



Urology **ADVANCES**

Multidisciplinary Team Delivers Comprehensive Options and Evaluates New Treatments for Patients with Low-risk Prostate Cancer

Clare M.C. Tempany, MD,
and Adam S. Kibel, MD

An expert team of urologists, radiologists, radiation oncologists, and medical oncologists at Brigham and Women's Hospital (BWH) and Dana-Farber/Brigham and Women's Cancer Center (DF/BWCC) are providing comprehensive care and studying innovative approaches to evaluate and manage low-risk prostate cancer.

"Unlike patients with advanced and aggressive cancers, low-risk prostate cancer may not need to be actively treated. The challenge is determining which patients with low-risk prostate cancer should be treated and what types of treatment are preferable in these cases," said Adam S. Kibel, MD, Chief of the Division of Urology at BWH and Surgical Director of the Lank Center for Genitourinary Oncology at DF/BWCC. "This has shifted our focus to both enhancing our diagnostic techniques and investigating less invasive treatment options. Our goal is to cure only those who need to be cured with reduced morbidity."

Extensive Prostate Biopsy Program Offers Customized Diagnostic Approach

The prostate biopsy program at BWH has been at the forefront of worldwide changes in prostate cancer diagnosis. The program's unique partnership between urologists and subspecialized genitourinary radiologists has led to pioneering work in performing biopsies using a transperineal approach with in-bore MR image guidance. Targeted biopsies using MRI to detect the targets have demonstrated a high yield of more significant cancer than non-targeted biopsies. With the advent of MR + ultrasound fusion, the in-bore MR guided biopsies are generally used for tumors in difficult locations.

The prostate biopsy program is one of few in the country that is experienced in the dual approaches of in-bore MR guided biopsy and MR + ultrasound fusion. These two approaches complement each other, enabling specialists to access lesions located in many areas of the prostate. Regular multidisciplinary

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**HARVARD MEDICAL SCHOOL
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Surgery Provides Overall Survival Benefit in Patients with Advanced Genitourinary Cancers



Quoc-Dien Trinh, MD, and Toni K. Choueiri, MD, and colleagues have led studies demonstrating overall survival benefit in patients with advanced genitourinary cancers.

Urologists and medical oncologists at Brigham and Women's Hospital (BWH) and Dana-Farber/Brigham and Women's Cancer Center (DF/BWCC) have led several registry studies demonstrating overall survival benefit in patients with advanced genitourinary cancers, including metastatic urothelial cancer of the bladder and metastatic renal cell carcinoma. Quoc-Dien Trinh, MD, a urologic surgeon in the Division of Urology at BWH and Lank Center for Genitourinary Oncology at DF/BWCC, and Toni K. Choueiri, MD, Director of the Lank Center for Genitourinary Oncology at DF/BWCC, were senior authors of the studies, which were published in the *Journal of Clinical Oncology*.

"These studies show that removing the primary tumor in the setting of metastatic disease, even with the availability of appropriate targeted and other systemic therapies, can be beneficial in two genitourinary cancers that carry a poor prognosis in advanced stages," said Dr. Trinh.

Surgery in Metastatic Urothelial Cancer of the Bladder

This study of 3,753 patients with primary metastatic urothelial carcinoma of the bladder within the National Cancer Data Base evaluated outcomes among those who received multi-agent systemic chemotherapy combined with high-intensity versus conservative local treatment (*J Clin Oncol*. 2016 Jun 6.). High-intensity treatment included patients who received radical cystectomy or ≥ 50 Gy of radiation therapy delivered to the bladder. The conservative local treatment group (92 percent of patients) included those who received no local treatment, transurethral resection of the bladder tumor alone, or < 50 Gy of radiation therapy. The researchers found that the median overall survival was significantly longer in the high-intensity group (14.92 months) compared with the conservative group (9.95 months).

"We have seen virtually no change in mortality rates among patients with metastatic bladder cancer over the past two decades," said Dr. Trinh, corresponding author of the study. "We hope that our study may open the door to large-scale randomized clinical trials to assess the benefit of this strategy in patients with advanced bladder cancer."

Cytoreductive Nephrectomy in Advanced Renal Cell Carcinoma

This study used the National Cancer Data Base to identify 15,390 patients with metastatic renal cell carcinoma who underwent targeted therapies between 2006 and 2013 (*J Clin Oncol*. 2016 Sep 20;34(27):3267-75.). Of these patients, 5,374 (35 percent) underwent cytoreductive nephrectomy. The median overall survival of patients who underwent cytoreductive nephrectomy was 17.1 months compared with 7.7 months among patients who did not receive cytoreductive nephrectomy. Cytoreductive nephrectomy was only performed in three of 10 patients with metastatic renal cell carcinoma who were receiving targeted therapy. Researchers found that patients who were younger, privately insured, treated at an academic center, and had lower tumor stage were more likely to undergo cytoreductive nephrectomy.

"This study may help to answer previously unanswered questions about whether there has been a decrease in cytoreductive nephrectomy since the introduction of targeted therapies, whether the procedure improves survival in patients being treated with targeted therapy, and whether some subsets of patients are more likely than others to receive the surgery," said corresponding author Dr. Choueiri.



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UROLOGY RESEARCH UPDATE

Screening Strategy May Predict Lethal Prostate Cancer Later in Life

Prostate cancer screening with prostate-specific antigen (PSA) has been shown to reduce death and the spread of prostate cancer to other parts of the body, but the PSA test remains highly controversial as it frequently leads to over diagnosis and over treatment of men who may not be at risk. Smarter screening strategies that can improve the accuracy of diagnosing lethal prostate cancer are urgently needed. Through a prospective study of US men, investigators from Brigham and Women's Hospital and the Harvard T.H. Chan School of Public Health have found that measuring PSA levels in younger men (between the ages of 40 and 59) could accurately predict future risk of lethal prostate cancer later in life. Their findings suggest that screening PSA levels in men at mid-life may help identify those who are at greater risk and should be monitored more closely.

"We found a single baseline PSA-level measurement during midlife could accurately predict future risk of lethal prostate cancer," said BWH urologist and co-lead author Mark Preston, MD, MPH. "These data identify subgroups of men, based on their PSA levels at a given age, who could benefit from screening intervals tailored to their actual magnitude of risk."

The current study leverages data from the Physicians' Health Study (PHS), a randomized, placebo-controlled trial that had its origin in testing aspirin and risk of cardiovascular outcomes. The PHS began in 1982 and US male physicians who took part in it provided blood specimens before the trial began. Those blood samples, and the detailed questionnaires filled out by the study participants over the next 30 years, gave researchers the information they needed to conduct the current research project. Using information from 234 men who were diagnosed with prostate cancer, including 60 who developed lethal prostate cancer, and 711 controls, all between 40 and 59 years of age at the start of the trial, the research team measured PSA levels from stored plasma samples and followed the men's outcomes over time.

The researchers found that this single, baseline PSA level measured at midlife could accurately predict future risk of prostate cancer: Of the lethal prostate cancer events, 82 percent, 71 percent and 86 percent occurred in men with a baseline PSA above the median at ages 40-49, 50-54 and 55-59, respectively.

The study also found that men who had a PSA below median (<1.0 ng/ml) at age 60 were unlikely to develop lethal prostate cancer in the future.

"These data support the recommendation that risk-stratified screening for prostate cancer based on mid-life PSA should be considered in men aged 45 to 59," said senior author Lorelei Mucci, ScD, associate professor of Epidemiology in the Department of Epidemiology at Harvard T.H. Chan School of Public Health. "Our study does not imply prostate biopsy or definitive treatment is immediately required in younger men with higher PSA levels at baseline, as this could lead to over diagnosis. Rather, these men should undergo more intensive PSA screening to enable earlier identification of cancer and potential cure while still possible."

The authors note that study limitations include that the study population consists primarily of Caucasian men, includes limited lethal events and that an unknown proportion of participants may have undergone opportunistic screening prior to the study.



Mark A. Preston, MD, MPH

Access to our Urology Services

At Brigham and Women's Hospital and Dana-Farber/Brigham and Women's Cancer Center, our specialists are available for timely consultations and will work with you to develop treatment plans for complex cases. Our Physician Liaison Tom Anderson can provide direct assistance with patient referrals and consultations. Tom can be reached at (617) 582-4760 or tanderson@partners.org.

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biopsy conferences are held with urologists, radiologists, and pathologists, to discuss cases and biopsy planning.

“With the availability of these advanced technologies, we can tailor the biopsy approach for each case and deliver individualized evaluation for each patient,” said Quoc-Dien Trinh, MD, urologic surgeon in the Division of Urology at BWH and Co-Director of the Prostate Cancer Program at DF/BWCC.

Managing Men with Low-risk Prostate Cancer

BWH urologists use a multi-pronged approach in developing a treatment plan for patients with low-risk prostate cancer:

- Conventional surgical treatments (including robotic, laparoscopic and open prostatectomy) and radiation therapy (brachytherapy and external beam radiation) are considered for low risk patients who have a family history of aggressive prostate cancer, especially those who have lost a family member to the disease;
- Based on the team’s published research on biomarkers that indicate a more aggressive tumor (*Cancer Epidemiol Biomarkers Prev.* 2016 Nov;25(11):1456-1463), they are investigating the role of biomarkers in predicting who needs active treatment;
- For patients with small volume, low-risk cancer, active surveillance is offered as an optimal option, especially for younger patients relative to quality of life.

“We provide a very specialized program for patients with low-risk prostate cancer,” said Dr. Kibel. “After expert evaluation, we carefully weigh the benefits and risks of treatments with the likelihood of disease progression within the patient’s expected lifespan. Our team collaborates to determine the best approach for each patient.”



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Focal MR-guided Focused Ultrasound

Urologists and interventional radiologists at BWH are among few in the nation and the only specialists in New England to participate in a new early-phase device study of MR-guided focused ultrasound surgery in patients with small volume, low-to-moderate risk localized prostate cancer. This prospective, single arm study (Focal MR-Guided Focused Ultrasound Treatment of Localized Low and Intermediate Risk Prostate Cancer: Feasibility Study) is enrolling up to 100 patients in 10 centers across the United States. Participants will be followed up for 24 months. The primary endpoints of the study include evaluation of overall safety and tumor control, as well as the incidence and severity of adverse events.

“This trial builds on a long history of pioneering research and clinical translation in MR-guided focused ultrasound surgery at BWH over the past 20 years,” said Clare M.C. Tempany, MD, Site Principal Investigator of the trial, Director of the National Institutes of Health (NIH) National Center for Image Guided Therapy (NCIGT) at BWH, and Co-Director of the BWH Advanced Multimodality Image Guided Operating (AMIGO) Suite. “We are optimistic that the concept of treating the tumor, not the prostate, will allow us to cure patients who need to be cured, while maintaining quality of life. We expect that this will be the first of many trials that will redefine management of small volume prostate cancer.”

(For more information regarding this trial, please contact Jason Lee at (617) 726-5866.)



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