to the American Cancer Society, and risk factors include smoking, excessive alcohol consumption, increasing age, a diet high in animal fats or salted, cured, or poorly preserved foods, chronic pancreatitis, and obesity.

UPMC CancerCenter specialists care for patients with all types of GI cancers, including anal, colorectal, esophageal, gallbladder, gastric (stomach), liver, pancreatic, and small intestine cancers. A complex subset of cancers, GI cancers often require a multimodality treatment approach, which typically includes surgery to remove as much of the tumor as possible, and pre- or postoperative chemotherapy or chemoradiation to shrink the tumor and/or prevent it from returning.

Surgery: A primary treatment for GI cancers

Led by **Herbert J. Zeh III, MD**, UPMC CancerCenter’s Division of GI Surgical Oncology is made up of faculty surgeons who have dedicated their careers to the treatment of patients with GI diseases and cancers. According to Dr. Zeh, the group covers all aspects of GI surgery and is known well for treating large complex abdominal tumors and tumors that have spread to the peritoneal cavity.

For some GI cancers, such as liver, pancreas, stomach, colon, and rectal cancers, a minimally invasive approach can provide the best outcome, while also decreasing surgical side effects for the patient. Minimally invasive surgery is typically performed robotically through four to five small (smaller than one inch) incisions in the abdomen

into which surgeons insert a camera and small instruments. The surgeon can control the instruments remotely to carry out the procedure. Benefits of this type of surgery include less bleeding, smaller scars, reduced pain, shorter hospital stay, quicker recovery, and earlier return to normal activity.

According to Dr. Zeh, the Division of GI Surgical Oncology also is using and having success with a single-incision laparoscopic technique for treating colon cancer. The procedure allows specially trained surgeons to perform a colectomy, or removal of any extent of the colon, through a single small incision, as the name suggests. The same instruments are used, as with the standard laparoscopic procedure, but benefits may include even faster healing, a shorter hospital stay, and lower risk of infection compared to the traditional laparoscopic procedure, due to fewer incisions.

“I see the single-incision technique as the natural progression of minimally invasive surgery,” says Dr. Zeh. “We are able to perform the same procedure using the same instruments, providing similar — if not better — benefits and outcomes.”

In addition to these techniques, a number of treatment options are available to patients with GI cancers, including the traditional and robotic-assisted pylorus-preserving pancreaticoduodenectomy or Whipple

procedure, a highly complex surgery used to treat a number of tumors of the pancreas, duodenum, and bile duct; and hyperthermic intraperitoneal chemoperfusion (HIPEC), a surgical procedure in which the surgeon removes as much of the tumor as possible and then bathes the cavity in heated chemotherapy, killing cancer cells confined to that area. HIPEC may be suggested for patients with cancers that have advanced beyond surgical removal, but still are limited to the peritoneum. Regional chemotherapy also can be applied to the liver for tumors that cannot be completely removed by surgery.

“Every patient presents uniquely,” says Dr. Zeh. “Our background, expertise, and treatment options enable us to provide patients with custom treatment to provide the best outcomes.”

UPMC Liver Cancer Center: Pioneering surgical advances for liver cancer

Approximately 60 percent of patients with a GI cancer will be diagnosed with a liver metastasis, or cancer that has spread to the liver. The liver’s large size and blood flow make it highly susceptible to attracting tumor cells. Still, according to the National Cancer Institute (NCI), approximately 28,500 patients are diagnosed each year with primary liver cancer, or cancer that originates in the liver. Physicians at the UPMC Liver Cancer Center have the expertise and technology to diagnose and treat a full range of liver diseases, including primary liver cancers, such as hepatocellular carcinoma (HCC), cholangiocarcinoma, and gallbladder cancer; metastatic tumors of the liver, such as metastatic colon/rectal cancer, neuroendocrine cancer, and melanoma; benign liver masses; and chronic, underlying diseases, such as hepatitis and cirrhosis.

Led by surgeon **David Geller, MD**, Richard L. Simmons Professor of Surgery, chief, Division of Hepatobiliary and Pancreatic Surgery, and co-director, UPMC Liver Cancer Center, the

center is a nationally recognized program offering a multidisciplinary approach and the latest surgical techniques, including traditional and robotic minimally invasive surgery. Since seeing their first patient in 2000, surgeons at the UPMC Liver Cancer Center have performed more than 500 laparoscopic liver tumor resections.

“Our physicians are pioneers of minimally invasive laparoscopic techniques for complex liver surgical procedures, and continue to lead the way using state-of-the-art technology to benefit our patients,” says Dr. Geller.

Minimally invasive surgery for liver cancer

During a minimally invasive procedure to remove a liver tumor, surgeons make five or six small bandage-size incisions across the abdomen, allowing for access to the liver from various angles. The surgeon inserts ports that serve as pathways for the laparoscopic instruments and other tools. The abdominal cavity is then filled with air to provide space to maneuver the instruments.

The surgeon cauterizes the liver tissue to seal off blood vessels and reduce bleeding. The tumor can then be separated from the remaining healthy liver, and removed through one of the incisions. Due to the liver’s ability to almost fully regenerate, surgeons can comfortably remove up to 75 percent of the liver. The incisions are then closed and covered with small bandages.

Following the procedure, many liver cancer patients are referred to a medical oncologist to start a chemotherapy regime. Patients who undergo a minimally invasive procedure may be able to start their chemotherapy sooner, due to the minimal side effects of the surgery.

Besides state-of-the-art clinical treatment options for liver cancer, the UPMC Liver Cancer Center offers innovative clinical research trials and serves as an educational resource for local physicians to participate in the care of their patients.



Dr. David Geller, center, chief of the Division of Hepatobiliary and Pancreatic Surgery and co-director of the UPMC Liver Cancer Center, uses minimally invasive surgical techniques to treat tumors of the liver.

“The UPMC Liver Cancer Center is one of only a handful of centers in the country to offer a minimally invasive surgical procedure for liver cancer, and we actually pioneered the procedure.”

—DR. DAVID GELLER



Dr. Lyn Robertson and her team from UPCI's Cancer Outreach Program screen at-risk populations for a variety of cancers, including colorectal cancer, by visiting the communities in which they live.

Grant allows study of experimental cancer therapy

In 2010, Dr. Geller was the recipient of a two-year, \$425,000 grant from the Kanzius Cancer Research Foundation, whose mission is to raise funds to support the ongoing research of the Kanzius noninvasive radio wave cancer treatment, an experimental cancer treatment developed by radio and television engineer John Kanzius in 2005. The therapy employs a combination of either gold or carbon nanoparticles and radio waves to heat and destroy cancer cells without damaging surrounding healthy cells.

The goal of Dr. Geller's research was to use the technology invented by Mr. Kanzius to thermally ablate, or destroy, inoperable liver cancer in a noninvasive manner. He had previously used gold nanoparticles to ablate liver cancer cells in the lab and by direct injection in rodent liver cancer. The grant from the Kanzius Cancer Research Foundation has allowed Dr. Geller to further study the mechanisms of cellular death caused by the experimental treatment, as well as develop antibody-labeled gold nanoparticles for the selective targeting of liver cancer in vivo, with the ultimate goal of developing a clinically useful strategy for noninvasive radio wave thermal ablation of liver cancer in patients.

Liver regeneration and the impact of hepatic growth factor

The liver is the only solid organ in the body, besides skin, that can naturally regenerate

if partially damaged. The mechanism of this regenerative liver growth is the subject of intense research by internationally recognized researcher **George Michalopoulos, MD, PhD**, professor and chairman of the Department of Pathology at the University of Pittsburgh. Dr. Michalopoulos and colleague **Reza Zarnegar, PhD**, professor of pathology, University of Pittsburgh School of Medicine, discovered a protein called hepatocyte growth factor (HGF) in 1980, which is responsible for cell growth, motility, and organism development. HGF has been shown to have a major role in embryonic organ development, wound healing, and adult organ — such as liver — regeneration. In a recent study, Dr. Michalopoulos' lab showed that genomic lesions associated with liver cancer occur in many genes associated directly or indirectly with signaling pathways operating in liver regeneration and hepatocyte growth regulation.

Dr. Zarnegar has devoted his research efforts to understanding this important signaling factor. HGF and its cell surface receptor (Met) play an important role in tissue regeneration, and the deregulation of these genes may lead to cancer. Dr. Zarnegar's group has mapped the interaction region in Met and Fas, a death promoting receptor. His lab currently is expanding these studies of Met. An in-depth understanding of the molecular mechanisms of HGF/Met function will not only shed light on normal tissue physiology, but also on understanding the basis of its pathogenic

COLORECTAL CANCER OUTREACH

Many experts agree that colorectal cancer could be greatly reduced if people got screened. Toward that end, colorectal cancer screenings for African-Americans — particularly men, who are the most reluctant to be screened — continue to be a top priority for UPCI's Cancer Outreach Program. **Lyn Robertson, DrPH, RN, MSN**, director of Cancer Outreach, and her team continue to develop mechanisms to screen those in need, according to established guidelines. One new test that looks promising is the InSure® FIT test, which tests the DNA in the stool and indicates people who are at a higher risk for developing colorectal cancer. Once identified, the outreach team can encourage them to undergo a follow-up colonoscopy. Because a colonoscopy can be costly for those without medical insurance, Dr. Robertson's team works closely with at-risk individuals to help them apply for assistance or make financial arrangements for colonoscopies at reduced rates.

effects, thus providing opportunities for rational drug design to combat various diseases, including tissue degeneration and cancer.

Satdarshan (Paul) Singh Monga, MD, and his lab are focusing on the signaling pathways of the Wnt and β -catenin gene to understand the molecular mechanisms of liver development, growth, regeneration, and cancer. Dr. Monga recently discovered that liver cancer caused by chemical carcinogens was more prevalent in animals that did not have the β -catenin gene. Absence of this gene also made the cancer cells more sensitive to certain chemotherapeutics.

Hypoxia and inflammation

Hypoxia (a low level of oxygen) often is found in solid tumors and is associated with tumor progression and poor clinical outcomes. The exact mechanisms related to hypoxia-induced invasion and metastasis remain unclear. Dr. Monga, in collaboration with Dr. David Geller and others, has elucidated the mechanism by which the nuclear-damage-associated molecular pattern molecule, high-mobility group box 1 (HMGB1), released under hypoxic stress, can induce an inflammatory response to promote invasion and metastasis in hepatocellular carcinoma cells (HCC).

Tumor cells survive hypoxic conditions by inducing autophagy, the process of self-digestion by a cell through the action of enzymes originating within the same cell. Dr. Geller and collaborators found that the microRNA miR-375 inhibits autophagy and impairs viability of HCC cells under hypoxic conditions. These miRNAs that inhibit autophagy of cancer cells also may be developed as therapeutics.

Expanding treatment options

For most GI cancers, adjuvant chemotherapy — or chemotherapy after surgery — is prescribed to shrink any remaining tumor and/or kill any tumor cells that may have spread. Led by **Edward Chu, MD**, chief, Division of Hematology-Oncology, and deputy director, University of Pittsburgh Cancer Institute

(UPCI), GI cancer specialists are collaborating to make better chemotherapy treatments available for GI cancer patients who have exhausted other treatment options.

Weijing Sun, MD, joined UPCI and UPMC CancerCenter in September 2012 as the director of the GI Cancer Section of Hematology-Oncology and co-director of UPMC GI Cancer Center of Excellence at the University of Pittsburgh. Dr. Sun is a member of the National Cancer Institute's Gastrointestinal Steering Committee-Hepatobiliary Cancer Task Force, the Eastern Cooperative Oncology Group (ECOG) GI Core Committee, and the American Society of Clinical Oncology (ASCO) Scientific Program Committee. At UPCI, Dr. Sun and his team are focused on the development of new drugs and biologic agents for GI cancers through Phase 1 and 2 clinical trials.

Clinical trials are research studies used to evaluate new, possibly more effective drug combinations for patients who often have exhausted their conventional treatment options. These trials help to further understand how cancer responds to different types of treatment. Each clinical trial acts as a stepping stone to the next, depending on its outcomes. Dr. Sun's group is focused on Phase 1 clinical trials, which allow researchers to determine the safe dose of a new drug or agent and learn about its side effects, and Phase 2 clinical trials, which test the effectiveness of the new drug or agent in stopping or controlling the growth of tumor cells in a certain type of cancer.

James Lee, MD, PhD, joined the Division of Hematology-Oncology in April 2012. Specializing in colorectal cancers, Dr. Lee is working alongside Dr. Sun to revamp the Phase 1 and 2 clinical trials program and offer more treatment options for patients.

Dr. Lee is currently investigating inhibitors of epidermal growth factor (EGF) receptors, which block proteins called growth factors, preventing them from helping tumor cells to divide, grow, and spread, and anti-angiogenic therapy, which



Dr. Edward Chu, chief of the Division of Hematology-Oncology and UPCI deputy director, and collaborators are working to develop new and better drugs and biologic agents for the treatment of GI cancers.

“We are working to identify and implement the most effective and least toxic drug combinations for our GI cancer patients. We’re looking to offer new treatment modalities through more clinical trials.”

—DR. WEIJING SUN

“UPMC CancerCenter has an impressive track record for treating and managing GI cancers with chemotherapy. But we can’t say, ‘What we have is good enough.’ We need to find new hope.”

—DR. JAMES LEE

COMMITTED TO COLON CANCER RESEARCH

In 2011, UPCI received a \$500,000 commitment from the **Chris4Life Colon Cancer Foundation** to support their colon cancer research and clinical efforts. Chris4Life is a nonprofit organization named after Christine “Chris” Sapienza, a Pittsburgh native who died from colon cancer in 2006.

In summer 2012, the foundation hosted the second Cookies4Chris Luncheon and Vendor Show, highlighting Pittsburgh’s famous “cookie table.” Another Cookies4Chris event is planned for spring 2013, and a Pittsburgh Scope It Out™ run/walk is planned for summer 2013. Proceeds from these events will benefit the Chris4Life Foundation to help support their commitment to UPCI’s colon cancer research program.

Chris’s son Michael, founder and executive director of Chris4Life, says the foundation selected UPCI because of its dedication to research and superior ability in treatment. “We’re very excited to continue to build on this partnership,” says Michael.

blocks the formation of blood vessels that supply the tumor with the blood and oxygen needed to grow and spread.

Also high on Dr. Lee’s priority list is personalized medicine. “This is not a new concept at UPCI and UPMC CancerCenter, but we continue to learn more about how we can tailor our treatments to work best for each patient,” says Dr. Lee.

According to Dr. Lee, the group is investigating gene sequencing, which can determine which genes in a patient’s body harbor the mutations that lead to colorectal cancer. Once determined, the sequence can be compared to existing information with the goal of determining the likelihood of disease risk.

Coordinating care for a better outcome

GI cancer experts at UPMC CancerCenter know that effective treatment of these cancers relies on both a multimodality treatment plan

and a coordinated approach to care. Employing a team approach, physicians from surgical oncology, thoracic oncology, medical oncology, radiation oncology, and the UPMC Liver Cancer Center meet with diagnostic and interventional radiologists, gastroenterologists, hepatologists, and pathologists weekly in a setting called the GI Specialty Care Center to review individual cases and create treatment plans for each patient. Ongoing reviews and updates of each case ensure that patients are continually receiving the most appropriate care for their type and stage of disease.

“Patients benefit from having their cases presented at the weekly meetings because multiple treatment options are discussed and weighed based on their specific disease and stage,” says Dr. Geller, who represents the UPMC Liver Cancer Center at these meetings. “A group consensus is reached and patients can begin their coordinated, specialized treatment plans as soon as possible.”

Vaccines offer personalized colorectal cancer immune defense treatments

The National Cancer Institute (NCI) lists colorectal cancer as the third-leading cause of cancer deaths in the United States, with nearly 52,000 deaths per year. Physician-scientists at University of Pittsburgh Cancer Institute (UPCI) are investigating a number of noteworthy vaccine clinical trials, not only to treat the disease, but to prevent it altogether.

Although a person’s immune system can mount an aggressive and typically effective defense against viral infection, it does not do so when infiltrated with cancer cells. Investigators

are aiming to condition a patient’s immune system into eliminating cancer as aggressively as it would a viral infection. UPCI researchers are taking a two-pronged approach using a novel type of dendritic cells — immune cells specialized in initiating immune responses — that are administered as a vaccine, and studying and implementing ways to manipulate the tumor microenvironment.

Personalized, targeted treatments

Pawel Kalinski, MD, PhD, professor of surgery, University of Pittsburgh School of Medicine, and Dr. Herbert Zeh and Dr. David Bartlett

have developed a new platform of personalized vaccines — Alpha type-1 polarized dendritic cells (α DC1) — that are grown from the blood of each individual patient over seven days. The hope is that this vaccine will instruct the patient's own immune system to recognize the colorectal tumor as cells that need to be eliminated rather than healed. This trial is being offered to patients who have failed first- and second-line standard chemotherapy, do not have another therapeutic option, and have roughly six months of anticipated survival. It will evaluate the ability of the treatment to prolong patients' lives. Similar vaccines are being developed for breast cancer and cervical cancer, and soon this approach will be applied for hematological malignances, as well.

Preventing cancer development

Olivera Finn, PhD, co-leader of the Cancer Immunology Program at UPCI, **Robert Schoen, MD, MPH**, a member of the UPCI Cancer Epidemiology, Prevention, and Control Program, and their team tested a vaccine that might prevent a person from developing colorectal cancer altogether. Dr. Finn developed the vaccine after two decades of research into understanding how cancer starts and progresses. The vaccine boosts the immune system to destroy cancer cells carrying the abnormal variant of the MUC1 protein on their surfaces. MUC1 is necessary for cancer cell survival and proliferation.

In the beginning stages of colon cancer, a polyp, a benign but abnormal cell growth, becomes malignant. Colorectal cancer forms when the MUC1 protein, which normally serves to protect the cell against pathogens, changes without producing a response from the immune system. Only after the cancer has taken hold and grown does the immune system react, but by then the cancer has already begun suppressing the immune response.

In a study published in *Cancer Prevention Research* in January 2013, the vaccine was tested on 39 patients between the ages of

40 and 70 with a history of advanced adenomas — polyps that have become precancerous. The trial proved successful in more than 40 percent of the patients by showing the vaccine had stimulated the production of antibodies against the abnormal variant of the MUC1 protein. In those who showed no response, it was found that their immune systems had already been negatively affected by the precancerous cells that stimulated expansion of an important suppressive blood cell population previously associated only with cancer.

The UPCI team's strategy is to inoculate people whose medical histories put them at high risk for colorectal cancer before benign polyps have a chance to become precancerous or induce immune suppression, which happens in more than 30 percent of cases. The next stage of human clinical trials will test the vaccine in multiple medical centers with as many as 200 patients at high risk of developing colon cancer. If successful, the vaccine someday could reduce or eliminate the need for high-risk people to undergo repeated colonoscopies.

Approximately one person in 20 in the United States will develop colorectal cancer in their lifetime.

Dr. Pawel Kalinski, a pioneer in dendritic-cell vaccines, has developed a new platform of personalized vaccines for the treatment of patients with colorectal cancer who have failed first- and second-line standard chemotherapy and are without other therapeutic options.



A final gift

The name may seem unsympathetic and impersonal to some, but the rapid autopsy program at Magee-Womens Hospital of UPMC is anything but the callous, rushed process it conveys. Rather, it's an opportunity for patients and families to leave ONE final gift in hopes of finding cures for deadly diseases.

Rapid autopsy vital to scientific research of cancer

Karen Perry, a special education teacher from Pittsburgh, was first diagnosed with breast cancer 15 years ago. She spent 12 years cancer free before receiving a second cancer diagnosis. A bilateral mastectomy and removal of her lymph nodes seemed to stall the disease until a year and a half later when a PET scan revealed that the cancer had spread to her clavicle. "The cancer returned with a vengeance," says Karen's brother, Craig Perry. "Everyone was astounded by the rate of metastasis. Not even radiation was successful."

As Craig watched his sister slip away, he asked Karen's medical oncologist **Shannon Puhalla, MD**, assistant professor of medicine at the University of Pittsburgh School of Medicine, and an oncologist at the Magee-Womens Breast Care Program, part of UPMC CancerCenter, about the possibility of donating Karen's organs. Because Karen's cancer had metastasized, she was not a candidate for typical organ donation, but Dr. Puhalla introduced Craig to the rapid autopsy program. "Tissue gathered through rapid autopsy gives us an invaluable opportunity to understand why we die of certain diseases," says **Adrian V. Lee, PhD**, professor, Department of Pharmacology and Chemical Biology, and director, Women's Cancer Research Center, University of Pittsburgh Cancer Institute (UPCI) and Magee-Womens Research Institute. "It allows us to get closer to the root of the problem. If we can't get to the root, we can't cure these diseases."

Rapid autopsy has been in use for more than 30 years, though primarily for research into Alzheimer's disease and multiple sclerosis. But it was **Naftali Kaminski, MD**, director, Dorothy P. & Richard P. Simmons Center for Interstitial Lung Disease at UPMC, who conducted UPMC's first rapid autopsy in 2002 at the request of a firefighter dying of lung disease. The patient was looking for a meaningful way to contribute to a better understanding of his disease for future generations.

Today, the program has evolved into part of the University of Pittsburgh's Health Science Tissue Bank and spans several medical specialties. There is no cost to take part in the rapid autopsy program, and UPMC absorbs any costs associated with the initiative, including transportation and funeral home expenses.

Karen passed away at the age of 56, but her legacy lives on through her organ donation. According to Craig, with the help of UPMC and Karen's hospice team, Karen's rapid autopsy process was seamless. Necessary paperwork was completed in advance, and when Karen died on October 25, 2012, she received an autopsy within hours of her death, allowing samples of the diseased tissue to be collected. Her body was then transported to the funeral home to be prepared for her memorial service. "Karen felt so strongly about organ donation that I have no doubts that being able to donate to the rapid autopsy program is what she would have wanted," explains Craig.

RAPID AUTOPSY EXPLAINED

Rapid autopsy, or warm autopsy, is the process of procuring organs, tissue, or other specimens within six hours of death. Obtaining samples immediately allows medical researchers to evaluate advanced-stage disease conditions in the recently deceased and compare them with tissue collected during biopsies done earlier during the course of the patient's illness, providing an opportunity to compare the disease at a cellular level at different stages. The goal of the program is to gain a better understanding of recurrence and why individuals die from disease.



Dr. Shannon Puhalla and Dr. Adrian Lee in the autopsy suite, where rapid autopsies take place.

Detecting and managing lymphedema in its earliest stages

“There is no cure for lymphedema. You can only manage the symptoms. The most optimal scenario is to diagnose patients in the preclinical stage.”

—DR. ATILLA SORAN

Experts in the Lymphedema Education, Monitoring, Early Detection, Intervention, and Prevention (LEMED) Program use advanced technology to detect lymphedema — the buildup of fluids after lymph node removal — in its earliest stages, when it's more treatable and manageable.

The fight against breast cancer has been an important battle fought hard on the front lines by dedicated physicians, patients, and their families. But there's one disease that is often associated with breast cancer that is often overlooked: lymphedema.

About 30 percent of breast cancer patients who undergo an axillary lymph node dissection, a common surgical procedure to remove the lymph nodes from the axilla (armpit) to stage breast cancer, will develop lymphedema, a painful condition in which lymph fluids build up in tissues of the extremities, causing swelling. Patients are often referred to a lymphedema

specialist after the swelling has occurred. Experts at the LEMED Program, housed at Magee-Womens Hospital of UPMC, advocate for multidisciplinary care and presurgery lymphedema consultations.

Led by **Atilla Soran, MD**, professor of surgery, the program is specifically for breast cancer patients. Experts work with UPMC CancerCenter breast surgeons to meet with patients prior to their axillary lymph node dissection procedure to perform a baseline procedure. Experts use noninvasive bioimpedance spectroscopy technology created by ImpediMed Limited to send low-frequency electrical currents through

KAREN VOGEL:

DEVELOPS LYMPHEDEMA 15 YEARS FOLLOWING BREAST CANCER SURGERY

Karen Vogel from Crafton Heights, Pa., was diagnosed with cancer in her left breast in 1996. She underwent a lumpectomy, an axillary lymph node dissection, and radiation therapy.

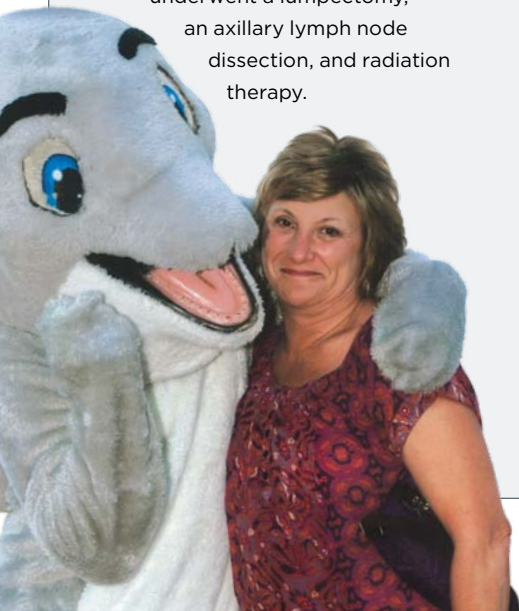
At the time, Karen was advised that the lymph node dissection could cause lymphedema, a buildup of lymph fluid that causes painful swelling.

“While removing lymph nodes is important to staging breast cancer, it can disrupt the flow of lymph fluid in that area,” says Dr. Atilla Soran. “As a result, sometimes excess fluids build up, causing lymphedema.”

Karen was initially diligent in doing daily exercises suggested by her doctor to prevent lymphedema, but the regimen waned as Karen began her life as a breast cancer survivor.

In July 2012, 15 years after her breast cancer diagnosis and treatment, Karen woke up with a swollen left arm and initially disregarded it as a bug bite. “The idea that this could be related to my breast cancer from so long ago didn't even cross my mind,” says Karen.

About a month later, however, she brought her slightly swollen arm to the attention of her radiation oncologist, **Melvin Deutsch, MD**, during her annual checkup. “He looked at my arm and immediately told me it was lymphedema,” says Karen. “I was shocked that it could appear so long



“Awareness is the key to discovering lymphedema in its earliest stages, when it’s more treatable.”

—DR. ATILLA SORAN

a patient’s arms and legs. Because these currents flow faster through fluid than muscle or bone, the procedure provides a baseline of the amount of fluid the patient is retaining. Before surgery, the patient’s baseline number should be normal. The patient returns to the clinic 90 days after surgery, and every three to six months thereafter to have the fluid levels tested and compared to the baseline number. If the test reveals that the amount of fluid has increased beyond a reasonable range, she is considered as having developed preclinical lymphedema — or lymphedema with no clinical symptoms — and is put on a track for treatment.

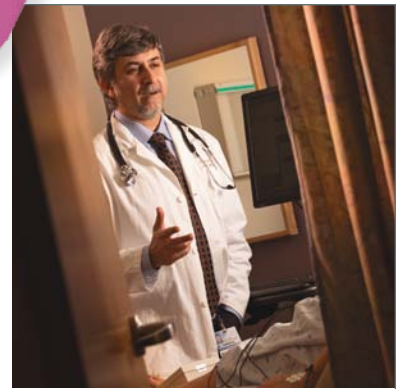
“There is no cure for lymphedema,” says Dr. Soran. “You can only manage the symptoms. The most optimal scenario is to diagnose patients in the preclinical stage. If you can catch the disease in this stage,

we may be able to prevent swelling, offer more treatment options, reduce the pain, aches, tightness, cramps, and infections often associated with clinical lymphedema, and, most importantly, improve the patient’s quality of life.”

Since the program was established in 2010, more than 500 patients have been measured to determine their baseline numbers, and 42 patients — or 14 percent — have been diagnosed with preclinical lymphedema.

Lymphedema treatment options

Lymphedema treatment depends on the severity of the disease, and more treatment options are available in the disease’s earliest stages. The Lymphedema Clinic at Magee, which also treats lymphedema patients unrelated to breast cancer, provides physical therapy, compression garments, new



Above, top and bottom: Dr. Atilla Soran advocates for lymphedema screenings before and after a patient’s surgery to catch the disease in its earliest stages.

after my cancer.” Dr. Deutsch referred Karen to Dr. Soran and the LEMEP Program.

According to Dr. Soran, breast cancer patients who undergo an axillary lymph node dissection, or those who receive radiation to the underarm area, are susceptible to lymphedema for the rest of their lives.

“Because lymphedema can creep up on a breast cancer patient at any time following their surgery — even up to 30 years post-surgery — it’s important to continue to monitor the patient so that if lymphedema symptoms arise, treatment is available

sooner, when it is more effective,” says Dr. Soran. “That is our goal with the LEMEP Program.”

Karen began laser treatments to clear the existing scar tissue that was causing the lymph fluid to back up. Her first and last treatments were administered by Dr. Soran at Magee-Womens Hospital of UPMC. The remaining treatments were performed at UPMC South Hills in Bethel Park, Pa., closer to Karen’s home. During the procedure, the therapist placed a small, hand-held device onto the skin under Karen’s underarm, which delivered low levels of laser therapy. “The treatment

was simple and finished in 10 minutes,” says Karen. “I didn’t feel anything.”

As part of her lymphedema treatment, following the laser therapy, Karen also received body massages to help open her lymph vessels so her lymph fluids could flow more freely.

Since completing treatment in November 2012, Karen’s lymphedema has regressed and the swelling in her arm has mostly subsided. As a part of the LEMEP Program, Karen’s lymphedema will continue to be monitored, and she knows that she’ll need to continue exercises and keep vigilant.



Dr. Joel Weissfeld and his team are working with experts at the Women's Cancer Research Center to analyze and infer possible trends concerning BMI and breast cancer risk, fertility drugs and ovarian cancer risk, and risk factors related to metastatic breast cancer survival.

WOMEN'S CANCER

generation pumps, and laser therapy as options for treating and managing the disease. According to Dr. Soran, in 2013 the clinic also will offer surgery, including lymphovascular anastomosis and liposuction, as treatment options.

Although lymphedema is a common complication of breast cancer surgery, only 36 percent of primary care physicians and 21 percent of nurse practitioners referred their at-risk patients to a lymphedema clinic, according to a recent study published in *Breast Cancer Research*.

"These figures represent a lack of nearby clinics or a lack of knowledge," says Dr. Soran. "Awareness is the key to discovering lymphedema in its earliest stages, when it's more treatable."

Educating patients and those at risk of lymphedema

The LEMEP Program is doing its part to educate lymphedema patients in western Pennsylvania by hosting quarterly meetings through the Lymphedema Educational Program.

"We facilitate communication by inviting experts in the coordination of care for lymphedema patients — such as physical therapists, dietitians, and our nurse coordinator — to speak to at-risk breast cancer patients and those struggling with the disease," says Dr. Soran. "At these meetings, we provide one-on-one, postoperative lymphedema education as a component in prevention; individual risk assessment, such as body mass index (BMI), lifestyle, occupation, and other possible risk factors; review of lymphatic function and anatomy; and discussion of early warning signs and risk-reduction strategies."

EPIDEMIOLOGY RESEARCH AND THE WOMEN'S CANCER RESEARCH CENTER

Cancer epidemiology is the study of factors that affect cancer for the purposes of identifying what causes cancer and, ultimately, developing improved treatments.

Joel L. Weissfeld, MD, MPH, co-leader of the Cancer Epidemiology Prevention and Control Program at UPCI and associate professor of epidemiology, Graduate School of Public Health, University of Pittsburgh, and his colleagues are working with experts at the UPCI Women's Cancer Research Center (WCRC) to identify possible trends and causes of cancers that may affect women. As a result, many exciting research initiatives are blooming:

- In a recent study, Dr. Weissfeld and his colleagues at the National Surgical Adjuvant Breast and Bowel Project determined that premenopausal women over 35 years old with high body mass indexes (BMIs) have an increased breast cancer risk. However, the group determined that this higher risk was not present in postmenopausal women.
- According to Dr. Weissfeld, previous studies examining the association between the use of fertility drugs and ovarian cancer risk have often provided conflicting results. Dr. Weissfeld and colleagues at the University of Pittsburgh Cancer Institute's (UPCI's) Cancer Epidemiology, Prevention, and Control Program analyzed data from the Hormones and Ovarian Cancer Prediction (HOPE) study and found that fertility drugs were not associated with an increased risk of developing ovarian cancer for women who succeeded in getting pregnant with the help of fertility drugs. The study also showed that women who use fertility drugs and are not pregnant may have an elevated risk for ovarian cancer.
- Women diagnosed with breast cancer metastases often have a poor prognosis. In a recent study, Dr. Weissfeld and colleagues identified the following factors as related to survival from this disease: a history of hypertension; tumor status, such as estrogen receptors (ER), progesterone receptors (PR), and HER2, a specialized protein found on breast cancer cells that controls cancer growth and spread; metastasis-free interval, or the time between the original diagnosis and recurrence; the location to which the cancer has spread, specifically, the brain, bone, and liver; and BMI at diagnosis.

UPCI and UPMC clinicians discover genetic mutations associated with lymphedema in breast cancer patients

Secondary lymphedema, or fluid retention and tissue swelling caused by a blockage of the lymph passages, is a frequent and serious chronic complication of breast cancer treatments, including surgery, chemotherapy, and radiation. Identifying those patients most at risk for developing secondary lymphedema would enable earlier interventions to prevent and treat this severe condition.

In a study recently published in *Clinical Cancer Research*, **David Finegold, MD**, professor of medicine and pediatrics, University of Pittsburgh School of Medicine; **Adam Brufsky, MD, PhD**, professor of medicine and associate chief, Division of Hematology-Oncology, associate director for clinical investigations, University of Pittsburgh Cancer Institute (UPCI), and co-director, Breast Cancer Program, UPMC CancerCenter; **Robert Ferrell, PhD**, professor of human genetics and associate dean for academic affairs, University of Pittsburgh Graduate School of Public Health, and scientific director, University of Pittsburgh Genomics and Proteomics Core Laboratory; and colleagues investigated potential genetic alterations that may predict the development of secondary lymphedema in breast cancer patients. By sequencing the DNA of 80 breast cancer patients with lymphedema, and 108 patients without, the research team uncovered four independent mutations in the GJC2 gene that were associated with lymphedema development.



The GJC2 gene encodes a protein called connexin 47, a critical component of cell-to-cell junctions that facilitate communication between cells and are known to play a role in major cell processes, including motility and cell growth. The research team claims that mutations in the connexin 47 protein impair function of these crucial cellular junctions, which in turn impairs how the lymphatic system behaves, resulting in lymphedema.

“We find it very intriguing that some women may have a genetic predisposition to lymphedema after breast cancer surgery,” says Dr. Brufsky. “Further refinement and understanding of these and possibly other inherited mutations that may predispose women to lymphedema, may allow us to tailor their breast cancer therapy to less invasive procedures.”

Dr. Adam Brufsky and his colleagues have discovered a predisposition to secondary lymphedema in some women, opening the doors for more tailored breast cancer therapies.

“We find it very intriguing that some women may have a genetic predisposition to lymphedema after breast cancer surgery.”

—DR. ADAM BRUFSKY



Dr. Lesley Butler has used blood and urine samples from the Singapore Chinese Health Study to evaluate the relationship between diet and cancer.

“Our goal is to establish whether a urinary metalloproteinase panel can be used as a biomarker for assessing breast cancer risk, which could ultimately result in fewer women dying from breast cancer.”

—DR. LESLEY BUTLER

Research project studies dietary relationship to breast cancer risk

The University of Pittsburgh Cancer Institute (UPCI) Cancer Epidemiology, Prevention, and Control Program, led by **Jian-Min Yuan, MD, PhD**, professor of epidemiology, and associate director for Cancer Control and Population Sciences, has long been studying the effects of diet on cancer risk. **Lesley Butler, MSPH, PhD**, recruited in 2012 as associate professor of epidemiology at the University of Pittsburgh Graduate School of Public Health, is continuing this effort by examining a woman's dietary relationship to her breast cancer risk.

For more than a decade, Dr. Butler has been a co-investigator on the Singapore Chinese Health Study, on which Dr. Yuan also participates as a principal investigator. The ongoing prospective cohort study has collected blood and urine samples from 63,000 Chinese individuals over a 20-year period, and has been solely and continuously funded by the National Cancer Institute (NCI). Dr. Butler has published numerous papers based on the cohort's key data, including such findings as an inverse association in dietary patterns characterized by intake of soy foods, vegetables, and fruits on the risk of breast cancer, to a positive association between black tea intake on the risk of prostate cancer.

In 2012, Dr. Butler received funding from the NCI to evaluate the association between prediagnostic levels of metalloproteinases, enzymes that break down proteins, such as collagen, that are normally found in the spaces between cells in tissues, in the urine of women with and without breast cancer through the Singapore Chinese Health Study. Her project will use a nested case-control study of 408 incident breast cancer cases and 816 individually matched controls within the Singapore Chinese Health Study.

“There is strong experimental evidence for the role of matrix metalloproteinases in developing early breast cancer, and in the change in the formation of cells that may result in a subgroup of dysplasia/carcinoma in situ that is prone to progression toward invasive disease,” says Dr. Butler.

“Our goal is to establish whether a urinary metalloproteinase panel can be used as a biomarker for assessing breast cancer risk, which could ultimately result in fewer women dying from breast cancer.” Because breast cancer is the most prevalent cancer among women in the United States, a noninvasive, highly reliable, and accurate biomarker panel would improve the early diagnosis of breast cancers in the growing population of women at high risk for breast cancer, as well as those at risk for cancer recurrence and second primary cancers.

Another project Dr. Butler currently is working on aims to evaluate the relationship between coffee intake and cancers of the breast and stomach, also evaluating data from the Singapore study. The study group offers a unique resource for analyzing the intake of tea and coffee on cancer risk, because this population is one of the only Asian populations that regularly consumes black tea, green tea, and coffee.



Pink Glove Dance

A NATIONWIDE YOUTUBE COMPETITION RAISES BREAST CANCER AWARENESS

In July 2012, UPMC CancerCenter entered the second annual **Pink Glove Dance™** contest, a nationwide competition to raise breast cancer awareness. Sponsored by Medline Industries Inc., more than 260 hospitals, schools, and other organizations throughout the United States and Canada submitted videos of staff and faculty dancing to music with pink gloves in hopes of winning a \$10,000 donation to a breast cancer charity of their choice.

Representing various UPMC CancerCenter locations and more than 15 departments, 200 advocates, including cheerleaders and Pittsburgh Steelers Quarterback Charlie Batch, rallied around the mission to raise awareness and funds for **Dignity Robes**, a local nonprofit organization that makes robes, designed like kimonos, for women undergoing breast cancer treatment.

As cancer can be discomfoting and a hospital gown unflattering, these robes are meant to preserve the women's dignity, reduce stress, and hug the patients during their treatment. The dignity robes are made from 100 percent cotton and are designed so women can wash and wear them more than once. They come in many colors and feminine patterns, and have pockets in the front with Velcro® sides so doctors can easily access the treatment area without completely undressing the patient. Made by volunteers, all of the materials are either donated or purchased in bulk at a reduced price.

"The Pink Glove Dance was a morale booster for our network," says **Nancy E. Davidson, MD**, director, UPCI and UPMC CancerCenter. "The excitement and pride surrounding our video was sensational. Not only was this an opportunity to raise money for a wonderful charity, it was a way to radiate the spirit of what UPMC CancerCenter is all about."

Through internal promotion, social media, and help from our local news and radio stations, UPMC CancerCenter finished in ninth place out of 260 submissions with a total of 3,923 votes. Although the video did not win a prize, it was a hit with employees, UPMC CancerCenter physicians, and the western Pennsylvania community.

"A main goal of our Pink Glove Dance was to bring happiness, hope, and courage to those who watched it," says **Chuck Bogosta**, executive vice president, UPMC, and president, UPMC CancerCenter. "No matter how old we are, what job title we have, and whether or not cancer has personally affected us or our loved ones, we wanted the world to know that we are in this together. UPMC CancerCenter is truly dedicated to the fight against breast and other cancers."

Medline produced the original Pink Glove Dance video in 2009, which has since been viewed more than 13 million times on YouTube. The video was so successful that Medline created a sequel featuring more than 4,000 health care workers and breast cancer survivors. In 2011, Medline hosted the first online national competition, bringing in more than 1.2 million views and half a million votes.



Women's Cancer Research Institute continues to make strides

“Discoveries such as this speak directly to the WCRC’s goal of translating laboratory findings into advancements in the treatment and prevention of women’s cancers.”

—DR. ADRIAN LEE

When **Adrian V. Lee, PhD**, professor, Department of Pharmacology & Chemical Biology, and director, Women's Cancer Research Center (WCRC), University of Pittsburgh Cancer Institute (UPCI), a renowned expert in the molecular and cellular biology of breast cancer, moved with his family from Houston to Pittsburgh in 2010, it was to lead the newly developed WCRC, a collaboration between UPCI and Magee-Womens Research Institute (MWRI). The center's mission is to reduce the incidence and death from women's cancer. Two years later, Dr. Lee and his team are entrenched in cutting-edge, high-impact translational science, and seeing real results.

Life-changing medicine

As recently as September 2012, Dr. Lee's team of researchers at the WCRC had made a major breakthrough in slowing triple-negative breast cancer, a particularly powerful form of the disease that disproportionately affects younger and minority women. Triple-negative cases typically don't respond well to traditional hormone therapies, such as tamoxifen, but his team discovered a cell-growth regulator that can impair triple-negative breast cancer when blocked.

According to Dr. Lee, combining this approach with chemotherapy in rodents has been shown to eliminate tumors. But perhaps even more exciting is that the discovery may lead to clinical trials in humans within the next couple of years. “Discoveries such as this speak directly to the WCRC's goal of translating laboratory findings into advancements in the treatment and prevention of women's cancers,” says Dr. Lee. “With the cooperation of basic scientists, oncologists, surgeons, and medical oncologists, we have the ability to make a major impact.”

Recognition and research

Housed at the MWRI in the Oakland neighborhood of Pittsburgh, the WCRC is co-directed by **Robert Edwards, MD**. **Steffi Oesterreich, PhD**, oversees the education program. The center is home to 173 members from a variety of medical specialties who are actively involved in women's cancer research initiatives and who have been published in some of the most highly regarded medical journals.

The WCRC and its investigators receive support from organizations such as the National Cancer Institute, the Department

OTHER RESEARCH INITIATIVES UNDER WAY AT THE WCRC

To date, more than 450 women have enrolled in the Cancer Family Registry (CFR), giving researchers at the WCRC unfettered access to members' medical histories, along with blood, urine, and in some cases, surgical specimens.

- Exploration into why breast cancer affects white women and African-American women differently. National studies reveal that mortality rates from breast cancer are 41 percent higher for African-American women than white women, underscoring the need for African-American women to ask their health care providers about clinical trials.
- Investigation into new biomarkers for invasive and in situ breast cancer and how those markers play into patient outcomes.
- Research of risk assessment and reduction of breast and ovarian cancers by utilizing information collected from the Magee-Womens Hospital High Risk Breast and Ovarian Cancer Program and the CFR.

of Defense, and Susan G. Komen for the Cure®. The RK Mellon Foundation and Scaife Foundation, alone, provided pilot funding for more than a half dozen studies during 2011 and 2012. And this past October, the Fashion Footwear Association of New York (FFANY) and QVC named UPCI, partner with UPMC CancerCenter, one of the beneficiaries of the 2012 QVC Presents “FFANY Shoes on Sale®,” a charitable shoe sale to benefit breast cancer research and education.

The FFANY grant will support research led by Dr. Lee and **Nancy E. Davidson, MD**, director of UPCI and UPMC CancerCenter. Dr. Lee and Dr. Davidson are using the funds to continue their research into why breast cancer recurs and what causes it to metastasize.

Banking on personalized medicine

Investigators at WCRC also have at their fingertips tissue and other biological specimens through the University of Pittsburgh’s Health Sciences Tissue Bank (HSTB). The HSTB is one of the most comprehensive in the world with more than 4,000 specimens and corresponding clinical data that serve as the critical basis for research, providing support to major research initiatives, including The Cancer Genome Atlas project (TCGA), and laying the foundation for the future of personalized medicine.

“The HSTB and TCGA are molecular dictionaries for breast and ovarian cancers,” explains Dr. Lee. “And by combining biology with informatics, we can move discovery into practice in the form of personalized medicine, making the treatment as individualized as the disease.”

Dr. Lee and researchers at the WCRC are involved in a personalized medicine breast cancer pilot program that will allow physicians and researchers to integrate patient genotype and phenotype data. The program helped to get a larger UPMC initiative off the ground — the creation of the Center for Innovative

Science — which highlights the strengths and challenges of such an expansive project.

The future of health care

In October 2012, UPMC announced a five-year, \$100 million investment in personalized medicine. Together with technology partners Oracle, IBM, Informatica, and dbMotion, UPMC is developing the Enterprise Data Warehouse that will enable scientists to mine more than three petabytes, equivalent to 500 billion pages of standard text, of patient data at UPMC alone and the 4,000 specimens from the HSTB, to start. Physicians, researchers, and administrators will focus in part on the biology of cancer and aging with the goal of developing new understandings of disease to improve patient outcomes while reducing over-diagnosis and unnecessary treatments.

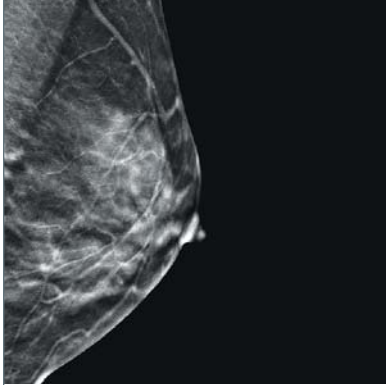
“The framework is in place,” says Dr. Lee. “Smart technology and good science will open the doors to new models of care. This warehouse will transform what we do as clinicians and researchers.”



Dr. Robert Edwards, left, and Dr. Adrian Lee, right, are co-directors of the Women’s Cancer Research Center; Dr. Steffi Oesterreich, center, oversees the education program.



Magee aids in advancing breast imaging



Digital breast tomosynthesis (DBT) generates a 3D 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.

For the past several years, breast radiologists at Magee-Womens Hospital of UPMC have participated in research evaluating breast tomosynthesis, also called 3D mammography, for screening and diagnosing lesions of the breast. Based on the success of this research, the same group of imaging specialists at Magee also was instrumental in translating this research to patient care, and is now offering patients this advanced 3D breast imaging, in conjunction with standard mammography, at Magee, Magee-Womens Imaging in Monroeville, and UPMC St. Margaret.

Approved by the Food and Drug Administration, tomosynthesis is an imaging procedure that uses low-energy x-rays to create a 3D image of the breasts. While conventional mammography takes pictures of the breast from two angles — up and down, and left to right — tomosynthesis takes multiple pictures from different angles, which creates images in thin slices of the breast, like a CT scan. Both the regular mammogram and tomosynthesis may be performed as a screening procedure. Tomosynthesis also is a valuable tool used in diagnostic breast imaging, which is done when a woman exhibits a symptom, such as a breast lump.

“For many years, women have been hearing that a yearly mammogram is the key to detecting and treating breast cancer in its earliest stages,” says **LaJuana Fuller**, director of Women’s Imaging. “But we didn’t just sit back and say, ‘That’s good enough for our patients.’ As frontrunners in women’s imaging, we have been eager to bring tomosynthesis from the bench to the bedside to provide the optimal breast imaging for our patients.”

How the procedure works

The technique for a tomosynthesis imaging session is essentially the same as a traditional mammogram. The radiologic technologist places the breasts, one at a time, on a platform on the mammography unit. The technologist then compresses the breast with a clear, acrylic paddle and captures four images of the breast tissue. With the breast still compressed, the 3D imaging commences. An x-ray tube rotates in a 30 degree arc, taking up to 50 low-dose images. These images are used to create the thin slices which allow the radiologist to get clear 3D images of every angle of the breast, helping to detect very subtle breast cancers.

The advantages of tomosynthesis

While tomosynthesis does not replace a traditional mammogram, it provides radiologists an opportunity to increase the level of imaging and care for their patients. Tomosynthesis helps to distinguish normal overlapping tissue from an underlying mass.

BREAST IMAGING LOCATIONS

Magee-Womens Imaging provides state-of-the-art breast imaging services at nine locations throughout western Pennsylvania.

MAGEE-WOMENS HOSPITAL OF UPMC *
300 Halket St.
Pittsburgh, PA 15213

MAGEE-WOMENS IMAGING HILLMAN CANCER CENTER
5115 Centre Ave.
Pittsburgh, PA 15232

MAGEE-WOMENS IMAGING MONROEVILLE *
Corp. One Office Park Building II, Suite 225
4075 Monroeville Blvd.
Monroeville, PA 15146

MAGEE-WOMENS IMAGING SOUTH HILLS
1300 Oxford Drive Suite 2A
Bethel Park, PA 15102

* Tomosynthesis is currently offered at these locations.

For instance, in a tomosynthesis image, a lesion that's missed in one image may be detected because of the thin slices that are produced by the tomosynthesis scan.

Tomosynthesis research

Research at Magee is ongoing to determine if tomosynthesis is helpful in decreasing the number of false-positives, or recalls, which may occur as a result of screening mammograms. According to **Jules Sumkin, DO, FACR**, chief of Women's Imaging at Magee, results from traditional screening mammograms may be reported as inconclusive, requiring the patient to return for another imaging session.

"Recalls occur in about 10 percent of patients who undergo traditional mammograms, and a very small number of those patients actually have cancer," says Dr. Sumkin. "This number is even higher in women who come for their first mammogram, called the baseline mammogram, because there is nothing to compare it to. The women with false-positive mammograms are asked to return for further imaging, which may result in considerable anxiety for the patient."

Dr. Sumkin is currently in the fourth year of an R01 grant from the National Institutes of Health (NIH), studying whether tomosynthesis, in conjunction with standard screening mammography, decreases recall rates in women having their initial baseline mammograms. Dr. Sumkin presented the study's preliminary results on the first 120 women at the Radiologic Society of

North America in 2011. These results have shown that the addition of tomosynthesis has decreased the recall rate by 28 percent.

In summer 2012, the NIH also awarded a two-year R21 grant to **Margarita Zuley, MD**, medical director of breast imaging at Magee and associate professor of radiology at the University of Pittsburgh School of Medicine, to evaluate novel imaging compression paddle systems used in tomosynthesis.

According to Dr. Zuley, tomosynthesis has the capability to reduce the need to compress the breasts during imaging. "One of the main reasons women don't schedule mammograms is because the compression required for standard mammography can be painful," says Dr. Zuley. "Because tomosynthesis has the ability to reduce the occurrence of overlapping tissue, compression becomes less important."

Dr. Zuley's study has three phases. She is currently collecting and analyzing data from the first phase of the study, which assessed by what percentage the compression could be reduced in order to have 90 percent of study participants experience no pain. The next phase will include testing a series of new paddle designs to determine which is best for tomosynthesis. Then, 100 women will undergo standard mammography on one breast and digital mammography with less compression from the new paddle on the other breast. Dr. Zuley will then determine if the diagnostic accuracy is equivalent between the two images.

"Magee has succeeded in being one of the first hospitals to offer tomosynthesis. We are excited to continue moving forward with these two NIH-funded studies so that we continue to be at the forefront of women's imaging and bring the best level of care to our patients."

—DR. MARGARITA ZULEY

MAGEE-WOMENS
IMAGING
PLEASANT HILLS
51 Professional Plaza
Suite 2100
850 Clairton Blvd.
Pleasant Hills, PA 15236

MAGEE-WOMENS
IMAGING
AT UPMC
ST. MARGARET *
815 Freeport Road
Suite 2160
Pittsburgh, PA 15215

MAGEE-WOMENS
IMAGING NORTH
2599 Wexford-Bayne Road
Suite 1000A
Sewickley, PA 15143

WOMEN'S
IMAGING NORTH
9000 Brooktree Road
Suite 402
Wexford, PA 15090

CRANBERRY
BREAST IMAGING
3 St. Francis Way
Building 3
Cranberry Township, PA
16066

* Tomosynthesis is currently offered at these locations.

Survivorship Clinic at Children's Hospital of Pittsburgh of UPMC

For the first time in history, a large population of college-aged individuals — estimated at 300,000 nationwide — has been cured of childhood cancers and survived into adulthood. Being a cancer survivor can present unique health issues later in life, but MANY of these former patients don't receive the proper follow-up care as adults. Children's Hospital wants to change that.

Strength in numbers

Top row, left: Dr. Jean Tersak is a pediatric medical oncologist and director of the Survivorship Clinic at Children's.

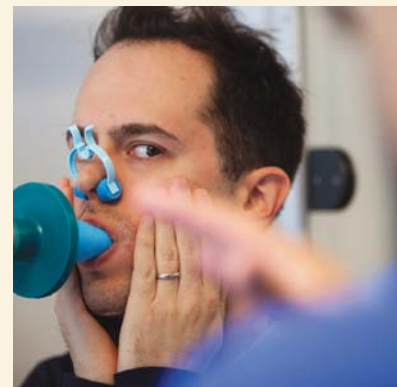
Bottom row, third from left, Aimee Costello, clinical coordinator, prepares documentation of each survivor's cancer treatments for their use later in their lives.

All other photos: Patients who are seen through the Survivorship Clinic receive preventive care focused on maintaining a high quality of life and proactively managing any late effects of their cancer treatment once they are no longer receiving follow-up care for their cancers.

Roughly one in 350 American children will develop cancer by the age of 20. Advances in treatment and supportive care have resulted in long-term survival rates of 80 percent, so that roughly one in 570 Americans ages 20 to 34 is now a survivor of childhood cancer. But their longevity is uncharted territory for primary care physicians and, often, for the survivors themselves — many of whom were too young to remember much about the specifics of their cancer care.

"A lot of former cancer patients don't know their own medical histories because they were so young at the time and their parents handled everything," says **Jean M. Tersak, MD**, medical oncologist and director of the Survivorship Clinic at Children's Hospital of Pittsburgh of UPMC. "Then when they grow up and move away from their families, they often don't have access to their complete histories or don't continue the follow-up care and early intervention that is recommended to maintain a high quality of life."

The Survivorship Clinic is a special program for young cancer survivors about to embark on their futures. Once patients hit the five-year mark following cancer treatment, they graduate





into Survivorship Clinic to transition out of the period of surveillance for disease relapse and into the rest of their lives as survivors. The program allows survivors to remain in contact with the oncology team that treated them, so that they can access information, education, and support, even years down the road.

“Greater than 60 percent of survivors who have been treated for cancer with surgery, chemotherapy, or radiation will develop chronic health conditions or ‘late’ side effects from the treatments,” Dr. Tersak says. “Of these late effects, about 25 percent of them will be considered severe or life-threatening, so it is important that survivors know their risks and understand the special needs they might have over the course of their lifetimes.”

Survivorship Clinic visits do not include screenings or scans to look for cancer recurrences; rather, visits establish baseline health assessments through tests such as echocardiograms, pulmonary function tests, and blood draws. Because these young people now must begin to take responsibility for their own health care, it is important that they understand the treatments they received to achieve a cure, and how those treatments may affect their health in the future. A team of professionals meets with survivors to provide one-on-one counseling focused on teaching them about their past medical and treatment histories, making healthy lifestyle choices, transitioning into the adult medical system, and being aware of their unique medical needs as cancer survivors.

One of the most valuable tools survivors take away from Survivorship Clinic is the comprehensive treatment summary that is prepared for each patient by the clinical coordinator, **Aimee Costello, RN, MSN, CRNP**. This documentation is complete with dates, diagnosis, duration of treatment, chemotherapy agents and doses received, radiation site and doses received, as well as contact information for their primary oncologist and Survivorship Clinic team. Importantly, the treatment summary also outlines potential late effects of therapy and an individualized plan of care for health promotion and prevention of complications. This data is helpful for survivors transitioning to adult PCPs, or for future surgeries where anesthesia will be used, and could be critical in an emergency situation.

Other members of the team are **Jessica Mink, MSW**, a clinical social worker, who helps survivors over age 18 gain access to health insurance or medical assistance once they’re on their own; and **Meghan Eberle, PsyD**, a psychologist, who helps survivors deal with late neurocognitive effects, such as attention, focus, and reading comprehension problems, anxiety, depression, and self-esteem issues, and to gain access to community mental health services, if needed.

The Survivorship Clinic recently held its first event — a reunion of sorts — at which survivors could meet one another and visit with their heroes: the surgical, medical, and radiation oncologists who treated them. The event drew 50 young adult and teenage survivors and an additional 150 family members, who gathered to support one another and celebrate their futures free of cancer.

Survivorship research

The Survivorship Clinic actively participates in a number of research projects related to survivorship, among them the Childhood Cancer Survivorship Study, the largest study of its kind. Children’s is one of 27 medical centers across the country reviewing the medical records of approximately 28,000 patients treated at their facilities for childhood cancers between 1970 and 1999. This body of information will yield important data on the types of health issues this cohort of survivors — some of whom are now in their 40s and 50s — are encountering as they age.

“Being a cancer survivor doesn’t define these former patients, but many do see it is an important part of their identities.”

—DR. JEAN TERSAK

Children’s recently received a two-year, \$100,000 grant from the Hyundai Foundation’s **Hope On Wheels** program to fund an outreach and database project called *SurvivorConnect*. Managed by **Noelle Conover, MS**, project coordinator, *SurvivorConnect* will track and maintain communication with survivors through the Web, email, Facebook, text, newsletters, and by other means, to keep survivors up to date on medical information and prevent them from straying from their follow-up care plans.

A successful transition and a promising beginning

In 1951, when Children's Hospital of Pittsburgh of UPMC founded its Tumor Clinic, marking its beginning in pediatric hematology-oncology care, the cure rate for childhood cancer was only about 5 percent. Today, the pediatric cure rate stands at about 80 percent, which is a dramatic improvement; yet the remaining 20 percent of incurable cancers has proved especially difficult and has not decreased much over the past 10 years, despite medical advances.

The cure rate for pediatric cancers has plateaued over the past decade, according to **A. Kim Ritchey, MD**, a pediatric hematologist-oncologist who has served for 14 years as chief of the Division of Pediatric Hematology-Oncology at Children's Hospital. "Several cancers, particularly neuroblastoma, brain tumors, and certain types of leukemia, still represent significant challenges," says Dr. Ritchey.

Dr. Linda McAllister, right, has been working closely with outgoing chief Dr. A. Kim Ritchey during the transition to her new position as chief of the Division of Hematology-Oncology at Children's. Dr. Ritchey was promoted to vice chair of the Department of Pediatrics.

"These remaining cases have been difficult to cure not just at Children's, but at pediatric hospitals across the country."

During his time as chief, Dr. Ritchey set a strong course for the research, clinical care, and academic activities related to pediatric hematology-oncology. Collaboration and research are critical to improving the cure rate for all cancers, particularly the difficult ones. Toward that end, Children's has shared in and contributed to the body of knowledge of Children's Oncology Group (COG), an international team of physicians and scientists at more than 200 medical institutions studying cancer in children.

Since 1955, COG has been the world's most experienced organization in the clinical development of new therapeutics for children and adolescents with cancer, and Children's was a founding member.

Children's also is a member of COG's Phase 1-2 and Pilot Consortium, a limited group comprising 21 premier pediatric oncology programs across the country. Selected through a peer-review process, this elite group serves as a national and international model for new agent development in pediatric oncology and provides the necessary infrastructure for conducting pediatric Phase 1 clinical trials



and pharmacokinetic studies. Dr. Ritchey has held numerous leadership positions in COG, and has served as the principal investigator of COG at Children's, supervising hundreds of COG protocols over the years.

In January 2013, Dr. Ritchey transitioned into a newly created position as vice chair for Clinical Affairs, reporting directly to **David Perlmutter, MD**, chair, Department of Pediatrics. As the vice chair, Dr. Ritchey will attend to the administrative needs of the entire Department of Pediatrics.

"The newly created position will call upon Dr. Ritchey's unique clinical expertise and leadership skills honed during his tenure as division chief," says Dr. Perlmutter. "Dr. Ritchey understands what physicians need to enhance patient care and optimize clinical practice across all pediatric specialties."

Charting the future in pediatric hematology-oncology

Following Dr. Ritchey as chief of the Hematology-Oncology Division is **Linda McAllister, MD, PhD**, who joined Children's in December 2012. "Some may call Dr. McAllister my successor, but she will actually pave a new path for pediatric cancer care at Children's," says Dr. Ritchey about the future of the program. Dr. McAllister brings with her a breadth of clinical expertise and research experience.

As a top National Institutes of Health (NIH)-funded professor at the University of Michigan, Dr. McAllister ran a basic research lab investigating the mechanisms by which inflammation triggers mucosa-associated lymphoid tissue (MALT) lymphoma. In this disease, chronic inflammation along mucosal surfaces promotes cancer growth at the site. Many of the disease-causing mechanisms discovered by studying MALT lymphoma were then found to also operate in other lymphomas, such as diffuse large B-cell lymphoma, a disease that is fairly common in children.



More than 200 people — 50 of them childhood cancer survivors — attended the first Survivorship Clinic event at Children's Hospital.

LATE EFFECTS OF CANCER TREATMENTS

A cancer diagnosis, treatment, and recovery can take a toll on a child's body that might cause some health problems down the road, so survivors benefit by knowing what to watch for as they age. Survivors may be urged to have screenings, such as mammograms and colonoscopies, at earlier ages than their peers, as well.

Late effects that might present years after receiving surgery, chemotherapy, or radiation therapy include:

- Fertility issues
- Premature menopause
- Cataracts
- Hypothyroidism
- Hypertension and other cardiac problems
- Lung problems
- Vitamin D deficiency
- Loss of bone density
- Chronic pain
- Neurocognitive deficits
- A treatment-related second cancer

As more and more childhood cancer patients become childhood cancer survivors, PCPs will be seeing more new patients who have complex medical histories and risks for these late effects of treatment. Doctors treating survivors can access the complete list of evidence-based Survivorship Guidelines and related Health Links, published by the COG, on the CureSearch website.

“I want to optimize Children’s relationship with UPCI. The infrastructure already in place at UPCI represents a real opportunity for us to enhance pediatric cancer research and expand the reputation for hematology-oncology at Children’s on a national scale.”

—DR. LINDA MCALLISTER

At Michigan, Dr. McAllister shared a joint lab with her husband, **Peter Lucas, MD, PhD**, a pathologist, and their research later branched out into studying other inflammatory diseases, including vascular and hepatic inflammation, and identifying additional connections between inflammation and cancer. Dr. Lucas also will join the Children’s team, continuing the couple’s inflammation and cancer research in Pittsburgh, and will collaborate with renowned University of Pittsburgh pathologist **Yuri Nikiforov, MD, PhD**, in conducting molecular diagnostics at UPMC.

Dr. Perlmutter predicts that the addition of Dr. McAllister will be a game-changer for Children’s Hospital and the Division of Pediatric Hematology-Oncology.

“Dr. McAllister’s ability to mentor, recruit, and lead research initiatives will have a fantastic trickle-down effect on our institution for years to come,” he adds. “Her investigative drive and approach to collaborative research is expected to bring new funding relationships, research opportunities, and the potential to expand on clinical trials, opening new doors for the department.”

“I have goals for myself and for the division,” says Dr. McAllister. “I want to further strengthen the relationships I have seen among my new research and clinical colleagues

at Children’s and capitalize on the exciting intellectual atmosphere here at the University of Pittsburgh. We will be recruiting talented physician-scientists to build a cohesive team who can collaborate in our efforts to better understand why pediatric cancer occurs and how to improve treatment.

“I want to optimize Children’s relationship with the University of Pittsburgh Cancer Institute (UPCI). The infrastructure already in place at UPCI represents a real opportunity for us to enhance pediatric cancer research and expand the reputation for hematology-oncology at Children’s on a national scale.”

As both Dr. Ritchey and Dr. McAllister begin new chapters of their careers, they will have the benefit of each other’s support. Dr. Ritchey will continue his clinical work in pediatric oncology, where he will be an asset to Dr. McAllister as she learns and grows within her new role. Conversely, Dr. Ritchey’s new responsibilities will be supported by the ongoing success of Dr. McAllister’s research and clinical development. “Dr. McAllister and I will have the unique opportunity to learn from one another, unlike most predecessor-successor relationships,” adds Dr. Ritchey. “I look forward to watching the department get to the next level.”

CANCER MEDICATION SHORTAGE REVEALS NEED FOR NEW DRUG DEVELOPMENT

What happens when there isn’t enough chemotherapy medication stockpiled to treat the pediatric patients who need it? That very scenario became a reality in spring 2012 when the Children’s Oncology Group (COG) called for mass rationing of methotrexate, one of the most commonly used forms of chemotherapy for children.

“The COG website regularly updates a list of medications and treatments that are considered at shortage levels in the United States,” explains Dr. Ritchey. “While the list’s length may be startling, the drugs typically aren’t high in demand or in regular use among pediatric oncology patients—until the methotrexate ration was initiated.” The rationing left physicians and clinicians unsettled and families frustrated.

Although back in supply, Dr. Ritchey’s team, and thousands of other physicians across the country, will be keeping a keen eye on methotrexate supply levels and are understandably more cautious about usage and utilizing alternative methods when possible. Scares such as this are further evidence of the need for more novel drugs to treat pediatric cancers and access the supply of established agents.



Pediatric bone marrow transplant: Expanding expertise beyond cancer

Bone Marrow Transplantation (BMT) is most commonly associated with treating cancers, but the Blood and Marrow Transplantation and Cellular Therapies department at Children's Hospital of Pittsburgh of UPMC is expanding its expertise to benefit children with nonmalignant diseases.

Recognizing the scope of BMT as a successful treatment for a number of cancers, blood diseases, and immune disorders, Children's Hospital has restructured the program by spinning it off from the Division of Pediatric Hematology-Oncology and establishing it as an independent entity.

The Bone Marrow Transplantation and Cellular Therapies Program, under the direction of **Paul Szabolcs, MD**, has begun to magnify the capabilities of BMT by focusing on individually rare disorders within immune deficiency syndromes, autoimmune diseases, and genetic disorders. Working closely with his wife, **Maria Escobar, MD, MS**, director of the Program for the Study of Neurodevelopment in Rare Disorders at Children's, Dr. Szabolcs now offers unrelated donor cord blood transplant (CBT) as a treatment for patients with rare metabolic disorders.

Through CBT, cord blood stem cells repopulate the bone marrow and give rise to circulating white blood cells that will provide the missing

enzyme for the patient's lifetime and also may detoxify the body from harmful byproducts. Dr. Szabolcs has overseen this treatment in myofascial pain syndromes, such as Hurler syndrome and Hunter syndrome, and also in leukodystrophies, such as Krabbe disease, metachromatic leukodystrophy (MLD), and others. The magnitude of the beneficial impact of CBT varies in each disease and also is greatly influenced by the timing of the intervention. Some children who receive CBT before the onset of disease symptoms may develop without obvious deficits to live productive lives for decades while, in other children, progression of the neurodegenerative disease will be halted to reduce suffering and preserve vision and hearing.

Although BMT often can offer a cure, high-dose chemoradiation and chemotherapy associated with BMT can be too toxic and dangerous for more fragile patients.

Dr. Szabolcs and members of his division are working to tailor treatment protocols toward a reduced intensity/reduced toxicity approach that can be used for children who are too sick to transplant through conventional BMT preparative regimens. Dr. Szabolcs is working to develop protocols for upcoming clinical trials using the reduced intensity/reduced toxicity approach, which may pave the way for improving cure rates and quality of life among patients.

From left, a patient and her mother at a checkup at the Bone Marrow Transplantation and Cellular Therapies Program; middle, Dr. Paul Szabolcs examines a tiny patient; right, Dr. Szabolcs, left, explains a procedure to the parents of a young patient, with help from Dr. Maria Escobar, far right, an expert in neurodevelopment and rare disorders at Children's.

With the expanded use of BMT and related enzyme-replacement therapies, Dr. Szabolcs and Dr. Escobar have seen favorable outcomes in seven children diagnosed with rare disorders since summer 2011.

Coping with cancer

It's common for a group of women to have similar interests, such as a favorite hobby or the same taste in movies, but MANY women are finding strength and comfort through specialized support groups that help them cope with something as serious and frightening as a cancer diagnosis.

Cancer support group unites young moms

Moms With Cancer is a networking group developed by the Cancer Caring Center in partnership with UPMC CancerCenter. Created and led by Jill Brufsky, PharmD, a mom and cancer survivor, this group offers support, advice, and companionship to mothers who have been diagnosed with cancer.

"Mothers with cancer face special challenges," said Jill, an Upper St. Clair, Pa., resident who was diagnosed with acute myeloid leukemia in June 2011. "The purpose of this group is to address those challenges — from how much about our disease to tell our children to how to manage being caregivers and having loved ones take care of us."

Jill is currently being treated at Hillman Cancer Center by **Mounzer Agha, MD**. Her personal fears about how her illness would affect her husband, **Adam Brufsky, MD, PhD, FACP**, a professor at the University of Pittsburgh and a medical oncologist at UPMC CancerCenter, and their three children, ages 15, 13, and 10, led her to start Moms With Cancer.

The group of 13 members gets together once a month at UPMC South Hills to talk about their experiences. The group is not focused on one specific type of cancer, but rather the concerns that arise from their diagnoses. "Everyone in this group is a mom, and a lot of the fears we have are related to our kids," says Jill. "We don't talk about specific treatments, but we'll discuss how we feel and what we're going through being moms with cancer."

Moms With Cancer member Cheri Lee moved to Upper St. Clair about a year and a half ago and is a chocolatier who sells candies and gifts to small businesses. She told her family, including her 11-year-old daughter, that she was diagnosed with liposarcoma and breast cancer in early spring 2012. Due to her treatments at Hillman Cancer Center with **Hussein Tawbi, MD, PhD**, which consisted of surgeries in addition to cycles of chemotherapy, Cheri put a hold on her work. She has been a part of the group since it was formed in September 2012.

Melanie Bleiweis joined the group after reading about it in *The Almanac*, a local newspaper. Having been friends for years, Jill and Melanie have supported and encouraged each other through their diagnoses. As a two-time melanoma survivor, Melanie was open with her children — a 14-year-old daughter and 11-year-old son — about her disease from the beginning. She was treated initially with surgery and interferon by **John Kirkwood, MD**, at Hillman Cancer Center and, when her cancer came back a few years later, she received surgery and ipilimumab treatment at UPMC CancerCenter, Upper St. Clair. Although it has been a tough road, she is thankful for the networking group. "I would have loved to have had a melanoma support group

CANCER CARING CENTER

Since 1988, the Cancer Caring Center has provided a wide variety of free support services to more than 65,000 area residents, including neighborhood network groups, counseling for individuals and couples, "Live Well With Cancer" programs, and pet therapy for children with cancer. The center's mission is to help cancer patients and family members move forward after a cancer diagnosis.

in 2008 when I was first diagnosed,” says Melanie. “It’s nice to hear from people who have gone through it. I love these ladies.” Melanie has been in remission for a year. The experience, however, is still a vivid memory. “It’s a drawing that never ends. It’s not fun, you don’t feel great. You’re doing it to stay alive.”

Sandy Dunkerley is a teacher’s aide for first and second grade students with learning difficulties. As a two-time cancer survivor — Sandy was diagnosed with breast cancer in 2007, and ovarian cancer in 2011 — she also read about Moms With Cancer in *The Almanac*. With the help of Dr. Brufsky, **Gretchen Ahrendt, MD**, and **Alexander Olawaiye, MD**, Sandy was able to beat both diseases. “I feel very supported when I come to the meetings because I’m with people who are going through or have gone through very similar experiences,” said Sandy.

Cheri, Melanie, Sandy, Jill, and the others are more than just individuals who meet every month to share their concerns. They are a group of friends who laugh together, cry together, and care for one another, brought together by an unfortunate disease.

Representatives of Moms with Cancer include, from left, Sandy Dunkerley, group founder Jill Brufsky, Melanie Bleiweis, and Cheri Lee.



“It gives you a place to talk about things that other people might not understand. When you talk to other moms and hear they are going through sort of the same things, it helps.”

—CHERI LEE

“Although the process is arduous, it represents a substantial honor to our practices and signifies a commitment of the utmost in excellence in care for our patients.”

—JAMES SINICKI

Network receives ACRO accreditation

UPMC CancerCenter recently became the largest health care system in the country to be accredited by the American College of Radiation Oncology (ACRO). The accreditation recognizes the highest quality of radiation oncology care.

“We know we deliver quality, state-of-the-art care for a variety of cancers. We know we do it across a large geographic area and with a great deal of safety. But it’s always helpful to have another set of eyes — external eyes — to look critically at what and how we do what we do,” said **Dwight E. Heron, MD, FACRO, FACR**, director of radiation services at UPMC CancerCenter. “We are constantly trying to improve the care we give our patients and strive to be better.”

For UPMC CancerCenter, ACRO accreditation is an external validation of the commitment to quality and excellence in patient care and treatments across its network of radiation oncology sites. For patients, it serves as a reassurance that they made the right decision to come to UPMC CancerCenter, as staff is dedicated to their well-being and offers the most up-to-date treatments and technologies. In addition, it is an educational process for our practices, pointing out what opportunities are available to improve upon.

The comprehensive ACRO accreditation planning process began in summer 2011. ACRO clinical and administrative experts reviewed detailed reports of patient charts, technology, staff certifications, and documentation of processes and site services for each radiation oncology site. Officials then visited each of the 20 UPMC CancerCenter radiation oncology sites to survey day-to-day operations.

Following the successful application and review of the findings by an ACRO committee made up of physicians, physicists, and administrators, UPMC CancerCenter was awarded accreditation — making UPMC CancerCenter the largest ACRO-accredited network in the United States.

“On a regular basis, everyone needs to be involved in the culture of safety and quality. It takes a team to provide this high level of care,” says **James Sinicki**, manager, Quality and Regulatory, UPMC CancerCenter Division of Radiation Oncology, who was responsible for ensuring each site was properly prepared for this detailed process. “Although the process is arduous, it represents a substantial honor to our practices and signifies a commitment of the utmost in excellence in care for our patients.”

Regardless of accreditation, UPMC CancerCenter is committed to continuously moving forward and advancing. “What we do is what we breathe,” said Dr. Heron. “Having the accreditation doesn’t mean our work is done. We’re still going to innovate and do all we can so that every patient gets the right treatment every time.”

ACRO was founded to represent both patient and practitioner interests and issues regarding radiation oncology. According to the Manual for ACRO Accreditation, ACRO has become a source of physician education, an advocate for patients and practitioners, and a forum for new technology.



International services

EXPANDING UPMC CANCERCENTER'S GLOBAL FOOTPRINT

For more than two decades, UPMC has been mastering clinical expertise in the western Pennsylvania region. Capitalizing on this proven foundation, the UPMC International and Commercial Services Division, in partnership with UPMC Global Care, continues to extend UPMC CancerCenter's international reach.

Ireland

The first of the international cancer centers was the UPMC Whitfield Cancer Centre in Waterford, Ireland, which opened in 2006. A year later, this expansion continued when UPMC CancerCenter took over the management of Beacon Hospital Cancer Centre in Dublin. The radiosurgery program at UPMC Beacon Hospital was recently awarded for excellence in delivering stereotactic radiosurgery treatment during a ceremony attended by local and national dignitaries, including Minister Alex White, TD, Minister of State at the Department of Health.

Kazakhstan

In addition to providing clinical expertise, UPMC CancerCenter offers international universities and organizations comprehensive feasibility studies. In summer 2012, UPMC was selected by Nazarbayev University in Kazakhstan to conduct such a study related to the development of a national oncology treatment and research center in that country. Kazakhstan President Nursultan Nazarbayev outlined a bold plan to build the nation's most advanced oncology treatment and research center for its citizens and others of Eurasia. More than 30,000 new cases of cancer are detected in Kazakhstan annually — with over half of all cancer patients being diagnosed at a late stage. The government-funded National Research Cancer Center, to be managed by Nazarbayev University, is expected to include a 300- to 400-bed hospital, outpatient care, a research facility, and a hotel complex. The UPMC CancerCenter feasibility study will significantly impact the inner workings and development of this center, potentially paving the way for future partnerships in the Eurasian region.

Italy

UPMC CancerCenter continues to extend itself to meet the needs of international patients with its newest endeavor, the management of UPMC San Pietro Fatebenefratelli (FBF) Advanced Radiotherapy Center in Rome, Italy. The San Pietro facility, which opened in early 2013, offers 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 San Pietro facility houses the only one in Rome.

The facility benefits cancer patients in Rome by fulfilling an unmet need for advanced radiotherapy treatment options, as patients had to travel to other regions for this type of treatment. The facility sets the stage for additional opportunities in Rome as it promotes UPMC's recognition among the international scientific and academic community. Patients at the San Pietro facility receive the same individualized, high-quality care and treatment that patients receive at all UPMC CancerCenter network sites in the United States and Ireland.

UPMC CANCERCENTER OPENS NEW SITE AT UPMC EAST

In July 2012, UPMC East in Monroeville, Pa., opened to provide the best health care practices and medical technology to patients in communities east of Pittsburgh.

UPMC CancerCenter at UPMC East is part of this state-of-the-art hospital, offering advanced radiation oncology treatment services to complement the existing medical oncology center nearby. UPMC CancerCenter at UPMC East treats an average of 21 patients a day, exceeding the expected volume of five. These patients have access to the latest therapies and clinical trials through the University of Pittsburgh Cancer Institute (UPCI), nutritional counseling and support services, patient and caregiver support groups, free parking, and more.

"With our team, patient care comes first. We develop very special bonds with our patients — we talk to them, listen to them, comfort them. Our patients are our neighbors, and we are proud to offer them the world-class care they deserve," says **Sanjeev Bahri, MD, FACRO**, chairman, radiation oncology, UPMC East.

UPMC East Radiation Oncology offers intensity-modulated radiation therapy (IMRT), image-guided radiation therapy (IGRT), respiratory gating, RapidArc®, prostate seed implantation, and high-dose rate brachytherapy.

As part of its work to give back to the community, UPMC East participates in many events, such as the Race to No Where, the Pink Glove Dance™, and Breast Cancer Awareness Day. In addition, the radiation oncology department had one of the first Above and Beyond winners for UPMC East.

Cancer Outreach Program committed to the many underserved



2012 OUTREACH BY THE NUMBERS

Children reached by *Health Choices for Students* program:

- 7,685 in 7 counties and 18 school districts during the school year
- 5,712 during the summer

Community-based education and screening activities:

- 55 community events
- 7,500 individuals educated
- 20,000 individuals reached in 5 counties
- 41 screening clinics
- 17 wellness fairs
- 11 "Ask the Nurse" sessions with the Salvation Army Food Bank, reaching 685 individuals (27% more than 2011)
- 433 individuals screened per guidelines (47% more than 2011)
- 336 participants in programs with *Health Care for the Homeless*

As a National Cancer Institute (NCI)-designated Comprehensive Cancer Center, the University of Pittsburgh Cancer Institute (UPCI), partner with UPMC CancerCenter, is committed to reducing the burden of cancer through a focused approach to education, risk reduction, screening, reducing barriers, and research.

The Cancer Outreach Program, funded, in part, by the Pennsylvania Department of Health, is the vehicle through which UPCI reaches the population at large, with a particular interest in meeting the needs of the region's underserved populations — among them, the uninsured and underinsured, minorities, seniors, the homeless and those living in transitional housing, people in rural areas, and those with mental and/or physical challenges.

To reach these groups who generally do not receive routine health care, **Lyn Robertson, DrPH, RN, MSN**, and her staff have developed innovative programs and partnerships with local social services agencies. "Our network continues to expand out into more of the places where our underserved and at-risk residents are — such as residential facilities, domestic shelters, and public libraries," says Dr. Robertson. "We're there regularly, so people know us and trust us."

The team regularly visits local community centers, YMCAs/YWCAs, food banks, support agencies, as well as businesses — such as barbershops, pictured at left, and beauty academies — to educate and provide screenings for these populations, including African-American men and women, who may be at higher risk for developing certain chronic diseases.

Cancer screenings

UPMC CancerCenter and UPCI support a number of community initiatives which provide no-cost or low-cost access to screening tests, according to medically accepted guidelines, that at-risk people otherwise might not receive. Included are prostate-specific antigen (PSA) blood tests to screen for prostate cancer in at-risk men, which are performed at no cost by the Pathology Lab at UPMC, and low-cost HPV tests and Pap smears to qualifying women to screen for cervical cancer.

UPCI also distributes vouchers for free mammograms, which are provided by Adagio Health with funding from Susan G. Komen for the Cure®, as well as vouchers for public transportation to and from these screening appointments.

Supporting research

Research is another area that Dr. Robertson's team supports, both in Pittsburgh and nationally. Her team actively assists UPCI researchers in obtaining blood samples from minority groups that might be underrepresented in research.

In addition, Dr. Robertson currently is the site primary investigator for a study with Cone Health and the Greensboro Health Disparities Collaborative in North Carolina. Geni Eng, DrPH, from the University of North Carolina, is the principal investigator of this study, funded by a five-year R01 grant from the National Cancer Institute, called

“We expend a lot of effort to save a few lives, and that reflects UPMC CancerCenter’s commitment to understanding and meeting the needs of the communities we serve.”

—DR. LYN ROBERTSON

Accountability for Cancer Care through Undoing Racism and Equity (ACCURE). African-American cancer patients, as compared to their white counterparts, tend to initiate treatment later and are less likely to complete recommended treatment, contributing to poorer outcomes and shortened survival rates. UPMC CancerCenter and the two sites in North Carolina have joined together to identify structures built into cancer care systems that make cancer care vulnerable to institutional racism. The study will investigate how these systems can be changed to reduce racial inequity in quality and completion of treatment for Stage 1-2 breast and lung cancer patients.

The first phase of this study involves looking at patient data from 2007 to 2011 for those diagnosed with early-stage lung and breast

cancer to examine treatment outcome measures and demographics, such as age, gender, and year. “Once we have this baseline data, we will then move forward to develop our intervention, hire an ACCURE navigator, and educate the health care teams caring for this group of patients on health equity issues,” says Dr. Robertson.

Phase 3 of the study, which will be a randomized, controlled trial, will include 150 patients with newly diagnosed Stage 1-2 breast or lung cancer from each of the two sites. Patients will be randomized to the ACCURE navigator or usual care. Data also will be collected in a “real-time registry” so that statistics can be kept regarding patient compliance with appointments and follow-up care, while controlling for demographic data and comorbidity.

Educating at-risk populations is an important goal of the Cancer Outreach Program. At left, Beth Simon, DrPH, RN, MSN, and at right, Dr. Lyn Robertson present frequent teaching programs for men at local treatment centers. Here the team presents a prostate cancer session at the Salvation Army’s Harbor Light Center on Pittsburgh’s North Side, a residential treatment and bridge housing program for adult men recovering from substance abuse.



COMMUNITY EVENT SUPPORT

Another form of outreach through which UPMC CancerCenter, partner with UPCI, touches the communities it serves is through participation in events and donated services and supplies to support community agencies and organizations.

Each of the more than 35 individual sites in the UPMC CancerCenter network is extremely proactive in building and maintaining close working relationships with their local community agencies, and partners with those agencies in many events and activities year-round. Support for these activities 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 **Glimmer of Hope Foundation**, the **Young Women's Breast Cancer Awareness Foundation**, the **Leukemia and Lymphoma Society**, and the **American Cancer Society**.

Volunteers find enrichment and fulfillment while helping others

UPMC CancerCenter, partner with University of Pittsburgh Cancer Institute (UPCI) has an active Volunteer and Community

Services Program whose central mission is 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.

Some people choose to volunteer at UPMC CancerCenter to gain educational and career-related experience, while others seek personal fulfillment, growth, or an opportunity to serve their community. Many of our volunteers are cancer survivors themselves, or have been moved to serve by friends or family members who have been diagnosed with cancer.

Hundreds of volunteers transition through our program each year, but we maintain a base of 150 to 200 volunteers at any given time. Our volunteers donated nearly 40,000 hours in 2012.

Volunteer opportunities are created wherever there is a need. Last year, we:

- Established a **pet therapy program**, which began in January 2012 with one pet. By the end of the year, the program had reached 11 pets, with an additional nine pets planned to join the program in early 2013.

- Showcased **volunteer service opportunities** to prospective volunteers at two University of Pittsburgh volunteer fairs.
- Collaborated with various schools to be a **host site for 40 student externs** who donated 5,400 hours to fulfill their school requirements. Extern roles included medical assistants and patient care technicians.
- Partnered with the **University of Pittsburgh School of Pharmacy to host 20 students** (10 in each of the spring and fall terms) for experiential learning studies in various clinical settings.
- Hosted 42 students who participated in the **UPCI Summer Academy program**. Funded by a grant from the National Cancer Institute, the program was designed to promote engagement in cancer research and cancer careers. Students were mentored by several research faculty members during the eight-week program. These students also participated in our "Oncology on Canvas" volunteer reception, in which they presented some of their findings from their summer experience.
- Collaborated with **educational programs through organizations such as Goodwill**, which focus on teen workforce development. We provided two teens the opportunity to gain first-time experience in a work setting during an eight-week summer youth employment program and to continue that experience in their after-school hours during the academic year. We also expanded our partnership to work with Goodwill's health care office skills program to recruit their students for entry-level administrative positions.



UPMC CancerCenter pledges support for American Cancer Society

Since 1994, UPMC has supported the American Cancer Society (ACS) through independent sponsorships, primarily focusing on events, galas, research, and receptions.

In 2011, UPMC CancerCenter agreed to provide a \$100,000 direct grant for ACS programs, services, and research efforts in exchange for ACS acknowledgment and recognition of this sponsorship at all western Pennsylvania programs and events. This year, UPMC CancerCenter and UPCI extended their arrangement with ACS through a two-year contract and will provide \$250,000 in support.

Events and initiatives covered by the sponsorship include:

- **Relay for Life** — An overnight event that celebrates the lives of people who have battled cancer, remembers those lost, and fights back against the disease.
- **Patient Navigator Program** — On- and off-site navigators help patients get the right information they need.
- **Making Strides Against Breast Cancer** — A walk to honor breast cancer survivors, raise awareness, and raise funds for breast cancer research, education, outreach, local services, and support. Representatives of UPMC CancerCenter and UPCI who participated in the walk raised nearly \$5,000, and the Hillman Healers team placed sixth overall out of 217 teams.
- **Look Good ... Feel Better** — A program that teaches beauty techniques to cancer patients to help them manage appearance-related side effects of cancer treatment.
- **Daffodil Days** — Allegheny County's Daffodil Days campaign is the largest in the country, raising more than \$400,000 annually. This program offers daffodils in the spring to donors in appreciation for their contributions to the fight against cancer.

In 2012, the Volunteers and Community Services program helped coordinate sales for more than 100 different departments across the entire UPMC hospital network. As a result, more than \$47,000 was donated to ACS — the largest amount given by a single participating organization in the Greater Pittsburgh Unit's fundraiser. More than \$11,000 of that total went to fund orders through **Project Care**, which provides stuffed bears to hospitalized children, and **Project Hope**, which provides daffodil bouquets for cancer patients in hospitals, treatment centers, and other facilities.

- **Support and education programs** — including **Man to Man**, a program that helps men and their families cope with prostate cancer; **Reach to Recovery**, a program that helps women and their families cope with breast cancer; **Road to Recovery**, a free transportation service offered by the ACS to help patients get to treatment appointments; and **I Can Cope**, a free educational program for people facing cancer.

Through this partnership, UPMC CancerCenter and ACS help roughly 2,500 patients annually to detect, prevent, and beat cancer, as well as obtain free transportation and lodging, provide emotional support and on-site navigation to information and resources, assist with financial and other cancer-related needs, and celebrate survivors. By working together, ACS and UPMC CancerCenter have built a partnership that has increased survival rates in breast, colorectal, lung, and prostate cancers through prevention and earlier detection.

Comprising more than 4 million volunteers, ACS offers nearly 100 programs and services and is the largest source of private cancer research funding in the United States.



Through this partnership, UPMC CancerCenter and ACS help roughly 2,500 patients annually to detect, prevent, and beat cancer.



The new frontier of cancer care



Under this initiative, a patient's medical records will be available digitally across all UPMC hospitals.

Precision medicine, also known as personalized medicine, is rapidly advancing as the new frontier of health care. After nearly a decade since the Human Genome Project was completed by the U.S. Department of Energy and the National Institutes of Health (NIH), the project continues to inspire clinicians and researchers alike to find better ways to diagnose disease and personalize patient care.

One of the original goals of the project was to use the information to pinpoint genes that cause disease, which researchers now know is much more complicated, involving the influence of genomic, transcriptomic, proteomic, and pharmacogenomic, as well as environmental information. Finding ways to identify, compile, and harness this information presents many challenges.

In cancer, principal among these challenges is the development of a comprehensive information management strategy in order to integrate cancer patient clinical data with complex molecular testing in such a way that clinical decision making regarding diagnosis and treatment can be made more precise and efficient.

According to **Steven Shapiro, MD**, executive vice president, chief medical and scientific officer, and president, Physician Services Division, UPMC is uniquely suited to take on this challenge.

"UPMC is a Learning Health System. Our payer, provider, and research partnership with the University of Pittsburgh, combined with our large, geographically diverse network of clinical care, gives us access to data that our advanced, secure analytics will mine, leading our efforts in precision medicine and allowing us to take advantage of emerging technology and care at the bedside," says Dr. Shapiro.

For more than a decade, UPMC has been at the forefront of investing in electronic health records, and interoperability and financial management systems. "Although this has

AN ENVIRONMENT OF ACCOUNTABLE CARE

We need medicine that is affordable, effective, and least toxic. Personalized medicine is about making the treatment as individualized as the disease. It involves identifying genetic, genomic, and clinical information that allows accurate predictions to be made about a person's susceptibility to developing disease, the course of disease, and its response to treatment.

The goal is to develop new models of patient care that are both high-quality and cost-effective. The NIH estimates \$750 billion is spent on unnecessary procedures each year. Both clinicians and researchers agree that we have an opportunity to both improve and eliminate unnecessary treatments and testing.

As patients and tumors become better characterized, there will be incremental improvements in defining therapy in terms of both effectiveness and toxicities using tools that can be applied in the clinic and acted on in real time. If this can be achieved, outcomes and quality of life could be dramatically improved. In addition, ineffective therapies could be avoided, which could save the health care system and patient considerable resources.

"While cost savings is a benefit, better patient outcomes are paramount," reflects Dr. Shapiro. "At UPMC, patients and their individual needs are always at the center of all we do and all we hope to accomplish for the advancement of medicine."

provided vast amounts of information to enhance the quality and safety of care, the explosion of data at UPMC alone is moving faster than our ability to transform that information into intelligence and improved decision making at the point of care," says Dr. Shapiro. "And with the rapidly decreasing cost of sequencing genes, huge amounts of genomic information will be added to that data base in the future."

Roadmaps for clinical practice

Many of today's treatments come from an outdated population-based clinical model, where at best 20 percent of our population may benefit from treatments, despite advances in the fields of genomics and proteomics.

Michael Becich, MD, PhD, pathology informatics leader and chairman and professor of the University of Pittsburgh Department of Biomedical Informatics, says that clinicians and researchers agree that our next focus in the evolution of medicine is to digitize patient information in an efficient way that creates opportunity for computational analysis and interpretation of patient care, so that treatment decisions can be made in the clinical environment.

"This is a very exciting time in research and medicine," says Dr. Becich. "We have the opportunity to make patient information and informatics 'come to life' and positively affect how we treat patients."

Leading the way

But feasibility isn't the only challenge. Achieving the goal of personalized medicine in cancer will require substantial input from clinicians, scientists, bioinformatics experts, information technology experts, and administrators.

With the help of its technology partners, UPMC over the next two years will install the hardware and software needed to create a comprehensive data warehouse that will bring

together data from more than 200 sources across UPMC, UPMC Health Plan, and outside entities, including labs and pharmacies. Clinicians, researchers, and administrators will have secure, real-time access to data and analytic tools that fit their particular interests and needs.

"UPMC's analytics initiative is one of the most ambitious and comprehensive efforts of its kind in health care," says **Scot Stevens**, chief information officer for UPMC CancerCenter and the University of Pittsburgh Cancer Institute.

This effort represents the new intersection of technology and patient care, enabling UPMC to find the most effective ways to manage and mine valuable health information.

Early analytics projects are expected to improve quality reporting and measurement across UPMC hospitals and physician offices; provide insight into the effectiveness of treatments and the cost of variations in care; and offer predictive alerts that will improve disease prevention.

"Given the size, scope, and influence of this leading academic medical center, the discoveries made here are likely to transform the practice of medicine far beyond the walls of UPMC."

—SCOT STEVENS

Dr. Michael Becich of the University of Pittsburgh Department of Biomedical Informatics and his colleagues across UPMC and UPMC CancerCenter are leading our efforts in personalized medicine.





The role of mind and brain in relation to cancer

The overall goal of the Biobehavioral Medicine in Oncology Program (BMOP) of the University of Pittsburgh Cancer Institute (UPCI) is to promote innovative and productive interdisciplinary research focused on the role of mind and brain in relation to cancer, with the long-term objective of contributing to a reduced risk of cancer development, earlier detection, improved treatment response, reduced symptom burden, and enhanced survival.

The BMOP has a rich history as one of the University of Pittsburgh's first National Cancer Institute (NCI)-supported programs, with more than two decades of scientific accomplishments investigating the impact of psychological and social influences on behavioral and biological pathways related to cancer initiation, progression, response to treatment, and patient quality of life.

Grounded in the behavioral sciences, program investigators are conducting a number of basic, preclinical, clinical, and translational research studies examining effects of stress and other psychological processes across the cancer continuum, including:

- At the basic science level, **Melanie S. Flint, PhD, Dana H. Bovbjerg, PhD, Frank J. Jenkins, PhD, and Bennett Van Houten, PhD**, are studying the effects of **chronic exposure to stress hormones on cultured human cells**. They found that under chronic stress, the cultured cells incur DNA damage, which in a person may increase the risk of cancer development. This adverse effect of stress hormones could be antagonized in cell culture by the appropriate antagonists, which also may work in people.
- **Eric Donny, PhD**, has expertise ranging from animal and human behavioral pharmacology to the regulatory science of tobacco control. His recent work focuses on understanding the **role of nicotine in tobacco use and dependence**, including how nicotine functions as a reinforcer and impacts the processing of other reinforcing stimuli in the environment. Dr. Donny currently directs the National Institute on Drug Abuse (NIDA)-funded Center for the Evaluation of Nicotine in Cigarettes, which aims to assess the potential impact of regulated reduction of the nicotine content of cigarettes as a means of improving public health.
- **Inna Belfer, MD, PhD**, is a human geneticist with a primary interest in the relationship between genotypes and complex traits, such as human pain, psychiatric diseases, and addictions. Her current research focuses on optimizing pain assessment, **acute and chronic pain phenotyping**, selection of pain candidate genes, and genotyping single nucleotide polymorphism (SNP) markers. Her primary research goal is to identify genetic and nongenetic determinants of human pain conditions, such as postmastectomy chronic pain, with a particular focus on the effect of genotype on neurobiology of neurons in human spinal ganglia.
- The research of **Hilary Tindle, MD**, focuses on the application of **mind-body therapies for tobacco dependence**, particularly among adult smokers with coronary heart disease (CHD). Cigarette smoking is the leading preventable cause of death in the United States, is associated with significant morbidity, and is a major cause of CHD and lung cancer. Despite standard therapy for tobacco dependence, the process of quitting smoking can produce mood, sleep, and cognitive disturbances, resulting in profound distress that hinders cessation attempts and hastens relapse. Smoking cessation therapies are needed to effectively address this gap in treatment.
- **Faina Linkov, PhD, MPH**, is surveying ovarian cancer patient and provider experiences to develop an **educational curriculum and decision support system** that promotes adherence to best evidence-based care. In particular, this information will help in areas where existing interventions traditionally failed to include patient input.
- **Chemotherapy-induced nausea and vomiting (CINV)** is a prominent side effect of several anticancer treatments.

Although antiemetics (antivomiting medications) have improved the management of CINV, a substantial number of patients with cancer still experience these debilitating effects. Using musk shrews as animal models, **Charles Horn, PhD**, found evidence of multiple biological pathways for CINV. Shrews were selectively bred into high- and low-emetic responders using motion exposure as the emetic stimulus. The biological pathway differences for emesis now are being studied, which could lead to testing novel antiemetic and antinausea agents.

- Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) have been shown to increase survival and improve quality of life for patients with non-small cell lung cancer (NSCLC). Because EGFR-TKIs are a new class of drugs, implications for taking the medication are unknown. **Catherine M. Bender, PhD, RN, FAAN**, and **Ahmad Tarhini, MD, PhD, MSc**, explored the process of **medication-taking for NSCLC patients receiving erlotinib TKI therapy** through extensive interviews of these patients. Their informative findings may provide the theoretical basis for developing patient-centered interventions to improve medication-taking, including peer support groups or group interventions.
- Dr. Bovbjerg and **Robert Schoen, MD, MPH**, found that the **successful recruitment of patients to a psychosocial/behavioral study** is most likely due to the established relationship with the health care team and flexibility regarding time and meeting location. These important observations could be implemented in future clinical studies.
- Women with ovarian cancer often experience many co-occurring, severe,

and distressing symptoms that directly impact their quality of life. Optimal symptom management depends on patients' abilities to negotiate the health care system. "Self-advocacy" is frequently promoted within cancer survivorship research and policy as a key factor ensuring patient participation and engagement in their care. **Heidi Donovan, PhD, RN**, and her nursing colleagues found that a **deepened understanding of self-advocacy** can lead to improved clinical support for and research approaches to improving patient-centered care, in addition to guiding potential interventions for women with ovarian cancer.

- Studies have shown a significant racial survival disparity in breast cancer patients. An intervention of Advocacy, Communication, Treatment Explanation and Support (ACTS) was developed by **Margaret Rosenzweig, PhD, CRNP-C, AOCN**, and colleagues to counter common symptoms related to **African-American treatment nonadherence**. Their results showed that the ratings for cultural appropriateness and acceptability of materials improved following implementation of suggested changes from the African-American Women's Speakers Bureau, a community advocacy group of breast cancer survivors.
- Head and neck cancer is a life-threatening illness, often with a poor prognosis. Although incidence rates are higher in men, a substantial number of women also are affected by this disease. It is unclear whether men and women differ in their emotional reactions to a new head and neck cancer diagnosis. **Donna Posluszny, PhD**, and Dr. Bovbjerg developed a study that showed that symptoms of emotional distress, characterized by anxiety rather than

depression, were more prevalent in women than in men, and that women were more vulnerable to the **emotional impact of a head and neck cancer diagnosis**. Efforts to further understand the emotional impact of this diagnosis in both men and women are important for future research.

- According to a study by **Paula Sherwood, PhD, RN, CNRN, FAAN**, and Dr. Donovan, **cognitive representation of symptoms** — such as severity, distress, consequences, controllability, cause, and timeline — may advance the understanding of patients' engagement in symptom-related coping efforts. The study aimed to describe relationships between representations of pain and numbness/tingling and coping in women with a history of ovarian cancer. They found that acceptance, or the belief that nothing can be done about the symptoms, was pervasive for numbness/tingling. Assessment of symptom representations may help practitioners identify patients' concerns about symptoms that may interfere with productive coping efforts.
- **Obesity has been associated with an increased risk of many diseases**, including certain types of cancer. **Lewis H. Kuller, MD, DrPH**, and colleagues found that weight loss was significantly associated with improvements in two proinflammatory adipokines, adiponectin and IL-6. When weight gain occurred, those changes were attenuated. Implementing strategies that support healthy behaviors and sustained weight loss can help prevent a state of chronic systemic inflammation and prevent adverse health outcomes.



Recruiting the best physicians and researchers to join our team of experts

The UPMC CancerCenter and University of Pittsburgh Cancer Institute (UPCI) network has expanded to more than 35 locations in western Pennsylvania and eastern Ohio so our patients get the best care at the cancer center closest to home. The goal of engaging new talent is to enhance our knowledge and expertise as an organization, so that patients have confidence in UPMC CancerCenter as the right place for their treatment. In addition, new recruits help us to continuously advance our education and research missions to discover new treatments and ways to prevent cancer.

Nduka Amankulor, MD

Neurosurgeon and assistant professor in the Department of Neurological Surgery. Dr. Amankulor specializes in spine surgery, neuro-oncology, and cranial base surgery. He received his medical degree from Yale University School of Medicine in New Haven, Conn. He completed his residency at Yale New Haven Hospital, and his fellowship at Memorial Sloan-Kettering Cancer Center in New York.

Julie Bauman, MD, MPH

Medical oncologist, assistant professor of medicine, director of the Head and Neck Cancer Section and Thyroid Cancer Section in the Division of Hematology-Oncology, and co-director of the UPMC Head and Neck Cancer Center of Excellence. Dr. Bauman specializes in the treatment of head and neck cancer and thyroid cancer. Dr. Bauman is board-certified in medical oncology and internal medicine. She received her medical degree from Tufts University School of Medicine in Boston, completed a residency in internal medicine at the University of Utah in Salt Lake City, and a medical oncology fellowship at the University of Washington Fred Hutchinson Cancer Research Center in Seattle.

Timothy F. Burns, MD, PhD

Medical oncologist focusing on the treatment of lung cancer. Dr. Burns has a special interest in patients with KRAS-mutant non-small cell lung cancer. Dr. Burns is board-certified in internal medicine and medical oncology. He received a medical degree and doctorate from the University of Pennsylvania and completed a residency and a medical oncology fellowship at The Johns Hopkins Hospital in Baltimore.

Lesley Butler, MSPH, PhD

Associate professor of epidemiology at the University of Pittsburgh Department of Epidemiology Graduate School of Public Health. Dr. Butler received her bachelor's degree in biology from the University of California Davis, and her doctorate in epidemiology from the University of North Carolina at Chapel Hill. She is a member of the American Association for Cancer Research and the Molecular Epidemiology Working Group.

Lijun Dai, MD, PhD

Medical hematologist-oncologist. Dr. Dai has a clinical interest in the management of hematologic disorders and the treatment of all cancers, including breast, gastrointestinal, and lung cancer. She received her medical degree from Sun Yat-Sen University of Medical Sciences (SUMS), Guangzhou, China, and completed residencies in internal medicine at the First Affiliated Hospital of SUMS, Guangzhou, China, and Texas Tech University Health Sciences Center at Amarillo, Texas. In addition, Dr. Dai completed a fellowship at the University of Pittsburgh School of Medicine and UPMC.

Emilia Diego, MD

Assistant professor in the Department of Surgery at Magee-Womens Hospital of UPMC. Dr. Diego specializes in premenopausal breast cancer, breast conservation therapy, locally advanced breast cancer, and high-risk breast disease. Board-certified in surgery, Dr. Diego received her medical degree from the University of the Philippines College of Medicine, Manila, Philippines. She completed a residency in general surgery at Mercy Catholic Medical Center in Darby, Pa., and a surgical breast oncology fellowship at the University of Pittsburgh School of Medicine.

Subarna Eisaman, MD, PhD

Radiation oncologist specializing in the treatment of breast, prostate, lung, and gynecologic cancers. Dr. Eisaman is board-eligible in radiation oncology. She received her medical degree from Pennsylvania State University College of Medicine in Hershey, and completed a dual residency in radiation oncology at Tufts Medical Center, Boston, and Brown University, Rhode Island Hospital, Providence, R.I.

Rafic Farah, MD

Medical oncologist specializing in allogeneic and autologous stem cell transplant and hematologic malignancies, including lymphoma, leukemia, and myeloma. Dr. Farah is board-certified in medical oncology and internal medicine, and received a medical degree from Saint Joseph University Medical School in Beirut, Lebanon. He completed his residency in internal medicine at Staten Island University Hospital in New York and his fellowship in medical oncology at the University of Washington School of Medicine Fred Hutchinson Cancer Research Center in Seattle.

Deborah Galson, PhD

Assistant professor of medicine at the University of Pittsburgh School of Medicine and director of the Pittsburgh Center for Bone and Mineral Research. Dr. Galson's areas of specialization and research interests include osteoclast differentiation, Paget's disease of the bone, and multiple myeloma bone disease. She received her doctoral degree from Brandeis University, Waltham, Mass., and completed a molecular biology fellowship at the Center For Cancer Research, Massachusetts Institute of Technology, Cambridge, Mass.

Marsha Haley, MD

Radiation oncologist specializing in the treatment of breast cancer, gynecologic cancers, and head and neck cancer. Dr. Haley is board-certified in radiation oncology. She received a medical degree from the University of Virginia School of Medicine in Charlottesville and completed a residency in radiation oncology at the University of Pittsburgh School of Medicine.

Nitin Kapoor, DO

Medical oncologist specializing in general hematology and oncology disorders. Board-certified in internal medicine and board-eligible in oncology and hematology, Dr. Kapoor received a medical degree from Ohio University College of Medicine. He completed a residency in internal medicine at Riverside Methodist Hospital, affiliated with The Ohio State University in Columbus, and a hematology-oncology fellowship at Grandview Hospital and Medical Center in Dayton, Ohio.

Brian Karlovits, DO

Radiation oncologist and director of clinical operations at Mary Hillman Jennings Radiation Oncology Center at UPMC Shadyside. Dr. Karlovits specializes in lung and prostate cancer. A Pittsburgh native, he is board-certified in radiation oncology. He received a medical degree from Kirksville College of Osteopathic Medicine, Kirksville, Mo., completed an internship in transitional medicine at the Naval Medical Center, San Diego, and graduated from the Naval Aerospace Medical Institute, Pensacola, Fla., as a naval flight surgeon. He completed a residency in radiation oncology at Allegheny General Hospital, Pittsburgh.

Sri Kottapally, MD

Radiation oncologist specializing in head and neck, prostate, and lung cancers, and general radiation oncology. Board-certified in radiation oncology, Dr. Kottapally received a medical degree from Kurnool Medical School in Kurnool, India, and completed a residency in radiation oncology at St. Francis Medical Center, formerly located in Pittsburgh. In addition, he is a fellow of the American College of Radiation Oncology.

Michal Krauze, MD, PhD

Medical oncologist with special interest in all areas of oncology. Board-certified in internal medicine, Dr. Krauze received a medical degree from the Medical University of Vienna, Austria, completed a residency at Albert Einstein College of Medicine in the Bronx, N.Y., and a hematology-oncology fellowship at the University of Pittsburgh School of Medicine and UPMC.

James Lee, MD, PhD

Medical oncologist specializing in Phase 1 clinical trials of new cancer drugs and the treatment of gastrointestinal (GI) cancers, especially colon, rectal, and liver cancer.

Dr. Lee's research has focused on the development of new cancer drugs, including cytotoxic chemotherapeutic agents, biologics, and natural herbal agents. He also has a strong interest in the basic and clinical research of colorectal cancer. He is board-certified in medical oncology and internal medicine. He received a medical degree from Seoul National University and a doctorate in immunology from The Johns Hopkins University School of Medicine. Dr. Lee completed an internal medicine residency at Albert Einstein College of Medicine/Long Island Jewish Medical Center in New York and a medical oncology fellowship at the National Cancer Institute (NCI)/National Institutes of Health (NIH) in Bethesda, Md. Prior to joining UPMC CancerCenter, he had been a faculty member at Yale University School of Medicine and Yale Cancer Center/Yale New Haven Hospital, focusing on GI cancers and Phase 1 clinical trials.

Amy Lowery, PhD

Assistant professor of medicine and clinical psychologist at the University of Pittsburgh Department of Medicine. Dr. Lowery's area of specialization and research interests include symptom management in psycho-oncology, sleep disorders in people with cancer, behavioral sleep medicine, distress screening in cancer care, geriatric psycho-oncology, clinical practice guidelines in cancer care, instrument development and validation, and cost-effectiveness of interventions. She received her doctoral degree from Alliant International University in San Diego. She completed her psycho-oncology fellowship and was the chief fellow in psycho-oncology at Memorial Sloan-Kettering Cancer Center in New York.

Brian McLaughlin, MD

Medical oncologist-hematologist specializing in the treatment of all cancers and benign hematology. Dr. McLaughlin is board-certified in internal medicine, medical oncology, and hematology. He received his medical degree from Stony Brook University School of Medicine, Stony Brook, N.Y., and completed his residency in internal medicine and fellowship training in hematology-oncology, both at UPMC.

Carola Neumann, MD

Associate professor in the Department of Pharmacology & Chemical Biology. Dr. Neumann's research is on redox reactions with a focus on DNA repair and breast cancer. She received her medical degree from Ludwig-Maximilian University in Munich, and her postdoctoral training in the Department of Genetics at Harvard Medical School and from Dana-Farber Cancer Institute, a teaching affiliate of the Harvard Medical School, in Boston.

Lidiya Orlichenko, PhD

Research assistant professor at the University of Pittsburgh Department of Medicine. Dr. Orlichenko's research interests include cellular and molecular mechanisms of onset and progression of ovarian and pancreatic cancers aiming at a better understanding of factors that lead to precancerous lesions, as well as factors that affect prognosis for patients at high risk of metastatic relapse. Her current research project is focused on development of novel tools for disease diagnostics. She received her doctorate in biological sciences at the University of Notre Dame and completed her postdoctoral training at the Mayo Clinic, Rochester, Minn. In addition, she completed her research fellowship in internal medicine at the Mayo Clinic Department of Biochemistry and Molecular Biology.

Rahul Parikh, MD, PhD

Medical oncologist in the Division of Hematology-Oncology. Dr. Parikh specializes in treating patients with genitourinary malignancies, with a focus on prostate cancer. Board-certified in internal medicine, he received his medical degree from Seth G.S. Medical College and K.E.M. Hospital in Mumbai, India, and his doctorate in human genetics, with an emphasis on DNA repair in cancer, at the University of Pittsburgh. Dr. Parikh completed his residency in internal medicine at UPMC Shadyside, where he received the I. Arthur Mirsky award for compassion and clinical integrity, and completed his fellowship in hematology-oncology at UPMC.

Kathy Shair, PhD

Assistant professor in the Department of Microbiology and Molecular Genetics at the University of Pittsburgh. Dr. Shair received her doctoral degree in virology from the University of Cambridge, United Kingdom, and completed training at the University of North Carolina at Chapel Hill. Her laboratory studies on the Epstein-Barr virus center on how virus-host interactions alter the biology of the infected cell and how modulation of the tumor microenvironment can contribute to cancer progression, maintenance, and metastasis.

Bernard Schneider, MD, PhD

Radiation oncologist specializing in the treatment of prostate cancer and gynecologic cancers, intensity-modulated radiation therapy (IMRT), 4D radiotherapy, patient education, and quality of life. Dr. Schneider is board-certified in radiation oncology and received his medical degree from the University of Virginia Medical School, Charlottesville. He completed his residencies in radiation oncology and pathology, and fellowships in neuropathology and clinical oncology, at the University of Virginia.

Weijing Sun, MD

Medical oncologist, professor of medicine, director of the Gastrointestinal Cancer Disease Section in the Division of Hematology-Oncology, and co-director of the UPMC Gastrointestinal Cancer Center of Excellence. Specializing in the treatment of colorectal cancer, Dr. Sun is board-certified in internal medicine and medical oncology. He received his medical degree from Shanghai Medical College, Fudan University, Shanghai. He completed his residency in internal medicine at Loyola University Medical Center in Maywood, Ill., and his hematology-oncology fellowship at the University of Pennsylvania in Philadelphia. In addition, Dr. Sun has been recognized on U.S. News & World Report's American Top Doctors list.

Paul Szabolcs, MD

Pediatric medical oncologist and chief of the Division of Blood and Marrow Transplantation and Cellular Therapies at Children's Hospital of Pittsburgh of UPMC, and professor of pediatrics at the University of Pittsburgh School of Medicine. Board-certified in pediatric hematology-oncology, Dr. Szabolcs received his medical degree from Semmelweis University School of Medicine, Budapest, Hungary. He completed his residency in pediatrics from Bellevue Hospital-New York University School of Medicine, and a hematology-oncology/bone marrow transplantation fellowship at Memorial Sloan-Kettering Cancer Center-New York Hospital Cornell College of Medicine, in New York.

Donald Woytowicz, MD

Medical oncologist and clinical assistant professor of medicine. Dr. Woytowicz specializes in myelodysplastic syndrome, myeloproliferative disorder, idiopathic thrombocytopenic purpura, and palliative care. He received his medical degree from the University of Maryland in College Park, Md. He completed a residency in internal medicine at the University of Miami, and his hematology-oncology fellowship at the University of Virginia, Charlottesville.

Nathan Yates, PhD

Associate professor in the Department of Cell Biology and Physiology at the University of Pittsburgh School of Medicine, and co-director of the UPCI Cancer Biomarkers Facility. Dr. Yates received his doctoral degree from the University of Florida in Gainesville, and completed his postgraduate degree at the University of Virginia in Charlottesville.

Mei Zhang, PhD

Assistant professor at the Department of Developmental Biology at the University of Pittsburgh School of Medicine. Dr. Zhang's research interests are cancer stem cells and tumor heterogeneity. She received her degree from the Baylor College of Medicine and her doctorate from The University of Texas, MD Anderson Cancer Center, Houston.

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★ **UPMC SHADYSIDE CAMPUS**

Hillman Cancer Center
Mary Hillman Jennings Radiation Oncology Center

▲ **RADIATION ONCOLOGY CENTERS**

- 1 Jameson Radiation Oncology¹
- 2 Heritage Valley Radiation Oncology (Beaver)¹
- 3 Heritage Valley Radiation Oncology (UPMC West)¹
- 4 St. Clair Hospital Radiation Oncology¹
- 5 Jefferson Regional Radiation Oncology¹
- 6 Washington Health System Radiation Oncology¹
- 7 Uniontown Hospital Radiation Oncology, Robert E. Eberly Pavilion¹
- 8 UPMC CancerCenter at UPMC East

■ **MEDICAL ONCOLOGY CENTERS**

- 9 UPMC CancerCenter, New Castle
- 10 UPMC CancerCenter, Beaver
- 11 UPMC CancerCenter, Steubenville
- 12 UPMC CancerCenter, Sewickley Medical Oncology
- 13 UPMC CancerCenter, Upper St. Clair
- 14 UPMC CancerCenter, Jefferson
- 15 UPMC CancerCenter, Washington
- 16 Arnold Palmer Medical Oncology (Oakbrook Commons)²
- 17 Arnold Palmer Medical Oncology (Mt. Pleasant)²
- 18 UPMC CancerCenter, Uniontown
- 19 UPMC CancerCenter, Windber
- 20 UPMC CancerCenter at UPMC Mercy
- 21 UPMC CancerCenter, Indiana
- 22 UPMC CancerCenter, Greenville
- 23 UPMC CancerCenter, Monroeville

● **DUAL CENTERS (RADIATION AND MEDICAL ONCOLOGY)**

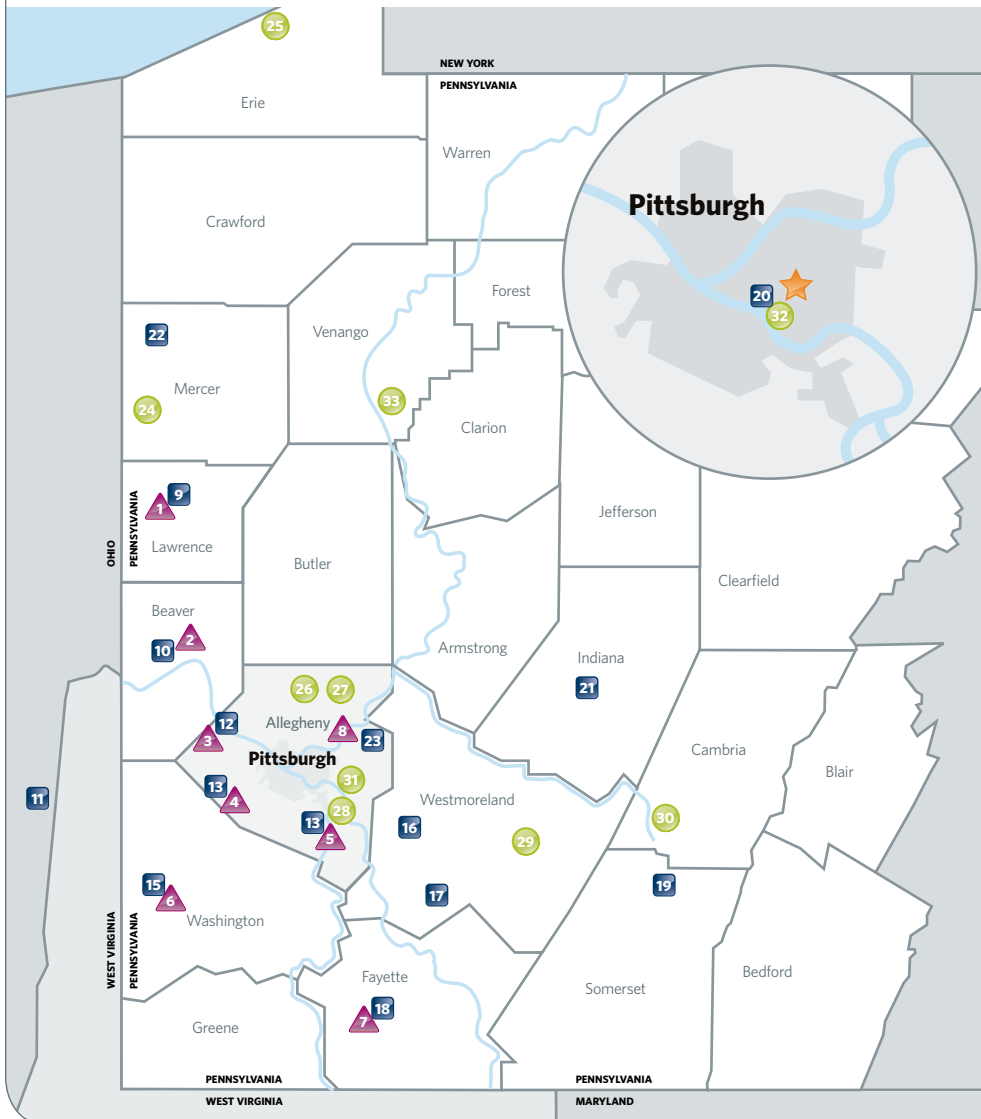
- 24 UPMC CancerCenter at UPMC Horizon
- 25 The Regional Cancer Center, Erie
- 26 UPMC CancerCenter at UPMC Passavant
- 27 UPMC CancerCenter, Natrona Heights
- 28 UPMC CancerCenter at UPMC McKeesport
- 29 Arnold Palmer Medical Oncology (Mountain View)² and Arnold Palmer Radiation Oncology (Mountain View)²
- 30 John P. Murtha Regional Cancer Center
- 31 UPMC CancerCenter at UPMC St. Margaret
- 32 UPMC CancerCenter at Magee-Womens Hospital of UPMC
- 33 UPMC CancerCenter at UPMC Northwest

▼ **INTERNATIONAL**

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

¹In partnership with UPMC CancerCenter

²A partnership of Excelsa Health and UPMC CancerCenter





UPMC CancerCenter *and* University of Pittsburgh Cancer Institute

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