SWEET HARMONY
Team care saves lives and lifestyles

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A Comprehensive Cancer Center
An integral part of one of the world’s most distinguished medical centers, the Massachusetts General Hospital Cancer Center is chosen by more cancer patients than any other hospital in New England. Its commitment to eradicating cancer is fueled by scientific investigation conducted as part of the largest hospital-based research program in the United States.

Known for providing individualized, compassionate care to both adults and children, the Cancer Center comprises 18 fully integrated, multidisciplinary clinical programs and a vast network of support and educational services.

The Cancer Center is consistently ranked as one of the best in the country by US News and World Report, and its nurses were the first in the state to achieve Magnet status in recognition of the hospital’s exceptional nursing care.

Through a powerful synergy between scientists in the laboratories and physicians at the bedside, the Cancer Center fosters innovation in basic, translational and clinical research.

It is a founding member of the DF/HCC, a Harvard Medical School consortium designated by the National Cancer Institute as a comprehensive cancer center. This prestigious seven-member center forms the largest cancer research collaboration in the country. Also, Massachusetts General Hospital Cancer Center and Dana-Farber/Brigham and Women’s Cancer Center collaborate on joint clinical trials, education, training programs, and quality of care improvements.

On the cover: Jules Eskin, principal cellist for the Boston Symphony Orchestra and bladder cancer survivor.
Dear Reader:

The history of medical discovery resembles a target, with each new finding bringing scientists closer to the bull’s eye — the most effective treatment with the fewest side effects. In cancer, this metaphor is particularly apt as we identify early cancerous changes in cells and zero in on them with highly specific drugs. This concept is already changing how medical science thinks about cancer: Ninety percent of current drugs in early clinical trials are “targeted” therapies.

At Massachusetts General Hospital Cancer Center, we are moving toward treating cancer by targeting the specific cellular change responsible for growth and spread of the tumor in addition to using the more traditional approach of classifying disease by the organ in which it originated. This more tailored therapy has the potential to transform cancer from a life-threatening disease to one like diabetes that is managed over a lifetime.

As more people join the ranks of cancer survivors, our clinicians investigate ways to ensure that these individuals are able to return to their families, careers, hobbies and friends with as few lasting reminders of their disease as possible. Our effort involves careful pathological characterization of tumor cells; development of minimally invasive and organ-sparing surgical procedures; precise, state-of-the-art radiation that destroys cancer while minimizing damage to healthy tissue; and large-scale studies to identify and address long-term effects of cancer treatment.

This issue of Synergy contains examples of our multidisciplinary approach to cancer, specifically in genitourinary cancers, which are those occurring in the bladder, prostate, kidney, urethra, penis or testicles. It covers breakthroughs in science and technology, including the exciting development of a microchip capable of capturing a single cancer cell from a billion circulating blood cells, as well as addressing the importance of communication in both scientific discovery and cancer care. As a whole, it demonstrates Massachusetts General Hospital Cancer Center’s commitment to saving both lives and lifestyles.

We hope you find it both interesting and informative.

Daniel A. Haber, MD, PhD
Director, Cancer Center

Bruce A. Chabner, MD
Clinical Director, Cancer Center
■ **Community Leaders Become Ambassadors for the Cancer Center**

Founding members of the Massachusetts General Hospital Cancer Center Leadership Council, comprised of prominent national business and civic leaders, gathered for the Council’s inaugural meeting in November. The Leadership Council was established to provide strategic advice and support for the Cancer Center.

The Cancer Center is poised to grow in key areas that have the potential to significantly affect the lives of cancer patients, and, according to Jeff Cunningham, chairman and CEO of NewsMarkets and the Leadership Council’s first chair, each council member will serve as an ambassador for the Cancer Center to friends, professional colleagues and the community at large.

■ **Drug Extends Life for Those with Non-Hodgkin Lymphoma of the Brain**

According to a recent study published in the journal *Neurology* by Tracy Batchelor, MD, executive director of the Cancer Center’s Stephen E. and Catherine Pappas Center for Neuro-Oncology, and colleagues, up to 40 percent of patients with primary central nervous system lymphoma (PCNSL) who achieve a complete remission with high doses of the chemotherapy drug methotrexate may be cured of their disease. The study involved adults with newly diagnosed PCNSL who received a high dose of the drug every two weeks for four months or until there were no signs of the brain tumor. After an average follow-up of seven years, over half of all patients achieved a complete remission, and 40 percent of these patients had not experienced a relapse. Patients treated with methotrexate alone at the time of diagnosis lived four times as long as patients who received whole brain radiation at the time of diagnosis. This multisite study was sponsored by the National Cancer Institute.

■ **Radiation Nurses Launch Study of Skin Care During Treatment**

Nurses in radiation oncology will investigate an approach to reducing the skin side effects for patients with head and neck cancers being treated with chemotherapy and radiation therapy. To date, there is limited research on this subject. This Institutional Review Board approved study is a collaboration among nursing co-investigators from Yawkey 8 Infusion, the Center for Head and Neck Cancers and the Mass General Hospital Burn Clinic. According to Laurel Radwin, RN, PhD, Yvonne L. Munn Nurse Researcher, “Nursing research has improved the quality of life for cancer patients in areas such as fatigue, mouth sores and depression. The nurses involved in this study have taken an important lead in reducing uncomfortable side effects and promoting healing for cancer patients.”

■ **Cancer Center Leader Named Harvard Professor**

Thomas Lynch, MD, chief of the Division of Hematology-Oncology and director of the Center for Thoracic Cancers, has been named a Professor of Medicine at Harvard Medical School, effective January 1, 2008. According to Bruce Chabner, MD, clinical director of the Cancer Center, “This appointment recognizes the many important contributions Dr. Lynch has made as a masterful clinician, an innovative translational researcher, an inspiring teacher and a national leader in the field of cancer medicine. Mass General Hospital is very fortunate to count this talented physician among its ranks of professors of medicine.”
Scientific Director Selected as Schwartz Professor

Harvard Medical School has selected Cancer Center Scientific Director Jeffrey Settleman, PhD, as the Laurel W. Schwartz Professor of Oncology. Settleman, who is also director of the Center for Molecular Therapeutics at the Cancer Center, studies the role of specific protein pathways that regulate cellular processes involved in cancer. His research focuses on understanding and improving “smart drug” therapies that zero in on a specific cancer-causing genetic change.

“This Professorship is made possible by the generosity of one of our long-term supporters,” says Daniel Haber, MD, PhD, director of the Cancer Center and the Professorship’s first incumbent. “Laurel Schwartz’s unwavering determination is accelerating the development of more effective cancer treatments, and her consistent support of the physician scientists throughout the Cancer Center is making a meaningful difference at a critical time.”

Student Generosity Boosts Cancer Program

Caroline Goss first learned about raising funds for cancer research through her father, Paul Goss, MD, PhD, director of breast cancer research at the Cancer Center. “When my father told me about the Friends of Mel Foundation and the extraordinary fundraising effort started by Pauline Alighieri and her colleagues at Delta Airlines, I immediately wanted to get involved,” recalls the younger Goss. With friend Emily Soukas, Caroline raised over $3,000 in three days for the Cancer Center by selling the Foundation’s beaded bracelets at school. The girls plan to continue their efforts with the Foundation, which has donated over $1 million to the Cancer Center in support of breast cancer research and education.

Surgical First Provides Hope for Rare Cancer

A 66-year-old woman with a history of non-Hodgkin lymphoma and a rare cancer of the bile ducts, cholangiocarcinoma, was recently the first Cancer Center patient to undergo a rare and complicated liver surgery. Prior to coming to the Cancer Center, Elaine Park had been told her cancer was inoperable. Indeed it was — by conventional methods. The aggressive procedure, performed by Kenneth Tanabe, MD, and other members of surgical oncology and transplant surgery, involved rerouting and severing blood flow from Park’s liver long enough to remove the tumor, then fashioning new blood vessels that were reattached to the liver. “Dr. Tanabe anticipated which experts would be needed for my care, and he was able to bring them together to do everything that could be done,” says Park. “I knew the surgery was complicated and that there was a chance I wouldn’t survive, but he gave me confidence. The next day, I was up and walking the halls. It was a nice miracle.”

Researchers Identify Cancer Outcome Predictor

A recent study by Rebecca Heist, MD, MPH, and colleagues, published in the Journal of Clinical Oncology, showed that two variations of the angiogenesis gene VEGF were associated with significant survival differences in early stage, surgically removed non-small cell lung cancer. The combined effects of the two variations were even more significant. In future studies, the investigators plan to assess whether these genetic variations may also help predict which patients are most likely to benefit from treatment with angiogenesis inhibitors, which are drugs that target the blood vessels feeding a tumor. Cancer Center investigators are currently conducting multiple clinical trials of angiogenesis inhibitors.

Melanoma Expert is Chief of Dermatology

David E. Fisher, MD, PhD, has joined Massachusetts General Hospital as chief of Dermatology, director of the Cutaneous Biology Research Center and director of the Cancer Center’s Melanoma Program. An expert in the biology of the skin, Fisher focuses his research efforts on the analysis of skin development; responses to the environment, such as ultraviolet rays and tanning; and skin cancer formation. He has discovered key roles for stem cells in the process of hair graying. In addition, he and his team have discovered human oncogenes in melanoma and in certain pediatric cancers. He currently serves as president of the Society for Melanoma Research.
HOPES Program Turns Ten

This year, the HOPES Program celebrates a decade of providing free wellness services, education and support workshops for cancer patients, their families and their friends. The celebration will include free demonstrations of massage, art therapy and other wellness services during the week of April 7, 2008.

HOPES focuses on taking care of the whole self — mind, body and spirit. Each month, the program offers over 25 free workshops on cancer-related topics and complementary therapies such as ear acupuncture, relaxation massage, music therapy, art therapy, qigong and yoga. These free services for patients and their families are primarily funded through donations and grants, including a grant from the Friends of the Massachusetts General Hospital Cancer Center. The Program also conducts fee-for-service acupuncture and massage clinics for patients. For more information, visit www.massgeneral.org/hopes.

Integrated Palliative Services Enhance Care

Jennifer S. Temel, MD, and Cancer Center colleagues recently published a study in the Journal of Clinical Oncology that examines the role of palliative care in patients with newly diagnosed, advanced lung cancer. Palliative care clinicians are specially trained in symptom management and in providing psychosocial and spiritual support to patients and families. However, they traditionally meet patients late in the course of their illness. In this study, researchers demonstrated that the palliative care and oncology teams could successfully integrate and collaborate to provide more comprehensive care to patients.

Walking for Cancer

Some 350 people laced up their sneakers and took to the streets in the first annual Granara-Skerry Walk for Pancreatic Cancer Research on September 29, 2007 raising $50,100 with the help of 800 donors. The 5K walk was started by Kathleen Granara-Skerry of Medford, who was diagnosed with pancreatic cancer two years ago. Granara-Skerry underwent surgery, subsequent rounds of chemotherapy and radiation at the Cancer Center. A month before her year-long treatment was finished, she participated in a walk to benefit cancer research that inspired her to do more — and thus the Granara-Skerry Walk was born. The second annual walk is scheduled for September 27, 2008. For more information, e-mail: Granara-SkerryWalk@comcast.net.

Gene Variation Marks Increased Risk of Liver Cancer

A recent study by Kenneth Tanabe, MD, chief of surgical oncology at Massachusetts General Hospital Cancer Center, and colleagues in France discovered that a single alteration in the epidermal growth factor (EGF) gene appears to significantly increase the risk that individuals with cirrhosis of the liver will go on to develop hepatocellular carcinoma, a liver tumor that is the third leading cause of cancer death.

“If these results are confirmed, this variation could be used to determine which patients with cirrhosis should be screened more intensively for tumor development,” says Tanabe. “In addition, the molecular pathway controlled by EGF and its receptor EGFR — which is known to be important in several types of cancer — appears to be an excellent target for drug studies. This is a deadly cancer, so progress in prevention and early detection is critically important.”

Teeing Off to Fight Kidney Cancer

The John Estrella Foundation for Cancer Research will partner with the Cancer Center to raise money for renal cell carcinoma (kidney cancer) during its fifth annual golf tournament on July 28, 2008, at the Georgetown Country Club in Georgetown, Massachusetts. The event includes a dinner, a silent auction, a movie and a short talk by a Cancer Center doctor or scientist.

Funds raised at the event support the work of Dror Michaelson, MD, PhD, a specialist in renal cell carcinoma at the Bertucci Center for Genitourinary Cancers. Michaelson has been using the funds raised to support a tumor bank for research and patient treatment. For more information, contact Elicia Estrella at 978-578-4913 or eae8@yahoo.com.
Investigators from Massachusetts General Hospital Cancer Center and the Biomicroelectromechanical Systems (BioMEMS) Resource Center in the Mass General Department of Surgery have developed a microchip-based device that can capture circulating tumor cells (CTCs) from a blood sample. CTCs from solid tumors are carried in the bloodstream at a level of one in a billion cells. Previously, the scarcity and fragility of CTCs interfered with the ability to get information from them that could help clinical decision-making, but the new device, called the CTC chip, has the potential to be an invaluable tool for monitoring and guiding cancer treatment.

“This use of nanofluidics to find such rare cells is revolutionary, the first application of this technology to a broad, clinically important problem,” says Daniel A. Haber, MD, PhD, director of the Cancer Center and a co-author of the report in the December 20, 2007 issue of Nature. “While much work remains to be done before the chip is ready for clinical use, this approach raises the possibility of rapidly and noninvasively monitoring tumor response to treatment — allowing changes if the treatment is not effective — and the potential of early detection screening in people at increased risk of cancer.”

The BioMEMS Resource Center research team, led by Mehmet Toner, PhD, senior author of the Nature report and director of the Center, and Ronald Tompkins, MD, ScD, chief of the Mass General Hospital Burn Unit and a co-author, developed a business-card-sized silicon chip covered with almost 80,000 microscopic posts coated with an antibody to a protein expressed on most solid tumors. The researchers also needed to calculate the correct speed and force with which the blood sample should pass through the chip to allow CTCs to adhere to the microposts.

“We developed a counterintuitive approach, using a tiny chip with critical geometric features smaller than a human hair to process large volumes of blood in a very gentle and uniform manner — almost like putting a hose through a microchip,” explains Toner. The chip was effective at detecting cells from various types of tumor.

CTCs can also provide the molecular information needed to identify tumors that are candidates for new targeted therapies and should help researchers better understand the biology of cancer cells and the mechanisms of metastasis.
Genitourinary Cancers
Saving Lives and Lifestyles

Around Thanksgiving 1999, Jules Eskin, the principal cellist for the Boston Symphony Orchestra, received some discordant news from his doctor. A routine urine analysis revealed too many blood cells, the first indication of a bladder cancer that he later learned had already penetrated his bladder wall. “I was very frightened,” recalls Eskin, whose only option appeared to be the complete removal of his bladder. At age 68 and an avid jogger and hiker, Eskin dreaded the prospect of spending the rest of his life wearing a urine collection bag on his stomach.

Then he learned that an equally effective alternative that preserves the bladder was an easy walk from Symphony Hall — at Massachusetts General Hospital Cancer Center. He chose that route, undergoing radiation and several months of intensive chemotherapy instead of surgery. Today, Eskin still relishes jogging, performing and an unchanged lifestyle.
Our bladder-sparing protocol significantly improves patient care and quality of life for those with invasive bladder cancer,” says Donald Kaufman, MD, director of the Cancer Center’s Claire and John Bertucci Center for Genitourinary Cancers. Kaufman, William Shipley, MD, lead radiation oncologist of the Cancer Center’s bladder cancer treatment program, and urologist Alex Althausen, MD, (now retired) were the physicians who treated Eskin. In the 1980s, Shipley, George Prout, MD, (now retired), Kaufman and Niall Heney, MB, MD, a senior Mass General Hospital urologist, helped pioneer the new treatment for patients whose cancer has penetrated the bladder’s muscle wall. “We’re still one of the few centers that can preserve bladders because most hospitals don’t have the necessary teamwork among urologists, pathologists, medical oncologists and radiation oncologists. But it’s our strength,” says Kaufman.

That multidisciplinary expertise has flourished at the Bertucci Center, which was established to bring comprehensive, integrated care to patients with cancers of the bladder, prostate, kidney, urethra, penis or testicles. According to W. Scott McDougal, MD, chief of the Department of Urology, “This Center treats hundreds of genitourinary cancers annually, giving us extensive experience in diagnosing and treating these diseases. Doctors elsewhere frequently solicit our opinions. If one has a rare or more complex cancer, this is the place to be treated.”

A Prostate Cancer Dilemma – Active Surveillance vs. Aggressive Treatment

Many of the Cancer Center’s treatment advances are benefiting patients with prostate cancer, a disease that often progresses slowly and that is so frequently detected early-on that many men are living for decades as survivors. They are also living longer with the sometimes-difficult side effects of treatment, a situation Cancer Center doctors are working to alleviate.

Although aggressive prostate cancer is life-threatening, many prostate cancers are so slow-growing that men with these forms of the disease may eventually die of other causes. Patients have an array of treatment options (see page 9) that are usually effective in curing the cancer, yet the treatments all may be associated with side effects that impact an individual’s quality of life. For example, hormone therapy, although very effective, may lead to hot flashes and sexual dysfunction.

For these reasons, Cancer Center doctors carefully counsel men about their treatment options. “We help men make more informed choices about the most appropriate treatment with the least damaging side effects,” explains Kaufman. “The best course of action is not always obvious, and, in carefully selected cases, we may advise the strategy of active surveillance,” which is a regimen of periodic digital rectal exams, monitoring of PSA (Prostate Specific Antigen), biopsies and imaging.

Because aggressive prostate cancers can often be distinguished from less dangerous forms by an experienced medical team, Cancer Center doctors have long recommended considering active surveillance. Currently, doctors here are defining criteria to determine which men could safely choose active surveillance instead of more life-altering treatments.

An elevated PSA may signal the presence of prostate cancer, but it could also indicate a benign condition. Even if a man with an elevated PSA does have prostate cancer, the level does not provide insight into staging, which is critical for treatment planning. More important is the Gleason score, a rating of microscopic cell appearance done by a pathologist. Patients coming to the Bertucci Center — whether for prostate cancer or for another type of genitourinary cancer — benefit from pathology readings performed by specialists in urologic pathology under the leadership of the Cancer Center’s Robert Young, MD. This specialized interpretation is not provided at most centers and is critical to accurate treatment decisions. Chin-Lee Wu, MD, PhD, a member of the urologic pathology group and director of the Urology Research Lab, is leading a team of molecular researchers whose goal is to identify metabolic markers and genetic profiles that indicate which types of cancer may progress. These criteria, along with clinical parameters, will help clinicians determine whether active surveillance is appropriate in a given case or whether aggressive treatment is necessary. (continued page 8)
■ Preventing Hormone Therapy’s Collateral Damage

Of the two million prostate cancer survivors in the United States, one third have received androgen deprivation therapy. In caring for patients undergoing this type of hormone therapy, Matthew R. Smith, MD, MD, PhD, director of the genitourinary section of the Division of Medical Oncology, observed that healthy, active men were suffering debilitating bone fractures. They were also losing muscle mass, gaining weight and developing unhealthy cholesterol, triglyceride and glucose levels. Smith embarked on seminal research into how these previously unappreciated problems stem from hormone treatment and how to prevent them.

“We learned that the hormonal pathway that regulates prostate cancer growth overlaps with normal bone growth, which may be why prostate cancer frequently metastasizes to bone,” Smith explains. Testosterone fuels the growth of prostate cancer cells, both when they reside in the prostate gland and when they spread to the bone. Hormone therapy lowers testosterone levels, which slows cancer cell growth but also accelerates bone remodeling, causing bones to thin. To prevent these unintended side effects in men who require hormone therapy, Smith is leading global studies to determine whether bone-targeted drugs can prevent bone fractures as well as bone metastases in prostate cancer survivors.

In related research, Smith determined that hormone therapy’s detrimental influence on cholesterol and metabolism sets the stage for cardiovascular disease, diabetes and obesity — chronic diseases that cause many health complications and shorten lifespan. Moreover, a 2007 study of men with prostate cancer revealed that overweight and obese men were more likely to die from their cancer than men who maintained normal weight. Smith is currently evaluating whether intensive exercise and lifestyle changes can prevent obesity and reduce the risk of diabetes and cardiovascular disease.

■ Precision Radiation

Many prostate patients require radiation therapy to destroy fast-growing cancer cells. “We pick the radiation treatment based on which of several options will cause fewer side effects for a patient,” says radiation oncologist Anthony L. Zietman, MD. “For a man with a small prostate and a small tumor, you often can’t beat brachytherapy, which is a tiny implant that produces internal radiation. Large prostates, though, would require so many seeds that the prostate would swell, impeding urination, so we’d use external radiation.”

The Cancer Center is one of six centers in the country offering proton beam radiation, a highly focused form that precisely targets tumors while sparing healthy surrounding tissue. “The jury is out whether proton beam for prostate cancer is superior to other forms of highly conformal external radiation,” cautions Zietman, who is researching the pros and cons of this much more expensive treatment option. He adds that standard radiation has improved and causes minimal damage to other tissue when planned by experienced radiation oncologists and administered by experienced technicians.

■ Canceling Kidney Cancer’s Growth Signals

One of the most exciting clinical advances in treating solid tumors in recent years has been the approval of new target drugs for treating advanced kidney cancer. “These drugs have entirely changed the prospects for patients with advanced, metastatic kidney cancer,” says medical oncologist Dror Michaelson, MD, PhD, who conducted pivotal trials leading to the 2006 approval of Sutent (sunitinib). Two related drugs, Nexavar and Torisel, have since been introduced, and more are in the pipeline. According to Michaelson, “Patients are surviving much longer than they would have just five years ago. Sutent is now available to patients everywhere, but our patients have benefited from it longer because they could enter these trials.”

Advanced kidney cancer is frequently resistant to chemotherapy and radiation, and most patients do not respond to the difficult-to-tolerate alternatives, interleukin and interferon, which turn the immune system against cancer cells. Sutent uses an antiangiogenic strategy that targets the blood vessels feeding the tumor. These drugs can temporarily shrink cancerous growths and help other anticaner medications work more effectively. Kidney cancers are uniquely sensitive to this approach, possibly because these tumors require a substantial blood supply.

Ten years of basic research at the Cancer Center helped determine that the genetic mutation that leads to kidney cancer also stimulates blood vessel growth. Sutent interacts with various biological targets to block this dual pathway, so tumors stop growing and sometimes shrink. (continued page 10)
Prostate cancer is the most common non-skin-related cancer in men, but thanks to prostate specific antigen (PSA) testing and improved treatments, the ten-year survival rate for men with prostate cancer is now 93 percent. Since men are living longer with this disease, doctors at the Cancer Center's Bertucci Center help patients make the treatment choice that will give them the best quality of life.

When chosen appropriately for an individual patient, all the treatments currently available are equally beneficial in killing prostate cancer cells. Each therapy entails some risk to quality of life, but skillful physicians minimize those risks.

**Active Surveillance** Because prostate cancer grows slowly, Cancer Center doctors often counsel men who do not have aggressive tumors to consider closely monitoring their disease rather than undergoing treatment that might compromise their general health and quality of life.

During regularly scheduled follow-up visits, doctors perform physical exams, track PSA levels and, if necessary, use surgical biopsy or bone scans to ensure the disease has not progressed to the point that curative treatment such as surgery or radiation should be used. With appropriate follow up, active surveillance is a safe and rational approach suitable for carefully selected patients.

**Surgery** Using either open, laparoscopic (minimally invasive) surgery or laparoscopic robotic surgery, surgeons remove the diseased prostate, seminal vesicles and lymph nodes for biopsy.

**Radiation** Radiation energy interferes with cell division, killing fast-growing cancer cells. All radiation methods deliver high doses of radiation to the cancer site to destroy 100 percent of these cancer cells and are equally effective when used appropriately.

- **Internal Radiation** or **Brachytherapy** uses a long needle to insert tiny radioactive “beads” or “seeds” in the tumor. This approach is preferred for a man with a small tumor in a small prostate.

- **External Beam Radiation Therapy** directs high-energy radiation at the tumor from outside the body.

- **Intensity Modulated Radiation Therapy (IMRT)** shapes multiple radiation beams to target the tumor with a high dose of radiation while sparing surrounding tissue.

- **Proton Beam Radiation** targets tumors precisely with atomic particles that, unlike the X-rays used in other forms of radiation, do not travel past the tumor.

- **Image Guided Radiation Therapy**, which allows the daily localization of targeted organ(s), is used with all forms of external radiation and is now a standard of care for precise radiation delivery.

**Hormone Therapy** Androgen Deprivation Therapy (ADT) lowers the level of the testosterone that stimulates prostate cancer cell growth, making the tumor stop growing or shrink. This approach is used for advanced metastatic cancer and for cancers that recur after previous prostatectomy or radiation. It may also be combined with radiation therapy or chemotherapy.

**Chemotherapy** Chemotherapy drugs kill rapidly dividing cells, like cancer cells. A medical oncologist decides which drug or combination of drugs will be most effective in fighting the particular type of prostate cancer.
Nanoparticle-enhanced MRIs help doctors search for early evidence of cancer's spread.

- **Smaller Openings for Faster Healing**

For small, localized kidney cancers requiring surgery, new minimally invasive procedures are reducing complications, shortening hospital stays and speeding patient recovery. In 1999, Peter R. Mueller, MD, division head of Abdominal Imaging and Interventional Radiology, adapted radiofrequency ablation, which was common in cardiac procedures, to treat selected small, peripherally located kidney tumors. Working together, radiologist Debra Gervais, MD, and Mueller insert a needle and guide it to the tumor, where a surge of energy destroys the malignant tissue. So far, this outpatient procedure, which is ordinarily done with only local anesthesia and light sedation, offers the same survival benefits as open surgery. Mueller and Gervais have extended the procedure to selective use in larger tumors. Many patients need all or part of their organs surgically removed in radical or partial nephrectomies (kidneys), cystectomies (bladders) or prostatectomies. In 2001, oncology surgeon Douglas M. Dahl, MD, introduced laparoscopy as an alternative to the large incisions of open surgery. In laparoscopy, surgeons maneuver instruments through several small incisions in the abdomen. This approach has become the standard of care for small, accessible tumors, and is particularly helpful in obese men, who tend to have more complications from open surgery.

- **Imaging Cancerous Nodes**

A weak link in cancer diagnosis involves the lymph nodes, explains Mukesh Harisinghani, MD, director of Abdominal Magnetic Resonance Imaging (MRI). “Because cancer cells travel from lymph nodes to other organs, knowing if cancer has invaded the nodes is important for deciding how to treat and also to assess the overall prognosis.” Yet surgical biopsies can only test so many nodes, and imaging relies on an unreliable yardstick, size, to determine if a node contains cancer cells. “The problem is, sometimes small nodes contain cancer cells and large nodes do not, and this has handicapped diagnosis.”

Building on research from the 1980s by Ralph Weissleder, MD, PhD, director, Center for Systems Biology and director of the Center for Molecular Imaging Research, Harisinghani is overcoming that handicap with specially designed nanoparticles. These ultra-small molecules tag normal lymph node cells and black them out on MRIs. Only spots containing cancer cells float out of the darkness on the scans, both near and far from the original tumor.

In international trials at the Cancer Center and elsewhere, nanoparticle-enhanced MRIs in genitourinary cancers lead to at least as many accurate diagnoses as surgical biopsies. In some cases, the imaging finds cancerous nodes missed by biopsies, enabling better staging and leading to better patient care. FDA approval is pending.

- **Help for Inherited Kidney Cancer**

A unique effort that spans the Bertucci Center and the Cancer Center for Risk Assessment is the Von Hippel-Lindau/Hereditary Renal Cell Carcinoma (VHL/HRCC) Clinic. This clinic, under the direction of Othon Iliopoulos, MD, treats individuals with VHL and evaluates those who may be at risk for inherited forms of kidney cancer. Since the disease can affect many organs, the clinic coordinates comprehensive care from relevant specialists in addition to facilitating access to genetic counseling and testing. The group developed referral criteria that has been adopted nationwide, as well as systematic follow-up for those found to carry a tumor-causing mutation. “Clinics like this one, that focus on inherited cancers, are a vital resource for patients and their families, health care professionals, and for the research community,” says Iliopoulos. “We enroll patients in clinical trials that help identify new markers for monitoring disease and that aid in the discovery of new treatment targets.”
Improving Care, Advancing Research

Cancer Center clinicians have spearheaded many advances in genitourinary patient care and research since Jules Eskin began his successful bladder-sparing procedure in 1999. Today’s bladder preservation patients benefit from more effective and better-tolerated chemotherapy and radiation techniques, for example. The Bertucci Center now occupies quarters in the Yawkey Center building that facilitate interdisciplinary exchanges. Partially thanks to that interaction and the research it powers, more patients are living longer with better quality of life.

Over Memorial Day Weekend in 2003, a sudden, withering pain on his right side and blood in his urine sent 58-year old David Page to an emergency room near his vacation home in New Hampshire. Eventually, the cause became clear: a large kidney tumor that had already metastasized to his lymph nodes, lungs and bones.

At that time, most doctors were telling patients with advanced kidney cancer that they had one, at most two years to live. But Page selected Dror Michaelson, MD, PhD, in the Massachusetts General Hospital Cancer Center as his medical oncologist, partly so that he could enter upcoming clinical trials with the targeted therapy drug known as Sutent. “Mr. Page and I were determined that he would go beyond the standard prognosis,” recalls Michaelson. “One reason for our optimism was the exciting research about this new class of drugs.”

These drugs, known as dual tyrosine kinase inhibitors, are related to “smart drugs” like Herceptin, Gleevec and Tarceva, except instead of disabling one critical cancer-causing pathway in the cell, Sutent and its cousins hit two. The other drugs silence a molecular “on switch” that drives the cell growth seen in cancer. These new drugs do so, too, but they also shut down blood vessels that nourish the tumors.

Previously, researchers at the Cancer Center had learned that a single genetic mutation, VHL for von Hippel-Lindau, stimulates two receptors that activate other genes. One receptor, VEGF, for vascular endothelial growth factor, fuels blood vessel growth. The other, PDGF for platelet derived growth factor, leads to cell proliferation.

Sutent blocks both of these receptors to inhibit both the blood vessels and the proliferating cells. This dual blockade is a very effective means for stopping tumor growth.

“It made intuitive sense to me to go after the source of tumor growth,” Page explains of his interest in entering the Sutent trial, “like cutting off the enemy’s food supply.”

That intuition paid off for Page. After he began the Sutent trial in the spring of 2004, his tumor went into a remarkable retreat. Although it has recently returned, Page feels “this trial truly improved my lifestyle. I could play golf, enjoy quality time with my wife and children, and live a full and normal life. I’ve had four years of wonderful time together with my family. I enjoy life one day at a time, but I am looking forward to another four great years.”

Michaelson and other researchers are now trying to understand how the tumor gets around the block, and whether cycling to other new drugs, or different combinations and doses, may help. He is optimistic that the continuing momentum of scientific progress will result in longer life and improved quality of life for many patients with advanced kidney cancers.

The innovative care Jules Eskin received at the Cancer Center has allowed him to continue his active lifestyle.
Prostate cancer surgery and erectile dysfunction are inextricably linked in the minds of many men and their sexual partners. While prostate cancer surgery may affect erections, says Pablo Gomery, MD, a urologist at Massachusetts General Hospital, a man’s past plays an important role in his sexual future. “Your medical history, your overall health, your relationship, your age and the quality of your sex life prior to treatment all contribute to your post-surgery sexual function,” Gomery explains. Older men, men who used erection drugs prior to surgery, or men who have medical conditions that reduce blood flow to the penis — such as high blood pressure, diabetes or high cholesterol — will find it more difficult to achieve or retain an erection following prostate cancer surgery. For those in good health, recovery is more likely. According to Gomery, “The reality is that your sex life will probably be different, but that does not mean it is over. Intimacy is about much more than an erection.”
Q. How does prostate cancer surgery impact potency?
A. Following prostatectomy, or surgical removal of the prostate gland, a man ceases to ejaculate fluid. Orgasms may not feel the same as they did prior to surgery. Men with more aggressive cancer may need to have one or both of the nerves responsible for erections removed as part of the surgery. However, most men having surgery now who have normal erections can expect to recover their erectile function after treatment.

It is important to note that function is not the same as desire. Cancer-related medications and other treatments can reduce the desire to have sex. The emotions surrounding cancer, such as anxiety or sadness, can impact your sexuality as well. You may also feel less attractive because of changes to your body such as surgical scars, weight changes, or tubes or drains.

Q. What can my care team do to preserve sexual function?
A. An integral part of caring for men with prostate cancer is to speak frankly about their sexual function prior to treatment. There are several choices of treatment for prostate cancer, and each of the options — external radiation therapy; brachytherapy, in which tiny radioactive particles are implanted into the prostate gland; and prostatectomy — presents a different risk of side effects. With the help of a multidisciplinary genitourinary oncology care team, men determine the treatment option that best suits them. Ongoing studies at Massachusetts General Hospital Cancer Center are aimed at getting accurate information about the impact of the various treatments on urinary, bowel and sexual function so that we can accurately counsel our patients and look for ways to reduce side effects.

Q. When can I start having sex again?
A. Regaining potency is less predictable than regaining urinary control, which returns in most men within four to six months (sometimes within weeks). Erectile function occasionally returns immediately, but can take over a year in some cases. Ask your doctor if you would like to try medication to help you obtain or maintain an erection. If you believe your cancer medications are interfering with your desire for sex, ask if they can be changed.

Q. What resources are available if I need additional help?
A. We consider post-surgical care, including counseling about erectile function, to be an important part of prostate cancer treatment. In our confidential support groups, men diagnosed with prostate cancer talk openly about their experiences and share solutions to issues in their relationships. We can also refer you to erectile function specialists, individual counseling, or couples’ therapy. Please let a member of your care team know if you are interested in knowing more about any of these services. You can also visit the Blum Cancer Resource Room on the eighth floor of the Yawkey building or the first floor of the Cox building for more information on prostate cancer diagnosis, treatment and recovery.
When Cynthia Calvin experienced disconcerting incontinence in 2002, she visited specialists at hospitals in and around Boston, finally receiving a frightening diagnosis of invasive bladder cancer and a recommendation for surgery to remove her bladder. Hoping for a better option, she came to Massachusetts General Hospital Cancer Center and to the Claire and John Bertucci Center for Genitourinary Cancers, where she met with Center Director Donald Kaufman, MD.

"Dr. Kaufman saved my life," says Calvin. "If I hadn't found this man, I probably wouldn't be talking to you today."

Calvin’s initial meeting with Kaufman was the first of many conversations that shaped her treatment, and her experience reflects the type of personalized care that defines the Cancer Center. At this meeting, in conjunction with the patient and family members, a pathologist, radiation oncologist, medical oncologist and a surgeon develop a unanimous treatment recommendation.

"Patients appreciate knowing that each of these specialists has contributed to the recommendation," says Kaufman. "Ultimately, however, it is the patient's decision."

These conversations, Kaufman continues, represent “the cornerstone of our whole clinic.”

This multidisciplinary team approach ensures a comprehensive review of the patient’s health. For Calvin, that meant taking into consideration her 1980 treatment for breast cancer. What the Cancer Center team saw — and what specialists elsewhere had missed — was that Calvin had a very rare case of recurring breast cancer cells that had invaded her bladder. Cancer Center doctors successfully treated her disease with a chemotherapy protocol she refers to as the “Red Devil.”

"Dr. Kaufman regarded me as a human being, a whole self," asserts Calvin, who says that elsewhere she felt the focus was on the disease rather than on her.
The Art of Good Conversation

“My idea of good company,” wrote 19th century English author Jane Austen, “is the company of clever, well-informed people who have a great deal of conversation. That is what I call good company.”

If Austen were to time travel from London in the early 1800s to the halls of the Yawkey Building today, she could well find herself in a great deal of “good company.”

“The art of medicine,” says Daniel Haber, MD, PhD, director of the Cancer Center, “is the ability to talk to everyone at the level they want to be talked to.”

That art — and skill — is a fundamental component of the translational research that is at the heart of a world-class academic hospital like Mass General. This term applies to the process of translating clinical findings from the patient’s bedside to the laboratory bench, where they are evaluated and used to inform the next phase of discovery. New scientific understanding of how cancer arises and spreads is also translated back to patient care through clinical trials. This complex process, rigorously repeated until safe and effective treatments are found, absolutely depends, says Haber, on conversations between physicians and scientists and between doctors and patients.

“It is a very special physician,” says Haber, “who can understand what is happening on the frontiers of medicine and also be able to communicate that to the patient.” The Cancer Center “greatly values clinical excellence and a strong commitment to patient care,” Haber continues. “It’s how we select our faculty.”

We Have a Lot to Talk About

Alan Costa, a 59-year-old manager of a golf club on Nantucket, recreational pilot, and avid golfer, can attest to the value of good communication among his doctors and with him. When he was diagnosed with an aggressive form of muscle-invasive bladder cancer six years ago, he talked to others who had had the same experience and asked questions of a number of doctors. After being told that his only option was to have his bladder removed — a complicated surgery with difficult-to-manage side effects — he came to the Cancer Center and met Kaufman, Niall Heney, MB, MD, and William Shipley, MD, vice chair for clinical research in the Department of Radiation Oncology.

“Dr. Shipley sent me in the right direction,” says Costa. “I felt confident that he was always going to level with me.”

Working together, Costa’s medical team recommended the course of action to attack his disease: an aggressive experimental protocol that spared his bladder while hitting the cancer with limited surgery to remove the tumor, followed by chemotherapy, radiation and then more chemotherapy. The year-long protocol required numerous conversations between Costa and his care team about how to take care of himself during treatment.

“What can I do to feel better?” Costa asked the infusion nurses as he received his chemotherapy. “They would tell me how to deal with side effects,” he says. “Nurses have a lot of information and they are extremely helpful in talking about options.”

For example, his treatment sometimes caused severe nausea, and one of his nurses told him to try taking his anti-nausea drugs in smaller doses continually rather than all at one time. It worked, he said. They also educated him about warning signs, such as a skin condition that might indicate internal bleeding.

“My favorite part of this work is the psychosocial part,” says Lorraine Nazzaro, RN, an infusion nurse at the Cancer Center. “A lot of patients don’t know what questions to ask. As I talk with them, I can answer some questions and help them formulate others for their doctors.” (continued on page 16)
Jackie Somerville, RN, MS, associate chief of nursing, says that the communication among nurses and between nurses and patients is fundamental to how care is delivered at the Cancer Center. “We want patients here to feel safe and feel known,” she says. “When there is a relationship, people participate in their care more effectively. They ask questions. They feel a connection to their providers. They feel safe and calmer.”

■ Real men talk, listen and dance

When Austen’s New England compatriot Ralph Waldo Emerson quipped: “Two may talk and one may hear, but three cannot take part in a conversation of the most sincere and searching sort,” he certainly never had in mind Marilyn Brier’s support group for men diagnosed with prostate cancer. In a private, comfortable part of the Yawkey Building, on the second Wednesday of every month for almost five years, the conversation among these 17 men is at once searching and sincere.

“The men are all so dynamic,” says Brier, a clinical social worker who has been at the Cancer Center since 2002. “They are up-to-date on new therapies and information, and they share this knowledge with one another. They’re all in this together.”

During a typical meeting, a member of the Cancer Center care team — a physician, social worker, nutritionist or nurse practitioner — joins the group for the first 45 minutes to talk about an issue of particular concern. On an unseasonably warm evening in January, W. Scott McDougal, MD, chief of the Department of Urology, discussed when to worry and when to be only mildly attentive to a rising PSA (a protein in the blood that can indicate cancer in the prostate) in the years following treatment. A lively question and answer period followed.

After McDougal left, the men talked openly about their concerns. Topics ranged from a request for a speaker to address sexual intimacy following prostate cancer treatment to the effect, if any, of diet on the risk of this disease.

Talking, say these men, is vital to both their emotional and physical health. One man recalled how conversations with his brothers about his own diagnosis following the death of their father from prostate cancer prompted each brother to be tested. Another encouraged the men to volunteer to talk with others who have been newly diagnosed.

But the most striking characteristic of this group of men, roughly aged 50 to 90, is their humor and their spirit. Brier notes that making friendships, even when their lives are challenging, has become fundamental. They realize they are not alone. This commitment to coming together, listening and talking through the good news and the bad, is at the heart of patient care at the Cancer Center.

“We work hard and we laugh a lot; it’s an upbeat group,” says Brier about the men.

“And on Tuesdays and Thursdays, I dance,” says one participant. That’s a good end to a good conversation in good company. ■ — Terri Rutter
Ten years ago, having had multiple biopsies and blood tests that finally resulted in a diagnosis of prostate cancer, Brad Ingalls wondered why better diagnostic tools didn’t exist. “There were many false negatives,” recalls his wife, Joan. “As an aeronautical engineer, Brad thought in engineering terms: He began thinking seriously about how to create diagnostic tools.”

Ingalls brainstormed with his Massachusetts General Hospital Cancer Center medical oncologist Matthew Smith, MD, PhD, about ideas for such tools. “Brad was a very intelligent man and initiated many in-depth discussions with me about why we needed new tools to diagnose prostate cancer and how they might be developed,” says Smith, director of Genitourinary Medical Oncology at the Cancer Center. “In a meaningful way, he both challenged and inspired some of our most important work in prostate cancer, and his gift has enabled us to translate some of those ideas into action.”

One idea that grew from Ingalls’ support was to use a microchip developed by Cancer Center researchers to capture cancer cells from solid tumors that circulate in the blood to better understand the biology of prostate cancer. Smith and his colleagues are now using the novel technology to determine whether this approach can complement or even replace traditional biopsies to diagnose prostate cancer.

Ingalls died on January 18, 2006, but his ideas about prostate cancer diagnosis and treatment live on at the Cancer Center through Joan’s $525,000 donation from the W. Bradford Ingalls Foundation.

“In many ways, Mr. Ingalls’ illness reflected the key unmet needs in the field of prostate cancer diagnosis and treatment,” says Smith. “The challenges of diagnosis, problems of bone metastases and side effects of treatment that he faced are problems shared by many men with prostate cancer. Thanks to his insights and generous support, we are making progress in each of those key areas.”

Smith is an international leader in prostate cancer research. He heads many multicenter clinical trials in prostate cancer, including studies on treatment and prevention of bone metastasis. In addition, he spearheads a research program to understand and prevent the unintended side effects of treatment in prostate cancer survivors including osteoporosis, obesity, diabetes and cardiovascular disease.

“Mr. Ingalls and I shared many hours discussing ways to improve prostate cancer diagnosis and treatment,” recalls Smith. “He decided he wanted to support the innovative prostate cancer research at Mass General Hospital in this field, and wanted to help other men with this disease.”

The generosity of donors like the Ingalls makes a profound difference in the lives of cancer patients. To find out how you can help people battling this disease, please contact Kate Todd, director of Development for the Massachusetts General Hospital Cancer Center, at 617.726.0402 or kstodd@partners.org.

Making a donation to the Cancer Center online is easy. To make your gift today, visit us at www.massgeneral.org/cancer/help/donate.asp
“I’m a fair-skinned Irishman,” Dick Finnegan says, acknowledging that his skin was the most likely place for melanoma to occur. But in December 2002, Cancer Center doctors diagnosed Dick with a rare form of the disease, which had blocked his digestive tract without ever showing itself externally. Dick was told he had stage IV melanoma with a ten percent chance of survival. Yet, more than five years later, his scans show no sign of disease.

Between 2002 and 2006, Dick’s cancer returned twice. Each time, Cancer Center doctors combated it with the most advanced treatment available, including specialized surgical procedures and a clinical trial that involved creating a vaccine from Dick’s tumor. This personalized therapy is designed to stimulate the body’s natural disease-fighting system into a more powerful attack on cancerous cells. When the cancer recurred a second time, Dick entered a follow-up to the clinical trial. This time, he received a human antibody, anti-CTLA4, that further boosted his immune system.

Pancreatic cancer took two of Dick’s older brothers, and Cancer Center doctors have counseled him about the genetic link between pancreatic cancer and melanoma. But for now, Dick’s attention isn’t on vaccines or genes. It’s on enjoying life with his wife, Joyce, and celebrating that, following his most recent checkup, the status of his digestive tract can be summarized in one word: unremarkable.