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Hillman Cancer Center is the academic hub of the UPMC Cancer Centers network. The state-of-the-art facility offers cutting-edge cancer care and is also home to the research activities of the University of Pittsburgh Cancer Institute (UPCI). UPMC Cancer Centers and UPCI are the only center in western Pennsylvania with the elite Comprehensive Cancer Center designation from the National Cancer Institute.

Changing the landscape of oncology

Physicians understand that breakthroughs in research won't make a real impact until they reach the patient.



At UPMC Cancer Centers and the University of Pittsburgh Cancer Institute, our physicians and researchers collaborate to rapidly translate basic science into effective new strategies for the prevention, detection, and treatment of cancer.

As one of the nation's top centers for care and research, our nationally and internationally recognized specialists are changing the landscape of oncology — from the development of vaccines to block the progression of many cancers, to the incorporation of new technologies that allow physicians to more precisely target treatment, to advances in minimally invasive surgical procedures that are leading to reduced recovery times and better outcomes for patients.

This inaugural issue of *Cancer Insights* features a wide variety of topics that translate to your day-to-day practice, including educating patients about the importance of clinical trials;

overcoming racial and socioeconomic barriers to care; and the development of pathways to ensure coordinated, consistent care throughout a patient's course of treatment.

This is an exciting time for cancer research and care. We are pleased to share examples of the cutting-edge therapies and technologies being developed and implemented at UPMC Cancer Centers and the University of Pittsburgh Cancer Institute. To learn more about our clinical research or patient care opportunities, please call 412-647-2811 or visit our website at www.UPMCCancerCenters.com.

SINCERELY,

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medical oncology

A roadmap for best practices

Physicians recognize that the most significant advances in cancer treatment have come from evidence-based care. A new program being developed by UPMC Cancer Centers' oncologists takes this approach a step further by combining innovative and promising clinical trial options with the best standard of care therapies for a specific disease.



Under the direction of Peter Ellis, MD, director, Medical Oncology Network, UPMC Cancer Centers has developed and successfully launched a clinical program called Pathways for a number of cancer disease types. Pathways are a tool developed to provide a uniform treatment plan for a type of cancer based on different disease and patient parameters.

“There are many advantages to offering Pathways throughout the network,” says Dr. Ellis. “It ensures that all patients treated at UPMC Cancer Centers, no matter where they are located, receive the same state-of-the-art, evidence-based care.”

This standardization will lead to better efficiencies, with fewer treatment errors, and improved patient satisfaction.

Pathways are constructed by disease-specific teams of physicians led by two co-chairs, a full-time academic faculty member with disease site subspecialty expertise, and a community-based practice physician. The physicians review

literature and clinical practices to determine the single best regimen for the specific disease, stage-by-stage, and its sub-categories. If more than one regimen fits the “best” category, then the regimen with the most favorable toxicity profile is chosen. As a top priority for each Pathway, whenever applicable, patients are recommended to participate in a relevant clinical trial. Pathways use the Eastern Cooperative Oncology Group (ECOG) performance status to develop lines of treatment for common patient presentations. These scales and criteria are used by doctors and researchers to assess how a patient’s disease is progressing, assess how the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis.

Pathways are re-evaluated every three months to ensure that the clinical applications remain to be the best and most efficacious.

Seven Pathways have been fully implemented in the network — breast, prostate, lung, colorectal, lymphoma, head and neck, and multiple myeloma — with a 92 percent patient participation rate. To ensure that patients are identified, scheduling tools have been developed to expedite the process.

Martin F. Earle, MD, medical oncologist, UPMC Cancer Center at Jefferson Regional Medical Center, co-chair of the colorectal working group, describes Pathways as a way to keep community physicians abreast of the latest, cutting-edge treatments and clinical trials.

“Patients on one of our Pathways can be sure that they are receiving the most state-of-the-art treatments, available right in their community,” says Dr. Earle. “Patients no longer have to travel to an academic setting to benefit from this type of care.”

For more information about UPMC Cancer Centers' Pathways program, contact Peter Ellis, MD, at 412-235-1077.

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Vaccine trial targets secondary cancers

Patients diagnosed with head and neck cancers experience high relapse rates and are at increased risk of developing secondary cancers later in life. To date, no prevention strategy or prevention drug exists for patients in this subset.

As part of a National Cancer Institute Specialized Program of Research Excellence (SPORE) grant, Robert Ferris, MD, PhD, assistant professor of otolaryngology and immunology, and co-leader of the Cancer Immunology, Immunotherapy, and Immunoprevention Program at the University of Pittsburgh Cancer Institute, is investigating a vaccine utilizing the tumor-suppressor protein, p53, to activate the body's immune system to prevent relapses and secondary cancers in head and neck cancer patients.

"Overall prevention strategies have been disappointing, because when treatment stops, they stop working," says Dr. Ferris. "However, the immune system has the power and the memory to protect the body against a particular target, making immune systems our best bet for finding a durable primary or secondary prevention treatment."

The main goal of this Phase I study is to evaluate the safety and toxicity of a semi-personalized vaccine using p53 peptide fragments infused with the patient's immune cells. By selecting already-made p53 peptides, it improves applicability and convenience factors by eliminating logistical problems associated with older methods of creating completely individualized vaccines, making it also easier to monitor the patient's immune response.

The success of the HPV vaccine has created enthusiasm for the field of vaccines to target the prevention of cancer. This enthusiasm has carried over to development of vaccines to prevent relapses and the development of secondary cancers.

"We need to find the best formulation, the best population, and the best timing for administering these new vaccines," says Dr. Ferris. "We also have to come to the realization that the auto-immunity caused by these vaccines may mean success. We may need to accept some side effects to show that these vaccines can kill cancer cells."

This study, which is only available at Hillman Cancer Center, is currently accruing patients. The study is restricted to patients with a particular HLA blood-type that is present in 50 percent of the population.

For more information on eligibility criteria or for patient referrals, contact Robert Ferris, MD, PhD, at ferrisrl@upmc.edu.

A conversation about clinical trials

Clinical trials are a crucial component in the development of cutting-edge, less toxic cancer therapies. Yet nationally, only a small percentage of adult cancer patients participate in clinical trials.

UPMC Cancer Centers has launched an educational website to help patients and their families learn about clinical trials. The goal is to allay patient fears and misconceptions about clinical trials by providing comprehensive information that can be easily accessed by patients in the privacy of their homes.

The site, which can be accessed at www.UPMCCancerCenters.com/Clinicaltrials, features interview clips with clinical trial participants who share their own personal views and experiences, and allows visitors to access an extensive menu of clinical trial topics and terms including:

- Why people participate in clinical trials
- Side effects and safety
- Apprehensions and misconceptions
- How to find a clinical trial
- Insurance coverage
- Definitions of common terms associated with clinical trials
- Minority involvement in clinical trials — including the impact of the Tuskegee Syphilis Study

The site is designed to stimulate conversation by allowing visitors to ask their own questions and receive video-based answers from cancer patients, as well as medical experts.

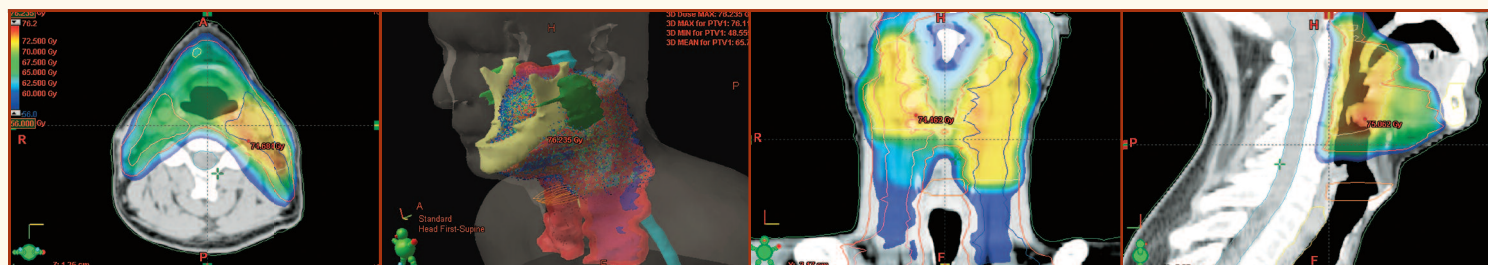
The website is a valuable resource for you and your staff to use in educating patients about the importance of cancer clinical trials.

Prevention — the spice of life

University of Pittsburgh Cancer Institute researchers are identifying the benefits of nutrition for cancer prevention, specifically the roles certain vegetables play as cancer-fighting agents. In a recent study, researchers found that an ingredient in red chili pepper, capsaicin, has cancer-fighting properties that prevent or slow the growth of pancreatic cancer tumors implanted in mice.



radiation oncology



A new dimension in radiation therapy

Radiation oncologists at UPMC Cancer Centers are employing four-dimensional, intensity-modulated radiation therapy (4D IMRT), a technology that marries new imaging modalities with targeted therapies to offer new hope for cancer patients.

“The fourth dimension adds the element of time,” explains Dwight Heron, MD, director of radiation oncology services at UPMC Cancer Centers. “The 4D imaging technology is a combination of software and hardware that allows a CT to capture the motion of the tumor. If 3D is like a photograph, 4D is like a video camera.”

When patients with chest, abdominal, or pelvic cancers breathe in and out, their tumors naturally move up and down or side-to-side with each new breath. Until now, these types of tumors have presented radiation oncologists with the challenge of treating the tumor while sparing healthy tissue.

Because 4D technology allows the radiation oncologist to trace the tumor at every point throughout the breathing cycle, the radiation beam can be more precisely targeted to the location of the tumor, decreasing the size of the margin and of the radiation field and ultimately sparing surrounding healthy tissue.

“As the patient breathes in and out normally, the tumor falls within a specified range and the radiation beam comes up,” says Dr. Heron. “When the tumor moves outside that range, the beam stops. With conventional 3D radiation, we were forced to treat the entire range of motion. But with 4D, we wait for the tumor to get to a certain position, and then we turn the radiation beam on.”

This 4D CT-based, gated approach to intensity-modulated radiation therapy packs a deliberate and powerful punch of radiation to the tumor while minimizing the impact on surrounding healthy tissue, resulting in fewer treatment-related side effects for the patient.

“It’s not an evolution in radiation therapy — it’s a revolution because it involves more than just varying intensity of radiation,” says Dr. Heron, who believes this new approach will become the next standard of care for almost all radiation therapy.

At UPMC Cancer Centers, nearly 500 patients have benefited from 4D CT technology, and preliminary data appears promising with reduced normal tissue side effects compared to more customary radiation approaches.

IMRT treatment outcomes validate care close to home

UPMC Cancer Centers’ hub and satellite model is designed to bring the same high-quality care available at the academic hub to patients closer to home.

A University of Pittsburgh study recently demonstrated the success of this unique and innovative model. The study showed that intensity-modulated radiation therapy (IMRT), a highly specialized and complex set of treatment planning and delivery techniques, can be delivered in a large health care system of academic and community cancer centers through a centralized planning and treatment process. Toxicity profiles from study participants revealed no significant differences between patients receiving care at the academic flagship facility compared to patients treated at a community cancer center, both large and small.

The 4D imaging technology is a combination of software and hardware that allows a CT to capture the motion of the tumor. If 3D is like a photograph, 4D is like a video camera.

In the study, 758 prostate cancer patients had their toxicity levels evaluated after being treated with IMRT at one of 12 UPMC Cancer Centers' community network facilities and Hillman Cancer Center, the flagship center for the region's only NCI-designated comprehensive cancer center.

To standardize the treatment network-wide, each facility followed the same clinical pathway guidelines for the radiotherapy management of prostate cancer, which included specific details on volumes for radiation treatment planning and recommended doses of IMRT.

Medical physicists based in Pittsburgh work in tandem with radiation oncologists at each of the community locations through telemedicine software to tailor specific treatment plans for each patient. The result is significantly lower treatment-related side effects with IMRT validating the approach of world-class cancer care closer to home.

Breaking down barriers

Evidence shows that geographical, cultural, and socioeconomic factors hinder economically disadvantaged populations from receiving much-needed radiation therapy services, including access to clinical trials.

A \$4 million grant from the National Cancer Institute is funding initiatives to address racial and socioeconomic disparities in radiation therapy, overcoming these barriers by helping rural and minority cancer patients gain better access to cutting-edge therapies.

The key goal of this grant is to use non-traditional outreach to make innovative clinical research studies, including radiation therapy, available to cancer patients in disadvantaged communities.

"A number of barriers, both real and perceived, are keeping these populations from receiving state-of-the-art radiation services and from accessing important clinical trials," said Dwight Heron, MD, principal investigator of the grant and director of radiation oncology services, UPMC Cancer Centers. "This grant allows us to provide access to radiation services to patients and communities with the greatest need."

The project, the Radiation Oncology Community Outreach Group (ROCOG), is based at UPMC McKeesport, part of the University of Pittsburgh Medical Center (UPMC) health system. ROCOG is comprised of five institutions including: UPMC McKeesport; Jameson Memorial Hospital in New Castle, PA; Mercy Hospital of

Pittsburgh; John P. Murtha Regional Cancer Center in Johnstown, PA; and Somerset Hospital, Somerset, PA. The consortium provides the research team with valuable information regarding health outcomes.

One of the unique components of this study is how it utilizes the patient navigator system. In an effort to "fast track" patient identification, each patient navigator is a registrar for the National Tumor Registry. Offering navigation services at the time of diagnosis reduces treatment delays, with the goal of healthier outcomes for patients with barriers to treatment.

Patient navigators work with oncologists to recommend the patient navigator program to qualifying cancer patients. Once patients are enrolled, the patient navigator works to identify and resolve obstacles that inhibit the patient from receiving care including — health insurance coverage, prescription coverage and co-pays, transportation, and child care. Each service area maintains a highly detailed database of available resources to assist patient navigators with patient needs.

To date, the ROCOG Patient Navigator Program has served 450 cancer patients throughout western Pennsylvania.

Exporting world-class care

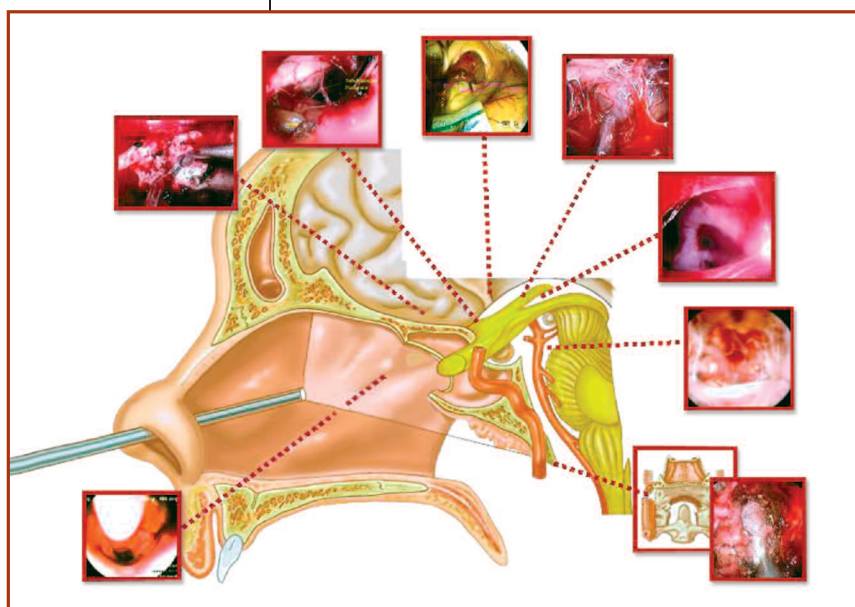
UPMC Cancer Centers clinical care network has expanded beyond U.S. borders with the opening of two new radiation oncology centers in Dublin and Waterford, Ireland. UPMC's "hub-and-satellite" telemedicine network links patients being treated in Ireland to the expertise and technology available at Hillman Cancer Center in Pittsburgh.



surgical oncology

Nasal passages opening new surgical treatment options for brain tumors

Through a new minimally invasive surgical technique, surgeons are able to remove often otherwise inoperable brain and spine tumors through the nasal passage. This expanded endonasal approach (EEA) is redefining the treatment of brain cancer, as well as other brain disorders.



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“Traditional surgical techniques involve peeling away the skin of the face and scalp and cutting open the skull, usually meaning some disfigurement and a long, painful recovery, says Amin Kassam, MD, FRCS(C), associate professor and chair, department of Neurological Surgery, and director, Minimally Invasive endoNeurosurgery Center (MINC).

In EEA, surgeons thread narrow scopes and custom-designed miniature surgical tools into the soft tissue of the nasal opening to gain access to benign or malignant brain tumors and blood vessels, minimizing damage to brain and surrounding tissue. Patients are often discharged within several days, leaving the hospital with no incisions or scars and few, if any, lingering side effects. Patients with malignant cancer can start follow-up

chemotherapy or radiation therapy almost immediately, giving the drugs a chance to work before the tumor potentially returns.

To provide comprehensive neurologic cancer care, UPMC Cancer Centers, in conjunction with the University of Pittsburgh Cancer Institute’s Brain Cancer Program and MINC, has established a multidisciplinary clinic with a minimally invasive skull base program.

“One of the most important functions for a disease-oriented program is to provide an infrastructure for physicians to collaborate, so that we are able to develop a comprehensive treatment strategy for the patient,” explains Frank Lieberman, MD, director of the Adult Neuro-Oncology Program.

The clinic’s multidisciplinary team includes the community referring physician, medical oncologists, radiation oncologists, and surgeons developing a treatment strategy that incorporates best practices and new therapies available through clinical trials. “Through this collaborative effort, we are able to provide a complete continuum of care, resulting in improved outcomes for the patient,” says Dr. Lieberman.

Novel treatment makes chemotherapy drugs more effective

A new therapy combining surgical intervention with concentrated chemotherapy is improving the prognosis for patients with metastatic tumors of the liver, abdomen, ovaries, and lung, as well as regional tumors such as melanoma of the limb. Unlike conventional chemotherapy, which when administered orally or intravenously becomes diluted in the blood stream, hyperthermic intraperitoneal chemotherapy (HIPEC) bathes the affected cancerous region with a high concentration of heated chemotherapy with minimal to no exposure to the rest of the body.

“Many tumors are too advanced for surgical removal, but remain confined to a single organ or region of the body,” explains David L. Bartlett, MD, chief, Division of Surgical Oncology, and director of the David C. Koch Regional Cancer Therapy Center at UPMC Cancer Centers. “HIPEC provides these patients with another option for treatment.”

After surgery to remove as much of the tumor as possible, the abdomen is closed off. Inflow and outflow tubes are placed through the abdominal walls and heated chemotherapy drugs are circulated through the abdominal cavity for 90 to 120 minutes. The lining of the abdominal cavity acts as a barrier to drug absorption into the blood stream, so that higher concentrations of drugs can be delivered directly to the tumor site safely. Recirculating the fluid through the abdominal cavity and manually moving the patient during the procedure assures even distribution of the drug and heat throughout the cavity. At the end of the procedure, the drug is flushed out to avoid further absorption.

A randomized trial demonstrated a 10-month improvement in median survival in patients treated with hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis from colon cancer. “The ultimate goal is to prolong quality survival, and we believe we’re able to accomplish that,” says Dr. Bartlett.

Dispelling misconceptions about pancreatic cancer surgery

A recent study in the *Annals of Surgery* determined that nearly 40 percent of Americans with early-stage pancreatic cancer are not offered surgery for potentially curable lesions due to a number of factors, including possible misconceptions about surgical outcomes.

Surgery for pancreatic cancer has improved dramatically over the last two decades. This study underscores the importance of a multidisciplinary treatment plan, with patient evaluation by a team of experts including surgical oncologists. The Pancreatic Cancer Center of UPMC Cancer Centers is a multidisciplinary clinic which focuses the expertise of gastroenterologists, medical oncologists, radiation oncologists, pathologists, radiologists, and surgeons on treating patients with pancreatic cancer.

The team works collaboratively with the referring physician to provide innovative patient-directed care for pancreatic cancer and pancreatic diseases.

Treatment strategies for pancreatic cancer often involve surgery – including minimally invasive options. UPMC surgeons have performed more than 175 pylorus preserving pancreaticoduodenectomy (Whipple) operations in the last two years, with a safety record of 0.56 percent mortality.

A treatment plan that combines surgery with chemotherapy, radiation therapy, and clinical trials when appropriate results in optimal patient benefits. Among the new treatment options available to patients is a Phase II clinical trial for patients with early stage pancreatic cancer. The trial provides patients an innovative chemotherapy approach followed by a short course of radiation prior to surgery. This approach is designed to reduce the risk of leaving cancer behind after surgery.

Endocrine surgeons reach milestone

The Section of Endocrine Surgery at UPMC and UPMC Cancer Centers is one of the leading centers in the country for the treatment of endocrine disease. Department surgeons recently performed their 2,600th surgery to treat parathyroid disease — a milestone in this specialty — using video-assisted or focused, minimally invasive surgical techniques.



upcoming events

2007 ASTRO Conference

Physician researchers from UPMC Cancer Centers and the University of Pittsburgh Cancer Institute (UPCI) will present findings from more than 21 studies at the 49th Annual American Society for Therapeutic Radiation and Oncology (ASTRO) Meeting, Oct. 28 to Nov. 1, 2007, in Los Angeles, including:

- Fractionated stereotactic radiosurgery in the management of primary, recurrent, and metastatic lung lesions: the role of PET/CT in pre- and post-treatment disease assessment
- Study of rotational set-up errors and their dosimetric impacts on head and neck IMRT treatments using kilovoltage cone-beam computed tomography (kV CBCT)
- Cells lacking the PolQ polymerase are more sensitive to irradiation in Vitro or in Vivo
- Intraesophageal administration of manganese superoxide dismutase plasmid/liposomes (MnSOD-PL) pre-irradiation results in increased engraftment of bone marrow progenitors' esophageal stem cells.

UPMC Cancer Centers' experts will be available at booth 361 in the ASTRO Exhibit Hall to discuss these and other presentations.

Pittsburgh Cancer Conference 2007

The 17th annual Pittsburgh Cancer Conference will be held Friday, Nov. 2, 2007 at the Herberman Conference Center, located at UPMC Shadyside hospital in the east end of Pittsburgh. Topic highlights for this year's conference range from prostate cancer to advances in treatment for multiple myeloma, including stem cell transplant.

For more information, contact Tricina Cash at 412-647-8257.

Third International Symposium on Regional Cancer Therapies

The Third International Symposium on Regional Cancer Therapies will take place Friday, Feb. 15 through Monday, Feb. 18, 2008 in Palm Desert, California. The symposium, sponsored by the David C. Koch Regional Cancer Therapy Center, the University of Pittsburgh School of Medicine Center for Continuing Education in the Health Sciences, and UPMC Cancer Centers, promotes the exchange of information and education among professionals for research, development and application of regional cancer therapies.

For more information, visit www.regionaltherapies.com or contact Rebecca J. Beward at 412-623-5993 or via email at bewardbj@upmc.edu.

UPMC Cancer Centers

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UPMC Cancer Centers has consistently received national recognition from *U.S. News & World Report* magazine as one of America's top centers for cancer care and research. For more information about UPMC Cancer Centers' clinical services, or University of Pittsburgh Cancer Institute research, call 1-800-533-UPMC (8762) or visit www.UPMCCancerCenters.com.