

PROSTATE HEALTH: A SURVIVAL GUIDE

- High-tech prevention, screening, and detection
- Feedback from the front lines
- Duke's best defensemen



FIGHTING THE MAN'S CANCER

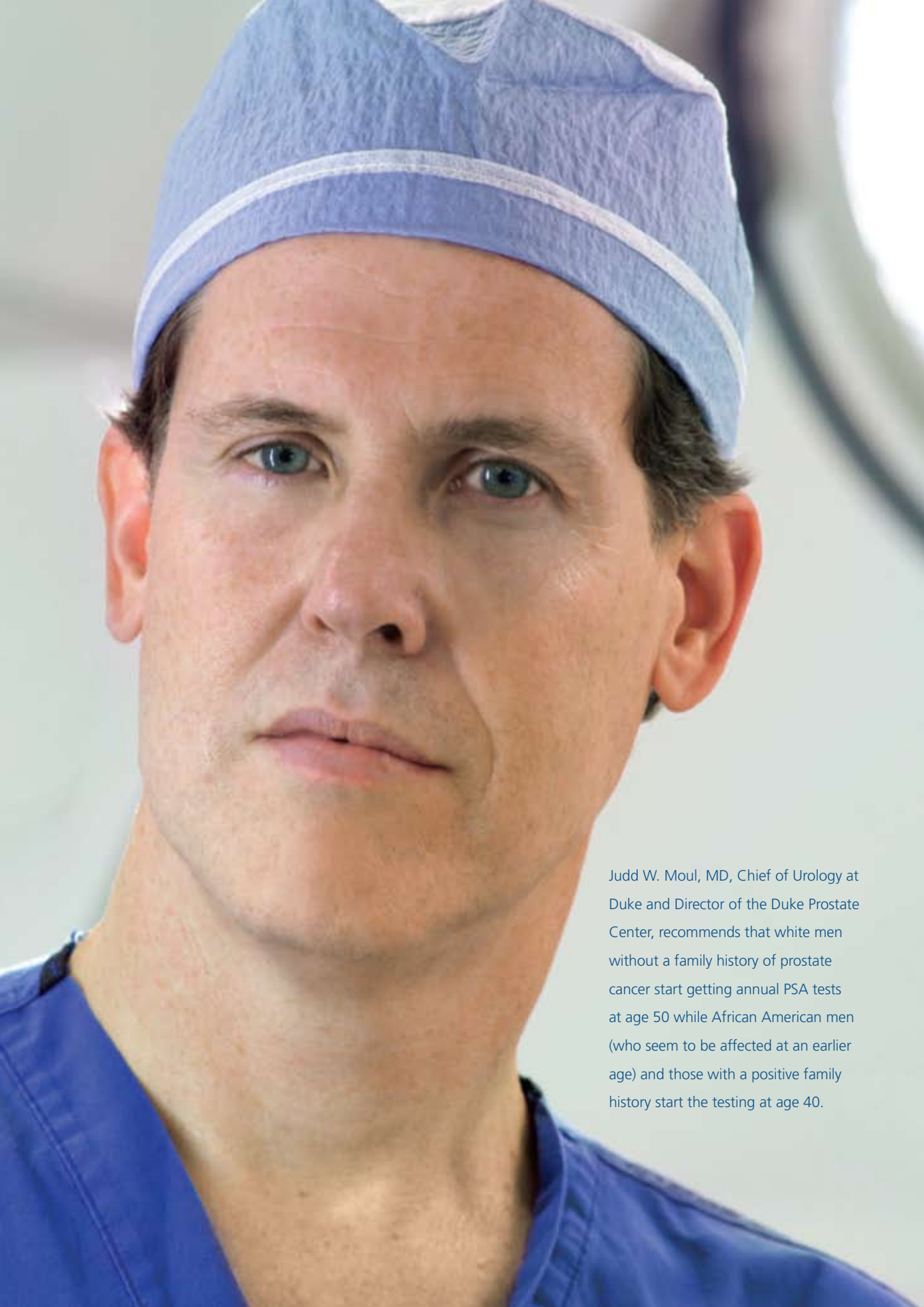
Offering an array of treatments and an integrated approach to care, Duke physicians are powerful allies in men's battles against prostate cancer.

BY DENNIS MEREDITH

"A MAJOR CHANGE IN THE DIRECTION OF MY LIFE" read the curious subject line of the e-mail message from my close friend of many decades. In our earlier years, I had certainly witnessed other major changes in his life. I had watched him receive much-deserved awards for his talents as a writer. I had watched him proudly walk his daughter down the aisle. But now, with both of us in our settled "middle" years—with grown offspring, happy marriages, and magically gorgeous grandchildren—I wondered what possible change could be "major."

He had prostate cancer, he announced. The fact shook me, though certainly not as much as it must have shaken him. The message and those that followed over the next few months introduced unfamiliar terms—Gleason score, brachytherapy, laparoscopic prostatectomy—that only dimly reflected the unfamiliar territory my friend's disease had brought him into.

For many men of my generation, prostate cancer has become an unexpected and unwelcome rite of passage, turning an innocuous gland somewhere in our nether regions into a malignant agent of unsettling life changes. Some 230,000 American men, many of them younger than 65, are diagnosed with prostate cancer each year—and as baby-boomers reach their middle years, the number of new cases is expected to rise to 300,000 a year by 2010, according to the National Prostate Cancer Coalition.



Judd W. Moul, MD, Chief of Urology at Duke and Director of the Duke Prostate Center, recommends that white men without a family history of prostate cancer start getting annual PSA tests at age 50 while African American men (who seem to be affected at an earlier age) and those with a positive family history start the testing at age 40.

“Duke takes the team approach to prostate cancer therapy, giving men state-of-the-art options in prevention, early diagnosis, and treatment.”

—Andrew J. Armstrong, MD ScM

The good news, for my friend and the other one in six men who will be diagnosed with prostate cancer in their lifetime, is that 85 percent will survive the disease. And there is enormous optimism among clinicians and researchers at Duke and other leading medical centers that this percentage will improve further in the decade ahead, thanks to promising advances across the spectrum of treatment modalities—from surgery, radiation therapy, and chemotherapy to vaccines and even nutritional therapies.

EARLY DETECTION DILEMMA

Yet there are challenges ahead as well. Ironically, one of the greatest has resulted from a major clinical advance—the advent of widespread testing for blood levels of the telltale marker prostate specific antigen (PSA).

“Better screening is catching these cancers earlier, which means that the population of men we’re seeing is getting younger and the cancers tend to be smaller,” says Judd W. Moul, MD, who was appointed chief of urology at Duke in 2004. “But it’s a double-edged sword, in that sometimes we’re diagnosing prostate cancer that may never need to have been diagnosed. It may grow so slowly it will never affect the health of the man—particularly if he is older.”

The fact that PSA tests flag some men who may not need treatment—while missing up to 15 percent of men who may in fact have prostate cancer—has caused some physicians to question the wisdom of wide-

spread screening. But Moul and other Duke specialists emphasize that PSA remains the best clinically available biomarker for detecting and tracking prostate cancer. “It’s a valuable test that has saved thousands of lives,” says Moul. He recommends that white men without a family history of the disease start getting annual PSA tests at age 50 while African American men (who seem to be affected at an earlier age) and those with a positive family history start the testing at age 40.

But because of fear of the “C word,” he says, “When we say prostate cancer—no matter how good or bad, small or big it is—we’ve trained the public very well to respond to that and say ‘Doc, get rid of it.’ The key challenge for the new millennium is to figure out how to aggressively treat cancers that are going to kill people, while not over-treating what we call ‘incidental’ cancers.”

Over-treatment is a concern even for men with more significant cancers, Moul adds. “If the man is younger, he may live with the effects of treatment for 30 years. So we need to consider how we can preserve his quality of life,” including potency and urinary function.

BRINGING CARE FULL CIRCLE

When treatment is warranted, says Moul, Duke’s goal is to offer patients expertise in the full range of treatment possibilities. And there are lots of options—among them nerve-sparing radical prostatectomy, robotic prostatectomy, external beam radiation,

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Andrew Armstrong, MD

brachytherapy, castration with surgery or medications in the form of periodic injections, oral hormonal therapy medications, cryotherapy, chemotherapy, nutritional therapy, and even “watchful waiting”—carefully monitoring a slow-growing cancer’s course with surveillance PSA levels, digital rectal exams, and biopsies to determine whether and when treatment is needed.

“All of these treatments have their advantages and disadvantages, and we try not to emphasize one over another,” says Moul. “They all fit into the armamentarium. Our goal is to bring urologists, radiation oncologists, and medical oncologists together to educate patients about their options and help men and their families make informed decisions.”

Such an approach is surprisingly uncommon. According to a major Prostate Cancer Foundation report released in September 2004, too many men are unaware of all the options available to them until they have late-stage disease, since multidisciplinary care is still not the norm in prostate cancer treatment.

To counter that problem, physicians at Duke established a multidisciplinary genitourinary oncology screening clinic, where patients can receive opinions from two or three specialists in a single setting. Says medical oncologist Andrew Armstrong, MD, “Duke takes the team approach to prostate cancer therapy, giving men state-of-the-art options in prevention, early diagnosis, and treatment.”

“Right now there are not enough men with prostate cancer going into clinical trials or otherwise participating in research,” says Moul, who has created a clinical trials unit and a prostate research database. “We invite patients to become part of the research team by contributing to banks of serum and tissue samples and participating in a comprehensive prostate cancer disease research registry. We’ll track their cancers and use the resulting data to better understand prostate cancer biomarkers and the effectiveness of various treatments.”

Prostate cancer patients at the Durham VA Medical Center also are offered the opportunity to participate in these research efforts, working with Duke urologic oncologist and Durham VA chief of urology Philip Walther, MD, Moul adds.

SURGICAL STRIKES

Since men with prostate cancer typically have multiple (and likely biologically distinct) tumors scattered throughout the prostate, most therapies today aim at eliminating the entire gland. The most widely used technique is nerve-sparing radical prostatectomy, in which surgeons carefully remove the diseased prostate while preserving the surrounding nerves that control urinary and erectile function.

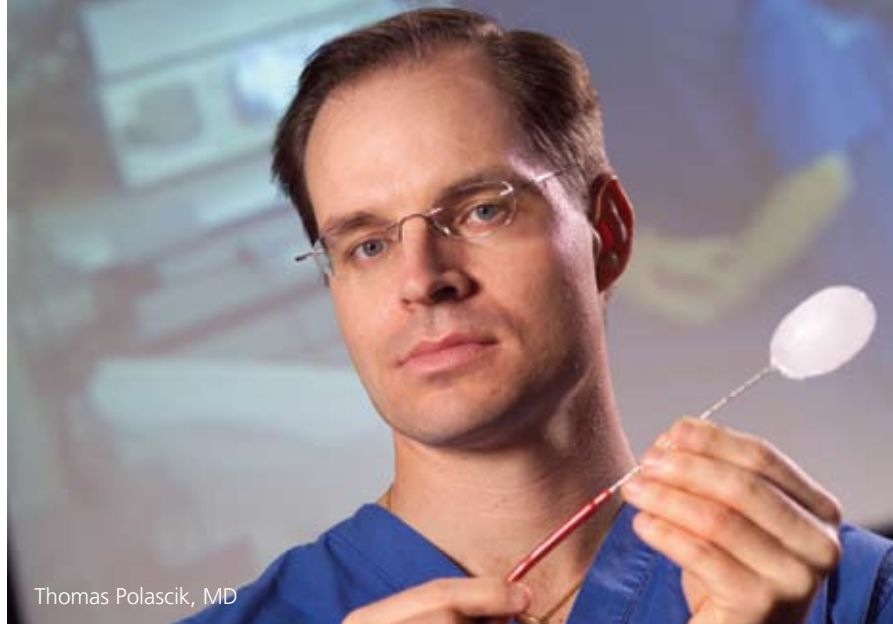
"This operation remains the gold standard for prostatectomies," says Moul. "We can now perform it in approximately two hours, through quite a small incision, with no need for a transfusion."

Men who undergo the procedure have a good chance of keeping their sexual function, he adds. "Up to 90 percent of men who are fully potent prior to the operation can regain erections sufficient for sexual intercourse," Moul says. "And by using some of the new erectile dysfunction drugs to aid men's sexual recovery earlier in the post-operative course, we are improving our results." In addition, many other treatments are available for sexual recovery, according to Craig Donatucci, MD, Duke Urology's nationally recognized expert in male sexual function.

Urologic surgeons are also using



David Albala, MD



Thomas Polascik, MD

Duke offers a wide range of treatments for prostate cancer, including cryotherapy, in which fine needles are inserted into the prostate and frozen, forming ice bulbs that kill the surrounding tissue (above), and brachytherapy, in which radioactive pellets are strategically delivered into the prostate via thin catheters.

technologies—such as robotic prostatectomy, offered at Duke since 2003. In this technique, surgeons perform the operation via a multi-arm robotic system that enables fine manipulation through very small incisions. Robotic surgeon David Albala, MD, says experience with over 300 robotic surgeries so far has been promising, with operating time currently averaging three to four hours and most patients well-satisfied with the results.

"The best candidate for this surgery is a patient who has been detected early with a small amount of cancer," says Albala. Certain physical attributes, including obesity, may eliminate a patient from consideration, he adds.

Despite these encouraging results, robotic prostatectomy is currently more expensive to perform than standard surgery, and most insurance companies do not recognize the added expense, Moul points out. "Duke clearly wants to be on the cutting edge of new technology, but we have to balance patient desires for the latest approaches with the realities of the added costs," he says. "Such are the challenges of modern medicine."

FREEZING IT OUT

Cryotherapy to ablate the prostate is an option for older men who do not want radical surgery or radiation therapy, or for those who have failed radiation therapy. In this technique, fine needles are inserted into the prostate and frozen with a mixture of cooled helium and argon. The cooling forms an ice bulb around

TREATMENT



Daniel George, MD

the needle that kills prostate tissue. Guided by ultrasound imaging, the surgeons can manipulate the needles to ablate the entire prostate without need for surgery.

Says DPC urologist Thomas Polascik, MD, a leading authority on the procedure, "About 80 percent of patients experience impotence, so we counsel patients to consider this option very carefully. If they are younger and have erectile function,

it may not be for them. But if they lack erectile function and want a less invasive method, cryotherapy is truly minimally invasive."

Brachytherapy is another minimally invasive alternative to surgery for certain patients with early-stage disease. Unlike external beam radiation—another form of radiation therapy—brachytherapy involves inserting radioactive seeds or pellets directly into the prostate, where they kill the tissue, ablating the prostate.

According to Duke radiation oncologist Robert Lee, MD, a national authority in this technique, brachytherapy minimizes damage to surrounding tissues, and new drug therapies to increase tissue protection will make the procedure more widely applicable in the future.

TARGETED TREATMENTS AHEAD

Duke oncologists are also making progress in treating patients whose cancers have progressed beyond the stage where surgery or radiation therapy alone can help. For example, DPC's Dan George, MD, and colleagues are currently testing a drug that inhibits the protein mTOR (mammalian target of rapamycin), which triggers the aberrant cells of prostate cancers to grow. And in a one-two punch, they are clinically testing a novel combination of drugs,

Docetaxel and a variety of other agents, to inhibit cancer cell growth.

Meanwhile, says George, scientists are also developing promising new technologies to characterize cancer cells on the genetic and molecular levels. "With better tools for investigating the disease and our rapidly growing knowledge of the genetics of prostate cancer," he says, "I think over the next decade we'll gain a far better understanding of the subtypes of cancer and how to treat them."

Phillip Febbo, MD, a physician-scientist with Duke's Institute for Genome Sciences and Policy, is launching a broad research program to better define the molecular sub-types of prostate cancer. His research program will organize the DPC's tissue banks and allow detailed analyses of genes in both human disease and cancer models to identify genetic events critical to prostate cancer's growth.

"Our ultimate goal," says Febbo, "is to provide a comprehensive understanding of the genetics of both the patient and the tumor so that clinicians can predict whether an individual's cancer will metastasize into the bone and cause death, or whether it will remain in the prostate—perhaps causing local symptoms such as difficulty in urination, but



“Our ultimate goal is to provide a comprehensive understanding of the genetics of both the patient and the tumor so that clinicians can predict [what an individual’s cancer will do].”

—Phillip Febbo, MD

otherwise doing no harm.” Febbo is convinced that over the next decade, such genetic insight will allow physicians to match molecularly targeted therapies with biologically susceptible tumors to improve the quality and duration of life for patients diagnosed with cancer.

While some Duke researchers pursue technically sophisticated treatments, others are finding that simple lifestyle changes may help. Studies have demonstrated the value of flaxseed in retarding prostate cancer. Flaxseed is the richest

source of plant-based omega-3 fatty acids and dietary lignans, both of which disrupt cell changes that lead to cancer. A pilot project involving 25 men with prostate cancer showed that those who ate low-fat diets supplemented with three tablespoons of ground flaxseed daily had lower testosterone levels and tended to have lower prostate specific antigen levels as well as tumors with lower proliferation rates. Researchers are now conducting larger clinical trials, as well as studies of how diet and exercise can help prostate cancer

survivors. The establishment of the DPC will help researchers fill such trials more quickly so they can yield answers sooner for men and their families, Moul says.

SUPPORT SYSTEM

With so many treatment options available, patients will rely heavily on their physicians to help them decide what strategies to pursue. But, emphasizes the DPC’s Cary Robertson, diagnostic and treatment expertise must be accompanied by a fundamental understanding that the

DETECTION

Improving prostate cancer detection in African American men

ONE OF THE MOST frustrating aspects of the battle against prostate cancer has been its disproportionate impact upon African American men, says urology chief Judd W. Moul, MD. The incidence of prostate cancer is 60 percent higher in African American men than in Caucasian males, and the death rate twice as high.

“When the PSA test first came out, there was clearly an ethnic and racial disparity in screening,” says Moul. “African American men were likely not as aware of their risk. And they weren’t getting tested for a multitude of reasons—distrust of the health care system, socioeconomic factors, and lack of insurance.

“Thus, African American men are in deeper trouble when their cancers are found, because they’re more advanced.” What’s more, he says, there are hints of greater genetic vulnerability to prostate cancer among African American men. “In my experience in the military health care system, where care was equal between ethnic groups, many African American men seemed to have a more aggressive variant of prostate cancer,” says Moul.

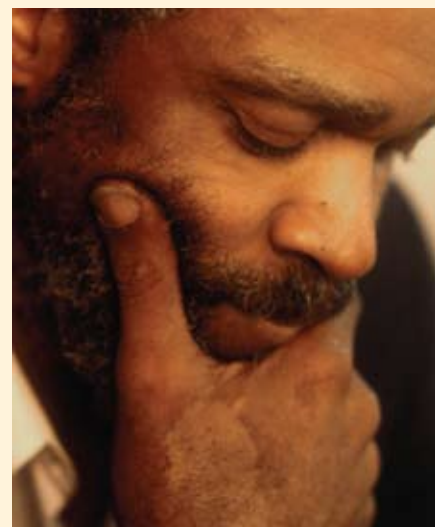
However, he adds, data from military, Veteran’s Administration, and private sector studies suggest that early diagnosis and effective treatment can help equalize outcomes between African Americans and Caucasians. For that reason, Moul encourages men in this high-risk group to begin PSA screen-

ing at age 40, using a PSA threshold of ≤ 2.0 to 2.5 ng/ml to prompt further evaluation.

By offering free annual screenings for prostate cancer, Duke researchers are exploring the reasons why some African American men may be reluctant to be tested. In a Department of Defense-funded study, School of Nursing faculty member and family nurse practitioner Marva Mizell Price, DrPH, and urologist Cary Robertson, MD, are identifying men who are likely to return each year for screenings and comparing them to men who do not return. Thus, Price and Robertson hope to uncover factors governing a man’s decision to take part in screenings, both initially and continually.

Between 1998 and 2003, the study screened 1,593 men. Early on, only about 60 percent who came in one year also came in the next, Price observed. But with community outreach and education, the return rate is improving, she says. This year’s screening was the best-attended yet—508 men were screened, about half of them African American—and return rates were also higher. “We’re getting a steady increase in both Caucasian and African American men taking advantage of the screening, and we hope to sustain that increase,” says Price.

Says Robertson, “It’s important to have a long-term, carefully designed project, because so often community screening is a one-day, feel-good event



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with no follow-through. I think our screening clinic is unique in that we track patients and offer them good information resources that encourage them to follow up individually with a physician.”



“Our major priorities are patient education and social support.”

—Cary Robertson, MD

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disease presents complex human dimensions.

“Our major priorities are patient education and social support,” says Robertson. “Once we’ve determined whether a patient needs a really aggressive form of treatment or can be treated less aggressively, we need to educate them carefully about their options.

“Most of these gentlemen will have a significant social support person—a spouse, child, or friend. And they really do need somebody to be a sounding board—to listen to the conversations and take notes and remind the patient of what was said and keep them on track in terms of self-education. Our research into

the dynamics of spousal support at Duke has helped us understand the need to tailor our comments and educate not only the patient, but his support person.”

The benefits of social support are clearly evident for my friend, who is faring well after his diagnosis with cancer, thanks to both a carefully considered course of treatment and a supportive wife. Indeed, if his experience is any indication, a bout with cancer may bring men and women even closer—sometimes in unexpected ways. When next we met in a crowded restaurant, my friend paused during the salad course and announced that he had to take a brief

moment to finish his hot flash first. The effects of the hormone therapy to shrink his prostate, he joked, had left him with a much deeper appreciation of the joys of menopause in women.

With excellent care available and even more encouraging prospects ahead, it’s reasonable to hope even more men will soon be able to go through the common experience of prostate cancer with a similarly sunny outlook. □



Patients or physicians’ offices can contact Terry Witting at 919-668-8108 to make an appointment at Duke’s multidisciplinary prostate cancer screening clinic.

For more information on prostate cancer services at Duke, physicians may call 1-800-MED-DUKE, patients 1-888-ASK-DUKE or visit dukehealth.org/prostate.

Learn about the Duke Cancer Patient Support Program by visiting cancer.duke.edu/support or contact Patrick Plumeri at 919-684-4497.

SEARCHing for answers

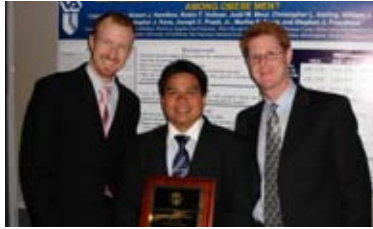
WITHIN THE DUKE PROSTATE CENTER (DPC), a movement is under way to examine which factors are related to prostate cancer recurrence after radical prostatectomy. While much of the focus has been on patients treated at Duke, there is also an effort to compare and contrast treatments at other centers.

One resource, which has been invaluable for this investigation, is the Shared Equal Access Regional Cancer Hospital (SEARCH) database. The SEARCH database, under the guidance and leadership of Duke urologist Stephen Freedland, MD, has collected information on nearly 2,000 men treated for early-stage prostate cancer with surgery at several different Veterans Affairs (VA) hospitals across the country.

What makes the SEARCH database unique is that VA centers contain a large number of African American men, a population that is hit particularly hard with prostate cancer.

According to Freedland, "Over 40 percent of the men in the SEARCH database are African American. This presents us with an incredible opportunity."

Indeed, recent studies from the SEARCH database have focused on



From left: Duke researcher's Robert Hamilton, MD, Lionel Banez, MD and Stephen Freedland, MD

the finding that African American men are at a slightly increased risk of cancer recurrence, though when they develop a recurrence, their cancers appear to be no more aggressive.

Freedland's SEARCH database research team has also led the efforts in examining the association between obesity and prostate cancer. Freedland's group was one of the first two to ever describe the increased risk of cancer recurrence after surgery among obese men. They have further gone on to show that when the cancer recurs, it tends to be more aggressive.

This in part may relate to the fact that obese men have larger prostates and lower PSA values, both of which may make finding cancer in obese men more difficult, such that when the cancers are eventually found,

they have become more aggressive.

While Freedland cautions that more research is needed, he says, "Our ongoing research clearly supports the idea that obese men fundamentally have a more aggressive form of prostate cancer. We are now trying to understand why. We hope that understanding this will lead to newer and better preventions and treatments for this disease for all men." □



RESEARCH

RESEARCH



Results by numbers

AT THE DUKE PROSTATE CENTER, our teams of urology and oncology specialists have in-depth experience and expertise in performing prostatectomies for treatment of prostate cancer—both the traditional retropublic radical prostatectomy (RRP) and the newer robot-assisted laparoscopic prostatectomy (RALP).

The high level of experience is gained through the volume of patients we care for; the expertise a direct result of our active participation in laboratory research and clinical trials.

To develop new treatment strategies on both fronts, Leon Sun, MD, PhD, Associate Research Professor for the Duke Prostate Center, has established a longitudinal research database to collect the follow-up data of men who underwent surgery and received other treatments for prostate cancer.

Says Dr. Sun, "Our research focuses on identifying patients with

a higher risk for disease progression and death, as well as outcomes after radical prostatectomy, including cancer control, urinary control, and erectile function."

Currently, we are working on comparing outcomes between patients who underwent RRP or RALP. From January 2003 through December 2006, a total of 298 patients underwent RALP and 335 patients underwent RRP at Duke.

In the age distributions of these patients, it is evident that a significant percentage of young patients under 60 years of age underwent either RALP or RRP. There are no significant differences in age when comparing RALP patients to RRP patients.

In the past, only patients with low-risk prostate cancer were given the option for the new robotic procedure, as long-term follow-up data was not available. Therefore, when comparing the risk for PSA recurrence,

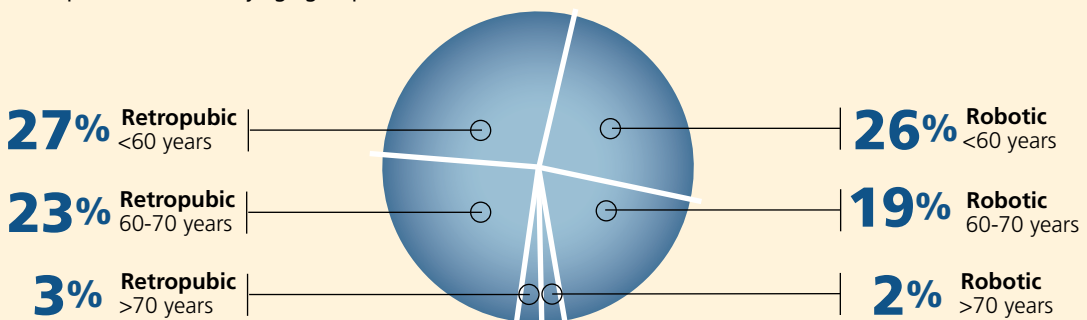
there is a trend for higher PSA recurrence-free survival in the patients who underwent RALP. However, this difference is not statistically significant, and when we adjust for prostate cancer risk factors, we achieve similar high cancer control rates with both RALP and RRP.

"The DPC Outcomes Research database and the SEARCH database together provide a powerful tool to learn more about prostate cancer in the new millennium," says Judd Moul, MD, chief of the Duke Division of Urology and director of the DPC.

Duke is also collaborating with the U.S. Department of Defense and other centers of excellence to conduct multi-center, mega-database outcomes studies. With the baby boomers entering their peak years of prostate cancer risk, these investigations over time are very important, according to Dr. Moul and Freedland. □

Radical prostatectomies at the DUKE PROSTATE CENTER

Retropublic vs. robotic by age groups



The **Duke Prostate Center** is dedicated to providing excellent care to men with prostate cancer and to discovering newer and better methods for detecting, treating, and preventing the disease.

Our multidisciplinary team is composed of nationally and internationally recognized surgeons, medical oncologists, radiation oncologists, basic scientists, and other medical professionals, all working together to deliver outstanding care and support to men and their families.

UROLOGISTS/UROLOGIC ONCOLOGISTS

Urologists specialize in the treatment of diseases of the urinary organs in women and the urinary tract and sex organs in men. Trained as surgeons, urologists are able to perform operations on these organs, including the treatment or removal of tumors. The urologists of Duke Prostate Center have also received special training in cancer treatment.

David Albala, MD
Greg Bianchi, MD
Craig Donatucci, MD
Stephen Freedland, MD
Tracey Krupski, MD, MPH
Kelly Maloney, MD
Judd Moul, MD *Chief, Division of Urology*
Thomas Polascik, MD
Cary Robertson, MD
Philip Walther, MD, PhD

MEDICAL ONCOLOGISTS

Medical oncologists are specially trained to diagnose and treat cancer with chemotherapy, hormone therapy, and other medications.

Andrew Armstrong, MD
Daniel George, MD
Philip Febbo, MD

RADIATION ONCOLOGISTS

Radiation oncologists are physicians who specialize in the delivery of radiation to target tumors.

Carol Hahn, MD
Bridget Koontz, MD
W. Robert Lee, MD
James Oleson, MD, PhD
Robert Prosnitz, MD, MPH

MEDICAL PSYCHOLOGISTS

Psychologists help patients deal with the emotional issues surrounding their diagnoses and treatment.

Christopher L. Edwards, PhD
Francis J. Keefe, PhD

PATHOLOGISTS

Pathologists diagnose abnormal changes in tissue removed during operations and can provide the oncologists with information to shape the treatment plan for each patient.

Leslie G. Dodd, MD
John Madden, MD
Robin T. Vollmer, MD

dukehealth.org/prostate

Appointments

To make an appointment at Duke's multidisciplinary prostate cancer screening clinic, please contact Terry Witting at 919-668-8108.

For other appointments or more information on prostate cancer services at Duke, call the Duke Referral Center at 1-888-ASK-DUKE (275-3853). Representatives are available to help you Monday through Friday, 7:30 a.m. to 6 p.m.

Specialty trained representatives can:

- Assist you in identifying a Duke doctor with the knowledge and expertise to care for your particular medical condition.
- Facilitate your initial appointment with a Duke physician in keeping with your insurance's guidelines for specialty visits and, whenever possible, in the location most convenient for you.
- Help you determine whether your insurance plan gives you access to Duke.
- Answer other questions you may have about care at Duke.
- Provide information and brochures about clinical services and programs at Duke.
- Access information and help register for community events sponsored by Duke, including classes, seminars, health screenings, and health fairs.





1-888-ASK-DUKE • dukehealth.org