Osteoarthritis Center Delivers Multidisciplinary Approach to Diagnosis, Treatment, and Clinical Research
Specialists in rheumatology, orthopedics, physical therapy, pain management, and bone and joint radiology are providing an expert, multidisciplinary approach to care for osteoarthritis patients, as well as clinical and basic research designed to advance options for patients with this difficult-to-treat disease.

Pioneering Novel Approaches to the Prevention, Diagnosis, Treatment, and Research of Venous Thromboembolism
Specialists in the Venous Thromboembolism (VTE) Research Group are advancing the prevention, treatment, research, and understanding of pulmonary embolism and deep vein thrombosis.

Discoveries in Renal Disease and Kidney Transplantation
Recent discoveries in renal disease and kidney transplantation are helping to identify kidney disease earlier, slow disease progression, control blood pressure, and improve kidney transplantation outcomes.

Injectable Gel Demonstrates Promise for Drug Delivery
Brigham and Women’s Hospital researchers have developed a potentially new way to treat diseases using a hydrogel that encapsulates and releases agents in response to specific enzymes that are significantly expressed in a diseased state.

Novel Multicultural Dermatology Program Offers Specialized Treatment
The Multicultural Dermatology Program offers specialized treatment of skin and hair conditions more commonly found in women and men of non-European ethnic heritages, including African, African-American, Asian, South Asian, Hispanic, and Middle Eastern descent.
Osteoarthritis Center Delivers Multidisciplinary Approach to Diagnosis, Treatment, and Clinical Research

Led by rheumatologist Antonios O. Aliprantis, MD, PhD, rheumatologist William P. Docken, MD, and orthopedic surgeon Andreas H. Gomoll, MD, the Osteoarthritis Center at Brigham and Women’s Hospital (BWH) offers a multidisciplinary approach to care for osteoarthritis patients, as well as engaging in clinical and basic research designed to advance options for patients with this difficult-to-treat disease.

“While more than 27 million people in the nation are affected by osteoarthritis, treatment plans are not usually straightforward and need to be tailored for each patient,” said Dr. Aliprantis. “We strive to maximize a patient’s care using a team-based approach.”

Composed of specialists in rheumatology, orthopedics, physical therapy, pain management, and bone and joint radiology, the Center aims to improve diagnosis and medical and surgical care. Specialists provide expert diagnostic evaluations and collaborate to develop an individualized treatment plan for each patient, including both non-surgical and surgical approaches.

Clinical Trials
Research at the Center is focused on all aspects of osteoarthritis, including basic mechanisms of joint degeneration, cartilage repair and regeneration, drug safety, the appropriate use of arthroscopy, and improving the quality of care for joint replacement patients.

Current studies offered by Center specialists include:
• A pain management study to assess the use of acupuncture to control knee osteoarthritis pain. Please contact Principal Investigator Ajay D. Wasan, MD, for more information at (617) 732-9579;
• A research study to evaluate predictors of pain and function after total knee replacement surgery. For further information, please contact Clinical Research Coordinator Christine Cahalan at (617) 732-9014;
• A study of strategies to optimize a patient’s experience throughout knee and hip replacement, from pre-operative evaluation to post-operative care. Please contact Principal Investigator John Wright, MD, at (617) 732-5352 for more information;
• A computer simulation model used to project the costs and quality-of-life associated with osteoarthritis and concomitant obesity, anterior cruciate ligament tear, and other clinical scenarios. Please contact Principal Investigator Elena Losina, PhD, for more information at (617) 732-5388.

Led by Principal Investigator Jeffrey Katz, MD, a recently closed multi-center trial is evaluating the efficacy of surgery to trim a torn meniscus versus non-operative management in patients with concomitant osteoarthritis. Preliminary data is expected in 2012.

Osteoarthritis can lead to joint destruction and deformities in multiple joints. The knee x-ray shows medial “bone-on-bone” joint space narrowing. The hand film depicts obliteration of the cartilage in the 4th PIP joint with osteophytes and bone cysts.

Basic Science Research
Basic science research includes ongoing study of osteoarthritis and bone biology. Dr. Aliprantis is evaluating the molecular pathways that cause osteoarthritis in animal models with the goal of identifying new drug targets. His group also is trying to identify osteoarthritis biomarkers by using a biorepository based at BWH that contains hundreds of clinical samples from osteoarthritis patients. Dr. Aliprantis also is collaborating with Jeffrey Karp, PhD, to investigate new drug delivery options using injectable gels for the treatment of arthritis (see Page 6 for more information).

Information and Referrals
For more information, or to refer a patient, please contact our Referral Coordinators at (617) 732-9894 or email bwhreferrals@partners.org. Patients can be seen at four locations: Brigham and Women’s Hospital main campus in Boston, Brigham and Women’s Ambulatory Care Center in Chestnut Hill, Faulkner Hospital in Jamaica Plain, and Brigham and Women’s/Mass General Health Care Center in Foxborough.
Pioneering Novel Approaches to the Prevention, Diagnosis, Treatment, and Research of Venous Thromboembolism

Specialists in the Venous Thromboembolism (VTE) Research Group at Brigham and Women’s Hospital (BWH) are advancing the prevention, treatment, research, and understanding of pulmonary embolism and deep vein thrombosis.

“Pulmonary embolism is the most preventable cause of death among hospitalized patients and accounts for up to 180,000 deaths per year in the United States,” said Samuel Z. Goldhaber, MD, Director, VTE Research Group. “Our goal is to prevent pulmonary embolism and deep vein thrombosis, as well as to improve outcomes among patients who develop these conditions.”

Computerized Physician Alerts Prevent VTE

The VTE Research Group and BWH Information Technologies have been at the forefront of developing computerized alerts for physicians with hospitalized patients who are at high risk for developing VTE. In a 2,500-patient randomized clinical trial led by Dr. Goldhaber and published in *The New England Journal of Medicine* (N Engl J Med 2005;352: 969-977), researchers found that computer alerts that encouraged prophylaxis use among high-risk hospitalized patients resulted in a 41 percent decrease in symptomatic pulmonary embolism (PE) and deep vein thrombosis (DVT). A subsequent and more sophisticated version of this alert system, designed to better ensure implementation of prophylaxis against DVT and PE in high-risk patients, has shown even greater effectiveness (Thromb Haemost 2010; 103: 312-317).

Groundbreaking Clinical Trials Shape Care

Dr. Goldhaber is the Chair of the Steering Committee for the ATTRACT (The Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-directed Thrombolysis) trial. This major NIH-sponsored, multicenter national trial for large DVT randomizes patients for either catheter intervention or usual therapy and then follows these patients for several years to determine which patients develop post-thrombotic syndrome. Having directed multicenter trials resulting in the FDA approval of tPA for treatment of PE and dalteparin for prevention of PE, Dr. Goldhaber is now active in national and international guideline committees to educate clinicians about optimal strategies to treat and prevent PE. For patients who are not candidates for tPA, BWH cardiac surgeons perform pulmonary embolectomy – with a 95 percent survival rate.

Dr. Goldhaber was the senior author of a recent trial that tested a novel oral anticoagulant medication, dabigatran, compared with warfarin in the treatment of acute venous thromboembolism (N Engl J Med 2009; 361:2342-2352.). The study found that, for the treatment of acute venous thromboembolism, a fixed dose of dabigatran is as effective as warfarin, has a safety profile that is similar to that of warfarin, and does not require laboratory monitoring.

Through the implementation of computerized decision support protocols, BWH specialists also are reducing the use of chest CT scans for PE diagnosis, thereby limiting radiation exposure and risks of renal failure and allergic reactions caused by contrast agents.

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Discoveries in Renal Disease and Kidney Transplantation

Brigham and Women’s Hospital (BWH) specialists have made recent discoveries in renal disease and kidney transplantation that are improving outcomes among patients.

**Acute, Chronic and End-stage Kidney Disease**

Led by Joseph V. Bonventre, MD, PhD, Chief of the Division of Renal Medicine, nephrologists are leading studies of new ways to identify kidney disease earlier, reduce disease progression, control blood pressure, and improve outcomes and quality-of-life among patients with renal disease. A select sampling of these studies includes:

- **Early Diagnosis of Kidney Disease and Improving Drug Safety** – The urine biomarker Kidney Injury Molecule-1 (KIM-1), discovered by Dr. Bonventre and Takaharu Ichimura, PhD, has been FDA-qualified for safety studies in drug development (Nature Biotechnology 2010; 28:478-485). With BWH colleague Sushrut Waikar, MD, other biomarker studies are ongoing in patients with various forms of chronic and acute kidney disease. These studies will evaluate the utility of KIM-1 and various biomarkers to detect kidney injury at an earlier stage to avoid drug complications and treat patients sooner;

- **Optimizing Dialysis to Reduce Complications** – Steven M. Brunelli, MD, MSCE, leads efforts to better understand the effects of various aspects of the dialytic prescription on intra- and peri-dialytic blood pressure, and how this interplay impacts cardiovascular health and survival. He has found that longer dialysis treatments are associated with greater survival (Kidney Int 2010; 77:630-6) and that higher rates of fluid removal are associated with increased cardiovascular complications and death (Kidney Int 2011; 79:250-7). These findings have influenced a national trend towards longer dialysis treatments;

- **TREAT study results** – Ajay K. Singh, MD, represented the BWH Division of Renal Medicine in the TREAT (The Trial to Reduce Cardiovascular Events with Aranesp Therapy) study (N Engl J Med. 2009; 361:2019-2032 and N Engl J Med. 2010 Sep 16;363(12):1146-55). This study, designed to determine the impact of anemia therapy in patients with chronic kidney disease and Type 2 diabetes, has greatly influenced the FDA to recommend major reductions in the use of erythropoiesis stimulating agents (ESAs) in patients with kidney disease;

- **Vitamin D and Omega-3 Fatty Acids in Hypertension and Kidney Disease Progression** – John P. Forman, MD, and Julie Lin, MD, MPH, are investigators in the NIH-funded VITamin D and OmegA-3 Trial (VITAL) study, which includes 20,000 older adults randomized to vitamin D and omega fatty acids in hopes of lowering cardiovascular and cancer risks. Dr. Forman is evaluating effects on blood pressure and Dr. Lin is examining progression of kidney function decline in diabetes;

- **Kidney Disease Progression and Regenerative Medicine** – Benjamin D. Humphreys, MD, PhD, Albert Q. Lam, MD, and Dr. Bonventre are conducting studies to develop technologies designed to limit the progression of kidney disease in patients. They also are evaluating the potential for use of stem cell therapies in patients with renal disease;

- **Kidney Stone Disease** – Gary C. Curhan, MD, SCD, studies factors involved in the formation of kidney stones. His studies have led to key changes in clinical practice for the prevention of kidney stone formation. Dr. Curhan is examining the role of individual nutrients, supplements, dietary patterns, lifestyle and genetics in the prevention of kidney stones.

**Kidney Transplantation**

Transplant surgeons in the Renal Transplantation Program perform an average of 80 kidney transplants each year –

**Hand-assisted Retroperitoneoscopic Live Donor Nephrectomy**

Transplant surgeons at BWH are among few in the nation to offer a laparoscopic retroperitoneal approach for living donor nephrectomies, including right side retroperitoneoscopic nephrectomy. Considered safer than traditional techniques, this approach to organ removal offers:

- Avoidance of the peritoneal cavity during kidney removal;
- Decreased blood loss and faster recovery;
- Shorter hospital stay.

**Incision and port placement for left-sided laparoscopic donor nephrectomy**

**Left-sided laparoscopic donor nephrectomy with hand port in place**

**Renal hilum has been dissected, this patient had two renal arteries**
BK infection rates from 28 percent to four percent and build on the group’s previously published data showing that quinolone antibiotics can target polyoma virus (akin to BK virus) by inhibiting the key helicase enzyme of the virus.

Dr. Chandraker is currently leading the BK Treatment Study – a multicenter controlled study to confirm the effects of levofloxacin, a new generation of quinolone antibiotic, against new onset BK infection in kidney transplant recipients.

New Trials in Kidney Transplantation
The Transplantation Research Center (TRC) has a rich tradition of not only conducting research but also training many of the leading transplantation researchers within the field. Currently, there are a number of transplantation clinical trials being conducted through the TRC. Many of these trials are large multicenter studies that are funded by the National Institutes of Allergy and Infectious Diseases through the Clinical Trials in Organ Transplantation. Trials include:

- **Rituximab in Kidney Transplantation (CTOT02)**, a study conducted in 22 transplant centers that has enrolled 740 kidney transplant patients to examine the effects and development of de novo anti HLA antibodies directed against the transplanted kidney;

- **An Observational Study to Assess the Prevalence of a Tolerance Signature in Renal Transplant Recipients (CTOT12)**, a collaborative study with the Immune Tolerance Network examining the prevalence of a profile of gene expression associated with tolerant kidney transplant recipients (off all immunosuppression medications).

For further information regarding clinical trials in kidney transplant recipients, please contact Christine Dyer at (617) 732-5883.

Managing Rejection and Complications from Immunosuppression
Specialists at BWH are evaluating new ways to address the increased risk of susceptibility to infections and cancer caused by immunosuppressive medications, including BK virus infection – the most common infection following kidney transplantation. There is no established treatment for BK virus, and the virus results in the loss of approximately 50 percent of transplanted kidneys among recipients who develop the infection.

Anil Chandraker, MD, Medical Director of Kidney Transplantation and Assistant Director of the Transplantation Research Center, and his colleagues have published data indicating that quinolone antibiotics appear to dramatically decrease the rate of infection of this virus (Clinical Journal of the American Society of Nephrology (2010 Jul;5(7):1298-304). This study showed that quinolone antibiotics reduced among the highest in New England. Recent findings in kidney transplantation have uncovered ways to improve outcomes in kidney transplantation among older patients. Stefan G. Tullius, MD, PhD, Chief of the Division of Transplant Surgery and Director of the Transplant Surgery Research Laboratory, is the lead author of a published study based on United Network of Organ Sharing (UNOS) data from more than 108,000 recipients of deceased donor kidneys transplanted between 1995 and 2008 (Ann Surg. 2010 Oct;252(4):662-74.). The study determined that older recipients have less acute rejections when they receive organs from older donors.

Information and Referrals
For more information, or to refer a patient, please contact our Referral Coordinators at (617) 732-9894 or email bwhreferrals@partners.org.
Injectable Gel Demonstrates Promise for Drug Delivery

Brigham and Women’s Hospital (BWH) researchers Praveen Kumar Vemula, PhD, and Jeffrey Karp, PhD, co-director of the BWH Biomedical Research Institute (BRI) Regenerative Therapeutics Center, have developed a potentially new way to treat diseases using a hydrogel that encapsulates and releases agents in response to specific enzymes that are significantly expressed in a diseased state. Their findings were recently published in the *Journal of Biomedical Materials Research (J Biomed Mater Res A.; 2011 May;97 (2):103-10).*

“Systemic drug delivery often has significant side effects,” said Dr. Karp. “Our research has found a new way to locally treat diseases while minimizing the potential for systemic toxicity.”

**Arthritis Discovery**

The team’s injectable, self-assembled nanofibrous hydrogel is made from a generally recognized as safe (GRAS) material that encapsulates and releases agents in response to specific enzymes, including matrix metalloproteinases (MMP-2 and MMP-9) and esterases, that are significantly upregulated in a diseased state, such as inflammatory arthritis. They also found that these self-assembled nanofibrous gels can withstand shear forces that may be experienced in dynamic environments (such as joints), can remain stable following injection into healthy joints of mice, and can disassemble in vitro to release encapsulated agents in response to synovial fluid from arthritic patients. (Additional information can be found at www.brighamandwomens.org.)

“This novel approach represents a next-generation therapeutic strategy for localized treatment of many diseases,” says Dr. Vemula, who was first author of the published study.

**Brain Tumor Research**

Through a grant from the Brain Science Foundation, Dr. Karp also is working with colleagues in the BWH Department of Neurosurgery, Harvard Medical School, and Massachusetts Institute of Technology on a basic science research study to evaluate the benefits of this approach in treating glioblastomas. With a median survival of nine to 15 months from the time of diagnosis, a major limitation to effective treatment for these patients is the inability of treatments to cross the blood-brain/blood-tumor barrier, and the presence of drug efflux pumps, which prevent adequate concentrations of drugs to be achieved at the tumor.

Many potential treatments fail due to their inability to target cancer cells that have invaded deep into normal brain tissue and inability to achieve drug concentrations required to kill cancer cells in the brain, as well as limited toxicity of existing chemotherapy drugs against resistant glioma cells.

To overcome these major limitations, Dr. Karp and researcher Lata Menon, PhD, are collaborating to use a new treatment approach that simultaneously delivers tumor cell sensitizers and chemotherapy drugs. They aim to develop a new approach that will serve as a paradigm shift in the treatment of glioblastomas using drug-based gels that can accommodate multiple drugs for combination therapy, can be designed to remain stable for months in healthy brain tissue, and can release drugs selectively in response to tumor growth or recurrence.

Dr. Karp and Dr. Vemula have applied for a patent on their work, which was sponsored by the Center for Integration of Medicine and Innovative Technology (CIMIT) through the U.S. Army and by the Harvard Catalyst Program. Dr. Karp was recognized for this work with the coveted 2011 Society for Biomaterials Young Investigator Award.
Novel Multicultural Dermatology Program Offers Specialized Treatment

Co-directed by Deborah Scott, MD, Vaneeta Sheth, MD, and Jennifer Lin, MD, the new Multicultural Dermatology Program at Brigham and Women’s Hospital (BWH) is one of the first of its kind in New England.

The Program offers specialized treatment of skin and hair conditions more commonly found in women and men of non-European ethnic heritages, including African, African-American, Asian, South Asian, Hispanic, and Middle Eastern descent, and provides specialized dermatologic care to individuals according to the natural color of their skin.

“The manifestations of common dermatologic conditions may be altered in these patients, and medical and cosmetic treatments may affect them differently,” said Dr. Scott.

State-of-the-art cosmetic treatments for persons with darker and other skin types include laser hair removal and other laser treatments, chemical peels, fillers, and Botox® injections. The Program provides an additional resource for patients with darker phenotypes to be evaluated and obtain treatment recommendations from physicians with extensive experience and interest in treating this population.

Referrals and Information

The Multicultural Dermatology Program offers individualized and expert care for:

- Melasma and other forms of hyperpigmentation;
- Vitiligo;
- Keloids;
- Acne keloidalis nuchae;
- Pseudofolliculitis barbae;
- Central centrifugal cicatrical alopecia.

To refer a patient, or for more information, please contact our Referral Coordinator at (617) 732-9894 or bwhreferrals@partners.org.

Pioneering Novel Approaches to the Prevention, Diagnosis, Treatment, and Research of Venous Thromboembolism... continued from page 3

Genetics and Epidemiology in VTE

BWH researchers also have made significant genetic and epidemiologic discoveries in PE. Paul Ridker, MD, MPH, Director, Center for Cardiovascular Disease Prevention, led a large randomized trial demonstrating the effectiveness of statin therapy in preventing venous thromboembolism in apparently healthy adults with elevated CRP levels. (N Engl J Med 2009; 360:1851-1861). The trial, called JUPITER (Justification for the Use of statins in Primary prevention: an Intervention Trial Evaluating Rosuvastatin), randomly assigned 17,802 apparently healthy men and women with both low-density lipoprotein (LDL) cholesterol levels of less than 130 mg per deciliter and high-sensitivity C-reactive protein levels of 2.0 mg per liter or higher to receive rosuvastatin, 20 mg per day, or placebo. Rosuvastatin reduced the occurrence of symptomatic venous thromboembolism by more than 40 percent.

Advancing Education

Specialists in the VTE Research Group established the North American Thrombosis Forum (NATF) – a non-profit organization dedicated to saving lives through thrombosis prevention and education. NATF’s annual Thrombosis Summit will take place on September 24, 2011 (www.NATFonline.org). Members of both BWH and the NATF have worked closely with the Office of the Surgeon General to communicate the importance of prevention of PE and DVT and to promote patient advocacy. A long-standing monthly pulmonary embolism support group led by Dr. Goldhaber and Ruth Morrison, RN, BSN, addresses the emotional and psychological ramifications of PE. Patients wishing to join this support group should contact Kathryn Mikkelsen at (857) 307-1932 or at kmikkelsen@partners.org.

Referrals and Information

BWH is a major regional referral center for patients with complicated PE and DVT. For more information, or to refer a patient, please contact our Referral Coordinator at (617) 732-9894 or email bwhreferrals@partners.org. In addition, Dr. Goldhaber can be reached directly at (857) 307-1932 or sgoldhaber@partners.org.
Continuing Medical Education

Brigham and Women’s Hospital is pleased to offer the following courses, occurring in late September and October 2011 through the Harvard Medical School Department of Continuing Education. Please call (617) 384-8600 or visit cme.hms.harvard.edu/ for more information regarding these and other CME courses.

September 21 – 23
Update in Hospital Medicine
Location: The Fairmont Copley Plaza Hotel, 138 St. James Avenue, Boston, MA
Directors: Glen M. Kim, MD, MPH; Christopher L. Roy, MD, SFHM
Offered by: Brigham and Women’s Hospital, Department of Medicine; Brigham and Women’s Hospital, Hospitalist Service

October 1 – 2
33 Challenges in Gynecologic and Obstetric Pathology: The 18th Annual Tutorial in Gynecologic and Obstetric Pathology
Location: Brigham and Women’s Hospital, Shapiro Conference Center, 70 Francis Street, Level 1, Boston, MA
Directors: Christopher P. Crum, MD; George L. Mutter, MD; Marisa R. Nucci, MD
Offered by: Brigham and Women’s Hospital, Department of Pathology

October 20 – 21
7th Triennial Brigham Cardiac Valve Symposium
Location: The Fairmont Copley Plaza Hotel, 138 St. James Avenue, Boston, MA
Directors: R. Morton Bolman, III, MD; Patrick T. O’Gara, MD; Stanton K. Shernan, MD
Offered by: Brigham and Women’s Hospital, Division of Cardiac Surgery; Brigham and Women’s Hospital, Division of Cardiovascular Medicine; American Association for Thoracic Surgery

Access to Brigham and Women’s Hospital

Physician Referral Service
(617) 732-9894 or 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

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.