Genitourinary Oncology Advances Improve Outcomes for Patients

Genitourinary cancer specialists at Dana-Farber/Brigham and Women’s Cancer Center are offering new clinical trials, a broader application of robotic surgery approaches, and radiation therapies using real-time image guidance to improve outcomes for patients.

New Diaphragm Pacing Option Enables Elimination of Ventilator Dependence

Directly stimulating the diaphragm muscle, a new device implanted by thoracic surgeons at Brigham and Women’s Hospital enables patients with spinal cord injuries and other conditions to reduce or eliminate their reliance on mechanical ventilation.

Electrophysiologists Develop Therapies for Complex Cardiac Arrhythmias

Electrophysiologists in the Cardiac Arrhythmia Service at Brigham and Women’s Hospital promote the development of new technology and innovative therapies, as well as support research into the mechanisms of arrhythmias.

Elizabeth G. Nabel, MD, Named Brigham and Women’s Hospital President

Elizabeth G. Nabel, MD, a board-certified cardiologist and former director of the National Heart, Lung, and Blood Institute (NHLBI), began her new role as president of Brigham and Women’s Hospital on January 1, 2010.

Continuing Medical Education

Learn about upcoming continuing medical education course offerings from Brigham and Women’s Hospital, through the Harvard Medical School Department of Continuing Education.
Genitourinary Oncology Advances Improve Outcomes for Patients

Genitourinary cancer specialists at Dana-Farber/Brigham and Women's Cancer Center are offering new approaches in caring for patients with genitourinary cancers.

The team of specialists at the Genitourinary Cancer Treatment Center at Dana-Farber/Brigham and Women's Cancer Center is offering new clinical trials of targeted and combination therapies, broader application of robotic surgery approaches across genitourinary cancers, and radiation therapies using real-time image guidance and immobilization and localization devices.

Minimally Invasive Surgical Techniques and Advanced Reconstruction
Urologic surgeons at the Center have completed more than 900 robot-assisted laparoscopic prostatectomy, nephrectomy, and cystectomy procedures using two da Vinci® Surgical Systems. In addition, partial nephrectomy is being performed to remove moderately large tumors, while preserving 50 percent or more of the kidney. Advanced reconstructive techniques include neobladder reconstructive surgery for select patients who have undergone radical cystectomy for bladder cancer.

Advanced Radiation Therapies
Radiation oncologists at the Center are delivering innovative treatment techniques designed to optimize cancer control and preserve normal function. Techniques include:

- The Center is one of few nationwide to offer image-guided radiation therapy using intraprostatic fiducials and a unique intra-rectal balloon designed to immobilize and localize the prostate for precise delivery of treatment.

Using these techniques, radiation oncologists have achieved prostate cancer control rates equal to or above the results seen with 3D-conformal radiation therapy, but with significantly less toxicity to the rectum, bladder, and prostatic urethra;

- Urethral-sparing brachytherapy, a technique developed by specialists at the Center, is performed using real-time, fused magnetic resonance imaging and ultrasound guidance, designed to minimize the risk of any urinary incontinence and markedly reduce acute urinary symptoms.

Pioneering Research
Several current research studies at the Center promote the development of personalized therapies including:

- Levi A. Garraway, MD, PhD, Philip W. Kantoff, MD, Anthony V. D’Amico, MD, PhD, and William C. Hahn, MD, PhD, are collaborating in studies of genomic characterization and profiling of prostate and bladder cancers to develop personalized therapies that improve outcomes for patients. A chip, held by Dr. Kantoff, holds hundreds of patient samples and is scanned for genetic mutations using cutting-edge genomic technologies.

Levi A. Garraway, MD, PhD, Philip W. Kantoff, MD, Anthony V. D’Amico, MD, PhD, and William C. Hahn, MD, PhD, are collaborating in studies of genomic characterization and profiling of prostate and bladder cancers to develop personalized therapies that improve outcomes for patients. A chip, held by Dr. Kantoff, holds hundreds of patient samples and is scanned for genetic mutations using cutting-edge genomic technologies.
Using a database of information gathered from more than 5,000 male patients, research led by Dr. D’Amico, Chief of the Center’s Prostate Cancer Radiation Oncology Service, has been able to identify patients who should avoid hormonal therapy. (JAMA, August 25, 2009). Based on these data, researchers found that men with low-risk prostate cancer and a history of heart attack or heart failure who are considering hormonal therapy in an effort to become eligible for prostate brachytherapy should be cautious. In this group of men, findings show that hormone therapy has no proven role in decreasing cancer death and may shorten survival.

**Innovative Clinical Trials**

Medical oncologists at the Center offer an average of 25 open clinical trials at a time. Current trials include:

**Prostate Cancer Trials**
- **Phase II study of neoadjuvant abiraterone combined with hormonal therapy prior to prostatectomy.** This trial evaluates the use of the new, highly-active androgen synthesis inhibitor (abiraterone) in combination with hormonal therapy in patients with high-risk prostate cancer prior to prostatectomy;
- **Randomized Phase III study of radiation and hormone therapy with or without chemotherapy for intermediate or high-risk prostate cancer, which is testing whether the addition of docetaxel chemotherapy improves outcomes in localized prostate cancer;**
- **Randomized Phase II study of angiogenesis inhibition (Avastin) with hormonal therapy in patients with rising PSA or metastatic prostate cancer who have undergone radiation therapy and/or surgery.** This trial is testing whether the addition of Avastin to standard androgen deprivation improves the response rate to ADT;
- **Phase II study of angiogenesis inhibition (Avastin) with chemotherapy (Docetaxel) and hormonal therapy (18 months) in patients with rising PSA who have undergone radiation therapy and/or surgery.** This trial is testing whether treating microscopic systemic prostate cancer aggressively with combined therapy will lead to durable remissions in a proportion of patients;
- **Novel hormonal agents – including abiraterone (CRPC pre-chemotherapy, randomized Phase III), MDV3100 (CRPC post-chemotherapy, randomized Phase III), TOK-001 (CRPC pre-chemotherapy, Phase I/II), and others – for metastatic, castration-resistant prostate cancer;**
- **Novel chemotherapy approaches for castration-resistant disease – combining GM-CSF with docetaxel;**
- **Novel immune therapy, including provenge and ipilimumab.**

**Kidney Cancer Trials**
- **Study of sunitinib or pazopanib in patients with advanced or metastatic kidney cancer.** This study is designed to compare and evaluate side effects and effectiveness of two FDA-approved therapies for kidney cancer.

**Bladder Cancer Trials**
- **Randomized Phase III study of gemcitabine/cisplatin chemotherapy with or without Avastin for patients with metastatic bladder cancer.** This study will test the role of angiogenesis inhibition in combination with chemotherapy in bladder cancer patients;
- **Phase II study of dose-intensified Dose-Dense MVAC to test whether Dose-Dense chemotherapy improves cancer outcomes in patients with muscle invasive bladder cancer;**
- **Randomized Phase II study of gemcitabine and carboplatin with or without AMG-386 for patients with advanced urothelial cancer who are not candidates for cisplatin.** This study will evaluate whether targeting an alternative angiogenesis pathway that appears active in bladder cancer improves outcomes in bladder cancer. Crossover is available for AMG-386 alone if patients are receiving placebo;
- **Phase II study of TKI-258 in patients previously treated with chemotherapy for bladder cancer.** This study targets the FGFR3 pathway, which is mutated in many bladder cancer specimens.

**Information on Clinical Trials**

For further information regarding any of these trials, please call David Flanagan at (617) 582-8313.
New Diaphragm Pacing Option Enables Elimination of Ventilator Dependence

Directly stimulating the diaphragm muscle, a new device offers improved quality-of-life, lower risk of respiratory infection, and other benefits for patients with spinal cord injuries and other conditions.

Brigham and Women's Hospital thoracic surgeon, Christopher T. Ducko, MD, was the first in New England and is among few specialists nationwide to offer implantation of a new diaphragm pacing system that enables patients with spinal cord injuries and other conditions to reduce or eliminate their reliance on mechanical ventilation.

Compared with an older device, which requires implantation of electrodes directly on the phrenic nerve in the neck or chest, the new system employs electrode leads that are implanted in the diaphragm at the motor point to directly stimulate the muscle. The leads are implanted laparoscopically during a minimally invasive outpatient procedure and connected to an external, battery-powered pulse generator that controls the stimulus regulating movement of the diaphragm muscle and affects respiration.

Electrode lead placement (Figure 1) is done laparoscopically with two leads on each diaphragm, placed at the point of maximal stimulation to capture the best muscle contraction. The leads are tunneled out of one of the port sites to exit the skin a few inches away (Figure 2).

The system’s battery-powered stimulator (Figure 3) is initially programmed by the surgeon and then can be powered on or off by the patient.

Indications for Referral

The diaphragm pacing device is suitable for select patients with:

- Intact bilateral phrenic nerves;
- High cervical spinal cord injuries;
- Central hypoventilation syndromes;
- Early-stage ALS with appropriate pulmonary reserve and muscle capacity (The use of the device for ALS patients is currently in clinical trial.);
- Acute respiratory changes due to sudden illness, such as H1N1 flu, with need for short-term support.

Generally, patients with stable, high spinal cord injuries, where the phrenic nerve is still intact, are eligible for device implantation. Patients with central hypoventilation syndrome and potentially select patients with early-stage amyotrophic lateral sclerosis (ALS) may be eligible for this device as well.

Patient benefits of the new device include:

- Better quality-of-life, including renewed sense of taste and smell, more natural eating and speaking capabilities, and easier mobility with less equipment;
- Lower risk of pneumonia and other respiratory infections;
- Delay in ventilator dependence in select patients with ALS.

Information and Referrals

For more information, or to refer a patient, please contact our Referral Coordinators at (617) 732-9894 or bwhteleservices@partners.org.
Electrophysiologists Develop Therapies for Complex Cardiac Arrhythmias

Electrophysiologists at Brigham and Women’s Hospital provide clinical expertise, sophisticated technology, and advanced therapies to reduce mortality and improve quality-of-life for highly-complex cardiac arrhythmia cases.

An international resource for treating complex arrhythmias, the Cardiac Arrhythmia Service recently transitioned into a new, state-of-the-art electrophysiology suite in the Carl J. and Ruth Shapiro Cardiovascular Center at Brigham and Women’s Hospital. The Service promotes the development of new technology and innovative therapies, as well as supports research into the mechanisms of arrhythmias.

Focus on Atrial Fibrillation

To address the expected increase in prevalence of atrial fibrillation (AF) as the population ages, Brigham and Women’s Hospital has created the Center for Advanced Management of Atrial Fibrillation. Led by Gregory F. Michaud, MD, the Center encompasses innovative patient care, as well as pre-clinical and clinical research into the causes of AF and identification of the most appropriate therapies.

Ventricular tachycardia

Electrophysiologists, including William Stevenson, MD, an internationally-recognized expert in treating ventricular tachycardia, also work with referring physicians to manage challenging ventricular arrhythmias (VT). Even with implantable defibrillators (ICD), VT episodes indicate an increased risk of mortality and hospitalizations, and symptomatic episodes reduce quality-of-life.

The Service is among a select few with extensive experience in epicardial mapping and ablation. Multicenter clinical trials have demonstrated that ablation therapy markedly reduces the risk of recurrent VT and is effective at reducing the frequency of VT in 70 to 75 percent of patients.

When the VT circuit is deep within the myocardium and cannot be reached either from the inside or the outside surface of the heart, electrophysiologists work with interventional cardiologists to perform transcoronary alcohol ablation or with cardiac surgeons who are skilled at creating pericardial windows to access the heart and ablate the VT circuits, or can directly perform ablations via open heart arrhythmia surgery.

New Clinical Trials

Physicians in the Center for Advanced Management of Atrial Fibrillation are offering participation in a variety of clinical trials, including:

- CABANA (Catheter Ablation Versus Anti-Arrhythmic Drug Therapy for AF) – An NIH-sponsored, multicenter, randomized trial evaluating catheter ablation versus antiarrhythmic drug therapy for symptomatic AF.

  This trial is designed to test the hypothesis that catheter ablation is superior to rate and/or rhythm control therapy and will reduce mortality in patients whose AF is incompletely controlled by medical therapy. Cabana Trial contact: Principal Investigator William Stevenson, MD, (857) 307-1948

- Pace-Guided Ablation Trial – Designed by Dr. Michaud, this trial – offered at only three centers worldwide – seeks to improve the one-time procedural success rate of catheter ablation for paroxysmal AF. Pace-Guided Ablation Trial contact: Principal Investigator Gregory F. Michaud, MD, (857) 307-1946

Dr. Michaud also is working on a hybrid AF protocol with cardiac surgeon Prem Shekar, MD, that will combine the benefits of catheter ablation with mini-MAZE surgery. The intent is to demonstrate that the combined procedure, approaching the heart from both the endocardium and epicardium, will allow them to create transmural lesions that will effectively ablate the arrhythmia. This approach also allows the removal of the left atrial appendage to reduce the risk of clots and stroke.

continued on page 6
Elizabeth G. Nabel, MD, Named Brigham and Women’s Hospital President

Elizabeth G. Nabel, MD, the former director of the National Heart, Lung, and Blood Institute (NHLBI), is the new president of Brigham and Women’s Hospital. A board-certified cardiologist who completed her internship, residency, and fellowship at Brigham and Women’s Hospital, she began as president Jan. 1.

“The opening of this door is a tremendous opportunity to share a personal passion with world-class clinicians and scientists to link excellent patient care to internationally respected research and then carry our collective wisdom forward to our students, the future leaders of medicine,” Dr. Nabel said. “All of this will be done with a keen focus on how we can make a difference in the lives of the people who depend on us, whether they live half way around the world or across the street from our front doors.”

Dr. Nabel is a graduate of Cornell University Medical College. She trained at Brigham and Women’s Hospital and completed a clinical and research fellowship in cardiovascular medicine at Brigham and Women’s Hospital and Harvard University. At the University of Michigan, she served as Assistant Professor of Medicine and then went on to become director of the Cardiovascular Research Center, professor of Internal Medicine and Physiology, and then chief of the Division of Cardiology.

Well respected for her research in vascular biology and molecular cardiology and for her gene transfer studies of the cardiovascular system, Dr. Nabel joined the NHLBI as scientific director for Clinical Research in 1999 and, in 2005, became director, overseeing an extensive national research portfolio and an annual budget of approximately $3 billion.

Dr. Nabel is a nationally-recognized scholar and author of 250 publications. She is also a mentor and teacher who has inspired her students, as evidenced by her selection for the Eugene Braunwald Academic Mentorship Award. Her colleagues have recognized her leadership by selecting her to the American Academy of Arts and Sciences, the Association of American Physicians (Council), the Institute of Medicine of the National Academy of Sciences (Council) and as a fellow of the American Association for the Advancement of Science. Dr. Nabel serves on editorial boards of the *New England Journal of Medicine* and *Science Translational Medicine*.

Electrophysiologists Develop Therapies for Complex Cardiac Arrhythmias… continued from page 5

On the Horizon
Another innovative technique involves MR imaging to replace fluoroscopic guidance during ablation procedures. Real-time MR images would allow operators to see the tissue they have ablated and to more effectively characterize lesions, improving the success of ablation and reducing the incidence of second procedures. Another is the use of focused ultrasound to perform MR-guided completely non-invasive ablation.

Information and Referrals
For more information, or to refer a patient, please contact our Referral Coordinators at (617) 732-9894 or email bwhteleservices@partners.org.
Genitourinary Oncology Advances Improve Outcomes for Patients... continued from page 3

About the Genitourinary Cancer Treatment Center
Offering more than a 90 percent cure rate for most patients with testicular cancer and improved outcomes for patients with prostate, bladder, and kidney cancer, the Genitourinary Cancer Treatment Center cares for more than 2,000 patients each year. A dedicated team of specialists, including urologic surgeons, medical oncologists, radiation oncologists, pathologists, and other cancer specialists, works together to develop and deliver the most effective treatment plan for each patient. Urologic pathologists and radiologists also employ advanced technologies and techniques to provide critical information that is used in treatment planning and assessing a patient’s response to treatment, including molecular pathology techniques and advanced imaging techniques.

Information and Referrals
For more information, or to refer a patient, please contact our Referral Coordinators at 1-877-332-4294 or email bwhteleservices@partners.org.

Continuing Medical Education
Brigham and Women’s Hospital is pleased to offer the following courses, occurring in May 2010, through the Harvard Medical School Department of Continuing Education. Please call (617) 384-8600 or visit www.med.harvard.edu/conted for more information.

May
May 11-14
Clinical Nuclear Medicine/PET
Location: Boston Marriott Long Wharf, 296 State Street, Boston, MA 02109
Director: S. Ted Treves, MD, FACP
Offered by: Brigham and Women’s Hospital, Department of Radiology and Harvard Medical School, Joint Program in Nuclear Medicine

May 22
Advances in the Treatment of Genitourinary Oncology
Location: Dana-Farber Cancer Institute, 44 Binney Street, Boston, MA 02115
Directors: Philip W. Kantoff, MD; Christopher Sweeney, MBBS
Offered by: Dana-Farber/Brigham and Women’s Cancer Center; Harvard Medical School

www.brighamandwomens.org
Access to Brigham and Women’s Hospital

Physician Referral Service
1-800-MD-TO-BWH (1-800-638-6294)
Experienced referral coordinators assist with outpatient appointments, access to our physicians, and information regarding our specialists and services.

Physician Liaison
Physician Liaison Ellen Steward provides direct assistance with patient referrals and consultations with our specialists. Ellen is available to meet with you in person and can be reached at (617) 732-9598, esteward@partners.org, or pager (617) 732-5700, ID #36031.

MD Connect
(Inpatient Transfers and Transportation Services)
1-877-637-3337

Care Coordination
(Facilitation of Care Plan and Discharge Planning)
(617) 732-6469

The Carl J. and Ruth Shapiro Cardiovascular Center

Cardiovascular Access Managers
Cardiovascular Access Managers Lisa Downey, RN, BSN, and Brian Laneau, RN, BSN, assist with inpatient transfers and consultations with our team of cardiovascular experts. They can be reached at (617) 543-4170.

Watkins Cardiovascular Clinic
(857) 307-4000