Choosing the Right Treatment for Prostate Cancer
Much of what we take for granted in medicine today—from the rigorous training of physicians and nurses to the emphasis on research and the rapid application of that research to patient care—emerged from innovations made more than a century ago at a brand new medical center in Baltimore: Johns Hopkins.

Hopkins now uses one overarching name—Johns Hopkins Medicine—to identify its whole medical enterprise. This $5 billion virtual organization unites the physicians and scientists of The Johns Hopkins University School of Medicine with the health professionals and facilities that make up the broad Johns Hopkins Health System.

A little history: Toward the end of the 19th century, American medical education was in chaos; most medical schools were little more than trade schools. Often, it was easier to gain admission to one of these than to a liberal arts college.

With the opening of The Johns Hopkins Hospital in 1889, followed four years later by The Johns Hopkins University School of Medicine, Johns Hopkins ushered in a new era marked by rigid entrance requirements for medical students, a vastly upgraded medical school curriculum with emphasis on the scientific method, the incorporation of bedside teaching and laboratory research as part of the instruction, and integration of the School of Medicine with the Hospital through joint appointments.
Hopkins medicine counts many “firsts” among its achievements during its early years: the first major medical school in the United States to admit women; the first to use rubber gloves during surgery; the first to develop renal dialysis and CPR.

Two of the most far-reaching advances in medicine during the past 25 years were made at Hopkins. The Nobel Prize-winning discovery of restriction enzymes gave birth to the genetic engineering industry and can be compared, some say, to the first splitting of an atom.

Also, the discovery of the brain’s natural opiates has triggered an explosion of interest in neurotransmitter pathways and functions. Other accomplishments include the identification of the three types of polio virus and the first “blue baby” operation, which opened the way to modern heart surgery. Hopkins also was the birthplace of many medical specialties, including neurosurgery, urology, endocrinology and pediatrics.
Since its inception, the mission of The Brady Urological Institute has focused on finding answers, solving problems, and coming up with medical solutions that will benefit not only its patients, but humankind as a whole.

Whether it’s developing a new therapy, fine-tuning an improved surgical technique, discovering a cure for a disease, or seeking better ways to educate patients, every time Brady medical experts set out to do something—through careful observation, study, and detailed research—they are always envisioning how improvements can be made.

As the leader in urology, the Brady Urological Institute has far more than a vision for the future. The Brady continues to create the future through discovery, intense focus, constant improvement, and an ethic of service.

Patients come to The Brady for medical treatment in the following areas: prostate cancer, benign prostate hypertrophy, bladder cancer, incontinence, kidney cancer, stone disease, testis cancer, ureteropelvic junction obstruction, Peyronie’s disease, erectile dysfunction, male infertility, female urology, pediatric urology, minimally invasive surgery, robotic-assisted surgery.
Who Was Brady and Why Does the Institute Bear his Name?

James Buchanan Brady (1856-1917), the second son of a New York saloon operator, remains a legendary character from America’s “Gilded Age,” a thoughtful philanthropist whose legacy continues to fuel urological research.

Brady started working at the age of 11 to support his family, eventually getting a job selling special patented steel saws used for cutting railroad tracks. He soon developed an eye for diamonds and other jewels, and as his success as a salesman grew, so did his vast diamond collection, earning him the nickname “Diamond Jim” Brady.

As renowned as he was for his business acumen, Brady, who consumed vast quantities of food daily, was also well known for his prodigious appetite. Culinary historians note that his breakfast often started with a gallon of orange juice, a half dozen eggs, pancakes, fish cakes, and chop in a dinner including dozens of oysters and clams, terrapin, lobsters, roasted meats, and a variety of game birds.

In 1912, Brady, who was already suffering from diabetes, kidney disease, and other ailments, developed severe prostate difficulties. After undergoing successful treatment at Johns Hopkins Hospital by Dr. Hugh Hampton Young, the ever-grateful Brady endowed the urological institute that now bears his name, allowing it to flourish right from its inception.
## ABOUT THE AUTHORS

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Dr. Mostwin, Professor of Urology at Johns Hopkins, is Director of the Division of Reconstructive and Neurological Urology. As a urological surgeon, he has performed more than 2,600 radical prostatectomies over the past 25 years. Among his major research interests are urinary continence issues and bladder function. Dr. Mostwin is the medical editor of the *Johns Hopkins Prostate Bulletin*.

**H. Ballentine Carter, M.D.**

Dr. Carter is a Professor of Urology and Oncology and the Director of Adult Urology at the Johns Hopkins University School of Medicine. He has written extensively on the diagnosis and staging of prostate cancer. In particular, he has researched prostate-specific antigen (PSA) levels: how they change as men age; their variability in men with prostate cancer; and their use in staging, predicting, and managing prostate cancer. Currently, he is working closely with the Baltimore Longitudinal Study of Aging to evaluate the development of prostate disease with age. Dr. Carter has had research articles published in *The Journal of Urology, Urology, Cancer Research, the Journal of the American Medical Association*, and the *Journal of the National Cancer Institute*.

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Dr. Wright is Director of Neurourology and Chief of Urology at the Johns Hopkins Bayview Medical Center. He completed a fellowship in female urology, reconstructive urology, and urodynamics. His clinical and research interests are in male and female urinary incontinence, complex voiding dysfunction, and pelvic genitourinary reconstructive surgery.

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Dr. Allaf is an Assistant Professor of Urology and Biomedical Engineering at the Brady Urological Institute and Director of Minimally Invasive and Robotic Surgery at the Johns Hopkins Hospital. His clinical interest includes performing nerve-sparing radical prostatectomy in all its forms (open, laparoscopic, and robotic). His research endeavors involve investigating approaches to minimize the morbidity of urologic surgery and the development of ways to decrease injury to the neurovascular bundles and hasten erection recovery following radical prostatectomy. Dr. Allaf has been the recipient of numerous academic awards, including placing first in the 2005 American Urological Association clinical and laboratory research annual essay contests. He has written and published numerous research articles and textbook chapters in the field of laparoscopic and robotic urologic surgery.

**Christian P. Pavlovich, M.D.**

Dr. Pavlovich, an Associate Professor of Urology and Director of Urologic Oncology at the Johns Hopkins Bayview Medical Center, is experienced in open, laparoscopic, and other minimally invasive surgery for the management of urologic tumors, including nerve-sparing laparoscopic and robotic radical prostatectomy. As Director of Urologic Oncology at Bayview, he continues to treat cancer with an emphasis on minimizing morbidity and maximizing quality of life, while exposing his patients to the latest treatment options and techniques.
If you have received a diagnosis of prostate cancer, you are far from alone. After skin cancer, prostate cancer is the most common cancer in American men and is second only to lung cancer as a cause of cancer deaths. The American Cancer Society estimates that there will be about 217,732 new cases of prostate cancer in the United States in 2010, with about 30,050 men dying from the disease. Prostate cancer may progress so slowly that some patients live with it for years and end up dying of something else; however, once it spreads to the bones it is often incurable. An American boy born today has a 16% chance of being diagnosed with prostate cancer at some point in his life and about a 3% risk of dying from it.

The good news is that reliable diagnostic tests and numerous treatment options are available for prostate cancer, and death rates from prostate cancer are on the decline. Nearly 100% of men are still alive five years after a prostate cancer diagnosis and about 93% are alive 10 years after diagnosis. Moreover, because most prostate cancer is slow growing, usually you can give yourself time to learn about and carefully weigh all the options available to treat prostate cancer. And it’s important that you take the time to do so. Of all the cancers, cancer of the prostate is unusual in that there is no consensus among doctors about the best treatment—or even whether any type of treatment is absolutely necessary.

This treatment decision guide can help you gain insight into your own situation and familiarize you with the options currently available for treating prostate cancer. Leading experts in the field at Johns Hopkins describe the major types of treatment and explain which patients are the most appropriate candidates for each type. They carefully review the advantages and disadvantages of each, and also present questions that they are asked most frequently by their patients with prostate cancer questions that are very likely on your mind as you make decisions about your treatment.

Of course, you will make final decisions about your treatment with your doctor. You should talk to your doctor about the relative risks and benefits of each treatment and also consider consulting physicians from different fields to get a broader spectrum of opinion (see page 10). The information presented here will provide you with the crucial issues to consider in treating your prostate cancer and the important questions to ask your doctor.
Many men are not aware of the location and function of their prostate gland until it begins to cause health problems. The gland is chestnut shaped and sits at the base of the bladder, in front of the rectum and behind the base of the penis. It produces prostatic fluid (a component of semen), functions as a valve to keep urine and sperm flowing in the proper direction, and pumps semen into the urethra during orgasm. The gland is about the size of a pea at birth and grows until it reaches its normal adult size (roughly 1.5 inches in diameter) in a man’s early 20s. When a man reaches his mid-40s or later, the inner portion of the prostate tends to enlarge, a condition called benign prostatic hyperplasia (BPH).

Physicians usually divide the prostate into three main zones (see illustration). The peripheral zone comprises the outermost portion of the prostate gland and accounts for about 70% of its volume. Because prostate cancer is most likely to develop in this area, doctors usually sample tissue from this section during a biopsy. Since much of the peripheral zone sits adjacent to the rectum, doctors can often detect prostate cancer with a digital rectal exam.

The transition zone is the innermost section of the prostate gland and accounts for roughly 5% of its volume in a healthy man. This zone surrounds the urethra, which passes from the bladder to the penis through the prostate. BPH begins in the tissues of the transition zone. Enlargement of this zone constricts the urethra and leads to the urination problems that are common in men with BPH.

The central zone, which sits between the peripheral and transition zones, makes up about 25% of the gland’s volume. The ejaculatory ducts, through which semen enters the urethra, pass through this zone. Prostate cancer and BPH are unlikely to develop in the central zone.
Current Treatment Options

The standard treatment options for prostate cancer include proactive surveillance (also known as expectant management), radical prostatectomy, radiation therapy, and hormone treatment. Radiation therapy can be delivered from an external source (external beam radiation therapy) or by implantation of radioactive seeds (brachytherapy).

Radical prostatectomy can cure prostate cancer, and radiation therapy is thought to cure or at least slow down the disease when it is in its early stages. Hormone therapy is not curative; it is generally used to slow the progression of the disease once it has spread to other sites. Though chemotherapy is effective in treating some types of cancer, it has been less successful for prostate cancer.

Key Factors to Consider in Choosing a Treatment

Men eventually make their treatment decision based on a variety of factors, including the potential for side effects, perceived long-term risks, psychological ramifications, and financial costs of each of the therapies. While aggressive treatment may prolong life, it can also damage the quality of life by compromising sexual performance and the ability to control urination, and, in the case of radiation therapy, rectal function.

Ultimately, however, prostate treatment depends on two factors: the clinical stage of the cancer (the extent of disease) and the age and general health of the individual. Researchers have found that, in healthy men who have more than a 10-year life expectancy, about 80% of prostate cancers detected by PSA testing have the potential to progress and thus warrant treatment. (The PSA test, which measures prostate-specific antigen—a protein produced in the prostate and released into the blood—is widely used as a tool to screen for the presence of prostate cancer.) Still, with increased use of PSA testing, some men will be diagnosed with small prostate cancers (which cannot be felt during a digital rectal exam but are suspected from PSA tests and confirmed by biopsy) that pose no immediate threat and, indeed, may never need treatment. Two recent studies suggest that 30% to 50% of cancers detected by PSA screening would never have become apparent otherwise.

Doctors use several methods to help predict the seriousness of prostate cancer, and this information is factored into the treatment decision. One method is the Gleason score, which ranges from 2 to 10. A score of 2 to 4 indicates a greater probability of an insignificant cancer—a cancer that is unlikely to grow rapidly and spread. Higher scores suggest a greater likelihood of a significant, potentially life-threatening cancer. Men with “high-grade” disease (defined as a Gleason score of 7 to 10) are considered poor candidates for proactive surveillance, since the high score indicates an aggressive cancer.

Another method helpful in determining the best treatment option is the Partin tables,
named after the Johns Hopkins physician who developed them. The tables help doctors predict whether cancer is confined to the prostate or has spread to adjacent tissue, seminal vesicles, or lymph nodes. (You can view the Partin tables on pages 18-19 and at the Brady Urological Institute website: http://urology.jhu.edu/prostate/partintables.php).

The prediction is based on the patient’s PSA levels, biopsy Gleason score, and clinical TNM cancer stage, which is a system for expressing the size and degree of spread of prostate cancer by separately describing the extent of tumor at its original location (T), whether and to what extent the cancer has spread to nearby lymph nodes (N), and whether and to what extent the cancer has metastasized (M) to other sites in the body. If cancer has spread outside the prostate, surgery may not be the best treatment option. You must also consider possible complications when deciding on a treatment option. If a man chooses surgery or radiation therapy, he risks the possibility of bowel, urinary, or sexual problems. If he chooses proactive surveillance (no treatment is provided, but the patient is closely monitored for cancer growth), he may be anxious about the progress of the disease, and urinary or sexual symptoms may arise if the disease progresses.

As you will read in the section about proactive surveillance by Dr. Ballentine Carter, Johns Hopkins researchers have also developed a way of determining which men are good candidates for proactive surveillance. They have found that the best candidates have the following characteristics: prostate cancers that cannot be felt on a digital rectal exam; PSA density of less than 0.15; signs of cancer in no more than two biopsy samples; cancer cells in less than 50% of any single biopsy sample; and a Gleason score no higher than 6. These criteria are evolving and currently being tested in larger populations, so the criteria for proactive surveillance may eventually change over time. (Any new developments will be reported in the Johns Hopkins Prostate Bulletin—see page 96).

Age also plays an important part in deciding whether to choose proactive surveillance or to treat prostate cancer more aggressively. Because prostate cancer generally progresses slowly, older men with small tumors can choose proactive surveillance more safely than younger men. Men in their 50s and early 60s with prostate cancer are more likely to live long enough for their disease to become life-threatening; men in their late 70s and 80s are more likely to die of another cause.

Understanding the Grade and Stage of Your Cancer

Obtaining and reading a copy of your pathology report can prove helpful in understanding your cancer and deciding on the best treatment. A pathology report outlines the diagnostic results of the prostate needle biopsy (or the biopsy specimen taken during prostatectomy). The pathologist who examined the biopsy specimen prepares the report.
Although you may not be offered a copy of your pathology report, your doctor will provide one if asked. Alternatively, you can obtain your report from the pathology laboratory where the biopsy specimen was sent. The report will have your name, patient number, and case number (which at Hopkins usually appears as S-year-number).

While benign (noncancerous) findings on the biopsied tissue cannot completely rule out cancer—it's always possible that the cancer lurks in other, unbiopsied prostate tissue—such findings indicate that an elevated PSA is likely due to other causes. These causes include chronic or acute inflammation and benign prostatic hyperplasia (BPH).

**Getting A Second (and Third or Fourth) Opinion**

In an often-cited study published in the *Journal of the American Medical Association* in 2000, researchers asked more than 1,000 specialists what treatment they would recommend for a man with early-stage prostate cancer who was expected to live at least 10 more years. Nearly all the urologists (93%)—who perform surgery—chose surgery as the preferred treatment, while most of the radiation oncologists (72%) responded that radiation therapy and surgery were equally effective treatments. The study authors' conclusion? Patients should schedule a consultation with a member of each specialty before making a decision.

If these specialists don’t agree, one option is to schedule a consultation with a medical oncologist, a specialist in cancer treatment who does not perform radiation or surgery. Another option is to see a second urologist or radiation oncologist. Doctors of the same specialty often have different approaches to treatment: For example, some radiation oncologists will recommend external beam radiation therapy; others, brachytherapy; and still others, a combination.

**The Importance of the Pathologist.** A final but not-to-be-overlooked reason to seek a second opinion is that, if done at a center that specializes in prostate cancer treatments, it involves having another pathologist review the slides from your biopsy specimen. An accurate pathology reading is essential because it forms the basis for treatment decisions.

Unfortunately, spotting cancerous cells and determining how abnormal they appear are difficult, and pathologists sometimes make errors. In one study, pathologists at Johns Hopkins reviewed biopsy samples of 535 men who had been referred for radical prostatectomy and reclassified 7 (1.3%) as benign. Upon subsequent clinical workup, 6 of 7 men were considered not to have prostate cancer, and their surgery was canceled. Getting an incorrect reading can limit your treatment options—or lead to having treatments that you don’t need.

**How To Get a Second Opinion.** Some patients are reluctant to bring up the matter of second opinions, thinking that their doctor may not be receptive to involving another physician. Today, however, doctors in step with current medical standards welcome such
discussions and support their patients’ desire for additional information whenever appropriate. Health insurers generally pay for second opinions, and some even require them before certain procedures.

Your primary care doctor and the urologist who performed the biopsy are the best sources for referrals. Request that, if possible, they suggest a colleague affiliated with a different hospital. Although this is not absolutely necessary, the practice is prudent, because doctors who work at the same institution often share similar views and may be reluctant to contradict one another. Also check to be certain the consultant is board certified in the appropriate specialty. The American Medical Association (www.ama-assn.org) and the American Urological Association (www.urologyhealth.org) offer referral services. Hospitals, local health departments, family, and friends are other possible resources.

If your referring doctor is unwilling to discuss the possibility of a second opinion or makes you feel uncomfortable about the matter, strongly consider changing doctors.

Before meeting with you, the consultant will require all relevant medical records. The first doctor’s office can send written reports and test results directly to the consultant. Be sure to call before your appointment to confirm their arrival, as it will be impossible to proceed without proper documentation; you can also choose to collect the records and deliver them personally.

During the consultation, the doctor will review the information and may perform a physical examination or order more tests. Recommendations made in a written report will be sent to the referring physician—and also to you if you request them.

Be sure that the specialists address all treatment options—surgery, radiation therapy, and proactive surveillance—and discuss the advantages and disadvantages of each. If your doctors don’t agree and you don’t know what to do, one or more of the following approaches can help you reach a decision:

- Have the specialists explain to you why they came to their respective conclusions.
- Suggest that the specialists discuss the matter with each other; sometimes such conversations produce an acceptable consensus.
- Ask your general practitioner—or, if you wish, another specialist—to help you sort through the options.
- Consider seeking an opinion at a nationally recognized cancer center, such as one affiliated with the National Comprehensive Cancer Network (www.nccn.org).
- Try talking to men who have been treated for prostate cancer.

Don’t panic if you’re having trouble making a decision. In many men, prostate cancer is generally a slow growing malignancy. These men can safely spend up to three months learning about the disease and consulting with the appropriate specialists.
Making an Appointment at Johns Hopkins

Many people facing a serious health crisis wish to get a second opinion from a leading academic medical center such as Johns Hopkins. There are several ways to make appointments at Hopkins. The most direct way is for your physician to call the Hopkins Access Line (410-955-9444 in Baltimore and internationally or 800-765-5447 in the rest of the United States).

If you prefer to make an appointment yourself, you may call the appointment service line (410-955-5464 in Baltimore or 410-955-8032 outside Baltimore, including international calls).

Finally, Johns Hopkins USA provides one point of contact for out-of-town patients. A representative can help you identify an appropriate physician or specialist, coordinate multiple medical appointments, arrange second opinions, and obtain general information about Johns Hopkins’s many services. To talk with a representative, call 443-287-0528 weekdays, 8:30 a.m. to 5 p.m. Eastern Time.
It is unusual for one individual to revolutionize a surgical procedure and in doing so have a major impact on a field as important as prostate cancer—the most common cancer and the second most common cause of cancer death in men in much of the Western world. Based on pioneering anatomic discoveries, Patrick Walsh’s innovations in radical prostatectomy surgery made it possible to preserve sexual function, improve urinary continence, reduce postoperative mortality ten-fold, and decrease progression to metastases and cancer specific mortality by 50%.

Furthermore, Dr. Walsh characterized genetic factors involved in the origin and development of the disease, and he demonstrated the value of serial PSA measurements to improve specificity for early diagnosis. Along with Dr. Alan W. Partin, he developed nomograms to predict probability of cure preoperatively. These graphic representations of numerical rela-
tions are also used for men who have a postoperative recurrence of cancer, to predict the time to metastases and death from the disease.

In the United States as recently as 1980, only 7% of men with localized prostate cancer accepted treatment with surgery because of major side effects: All surgical patients had severe erectile dysfunction, life-threatening bleeding was common, and 10 to 25% suffered severe incontinence. In an effort to reduce this morbidity, Dr. Walsh embarked on anatomic studies; he quickly realized that these side effects resulted from an imperfect understanding of the anatomy surrounding the prostate.

His research convinced him that it was possible to prevent these side effects through 1) the discovery of the location of the pelvic plexus that provides autonomic innervation to the corpora cavernosa; 2) identification and preservation during surgery of the microscopic neurovascular bundles needed to preserve sexual function; 3) characterization of the venous anatomy of the dorsal vein and Santorini’s plexus, which permitted the prostate surgery to be performed more safely in a relatively bloodless field; and 4) the delineation of the fascia surrounding the prostate and of the sphincteric complexes, which improved both cancer control and urinary continence.

In making these advances, Dr. Walsh single-handedly changed the prostate cancer field, with his discoveries forming the basis for the anatomic approach to radical prostatectomy that is now used worldwide in open, laparoscopic, and robotic procedures. Over the course of the decade following his discoveries, the 30-day mortality following radical prostatectomy fell ten-fold (from 2% to 0.2%) and by the mid-1990s 34% of men with localized prostate cancer in the U.S. was treated with surgery. Experienced surgeons have reported that serious problems with urinary continence have been reduced to 2%, and in men with normal sexual function who are under 65, sexual function can be preserved in 60 to 90%.

Validation of the technique’s influence on cancer control was provided by The Scandinavian Prostatic Cancer Group’s randomized controlled trial that compared radical prostatectomy using the anatomic approach developed by Dr. Walsh to watchful waiting. They reported that within eight years surgery reduced progression to distant metastasis and death from prostate cancer by 50%. At 10 years, surgery resulted in a significant improvement in overall survival.

These findings are relevant to the 25% decline in prostate cancer deaths that has occurred in the United States over the last decade. In addition to a direct impact on reducing deaths from prostate cancer in this country and abroad, the widespread application of the radical prostatectomy has had a powerful indirect effect by facilitating prostate research. When few men underwent surgery, there was little or no tissue available for pathologic evaluation or biochemical/molecular investigations. Today, tissue harvested from surgical specimens provides an invaluable resource for researchers.

Under Dr. Walsh’s stewardship, Johns Hopkins has developed the leading department
of urology in the world. Dr. Walsh and his colleagues used the clinical material from his patients to make important contributions to the understanding of the natural history of prostate cancer and the influence of genetic factors. Using the Baltimore Longitudinal Study of Aging, serial PSA measurements (PSA velocity) were shown to improve the specificity of PSA for the diagnosis of prostate cancer, especially at low PSA values. Recently, with the recognition that many men with low PSA levels have prostate cancer, PSA velocity has taken on a new importance.

Based on pathologic findings from his radical prostatectomy patients, Dr. Walsh developed a set of tables that used a combination of clinical stage, PSA, and Gleason score. These tables enabled physicians and patients for the first time to preoperatively estimate the likelihood of cure, thereby eliminating unnecessary surgery in many patients who were not curable.

Finally, based upon the follow-up evaluation of his patients who developed an elevated PSA following radical prostatectomy, Dr. Walsh developed two nomograms that make it possible to determine when this early biochemical finding will progress to distant metastasis and when patients who develop metastasis will die from the cancer. This vital information is useful in planning intervention and for stratifying patients for clinical trials.

In the mid-1980s, Dr. Walsh noted that a number of younger men who came to him for evaluation of prostate cancer had a strong family history. Pursuing this observation, he demonstrated the strong association between family history and the relative risk of the disease. Subsequently, he and coworkers performed a segregation analysis suggesting that this association is characteristic of an autosomal dominant disorder. Based on the factors that most strongly influenced this model, the team developed a definition of the syndrome of hereditary prostate cancer, and Dr. Walsh put together one of the largest collections of multiplex families for linkage analysis.

The Hopkins team in collaboration with Dr. Francis Collins and Jeff Trent from the National Institute for Human Genome Research went on to identify linkage to the first prostate cancer susceptibility locus on chromosome 1 (HPC1). Along with investigators from Wake Forest University, they cloned two rare but highly penetrant cancer susceptibility genes (RNASEL, MSR1). Because these genes are part of the innate host defense against infections, this finding supports the concept that infection and/or inflammation may play a major role in the pathogenesis of prostate cancer.

By revolutionizing surgery for prostate cancer and improving our understanding of its natural history and genetics, Dr. Walsh has made a major impact on the most common cancer in men in the Western world. In everything Dr. Patrick Walsh has done, and in all that he has accomplished, his legacy—of steadfast commitment to advancing the mission of the Brady Urological Institute, extending its impact, and expanding its contributions to the field of prostate cancer treatment—will remain an everlasting model for those who follow in his footsteps.
CONVERSATION

Pioneering prostate cancer expert Alan Partin on the benefits of surgery for treating organ-confined prostate cancer

Alan W. Partin, M.D., Ph.D., a world-renowned expert in the study and treatment of prostate cancer, is the fourth director of the Johns Hopkins Department of Urology and the Brady Urological Institute, and the urologist-in-chief of The Johns Hopkins Hospital. He succeeded Patrick Walsh, M.D., who led the department for three decades and who remains on the urology faculty devoting himself full-time to patient care, surgery, and research.

Dr. Partin is one of the world’s leading investigators into the early detection and treatment of prostate cancer. His laboratory, clinical, and surgical interests are focused on developing and testing new and existing methods for predicting the aggressiveness of prostate cancers so that both patients and physicians can make rational treatment decisions. He is renowned for his role in developing the Partin tables, which have given thousands of men with prostate cancer an accurate prediction of their likelihood of being cured.

The recipient of numerous professional honors, he was awarded the American Urological Association’s prestigious Gold Cystoscope Award, given yearly to the urologist who makes the greatest impact within the first 10 years after residency. Dr. Partin was the first urologist to receive this award after only five years of practice.

Dr. Partin is a Johns Hopkins-trained physician and surgeon. After receiving his B.A. in chemistry from the University of Mississippi in 1983, graduating first in his class, he came to Johns Hopkins for his medical training, receiving his Ph.D. degree in 1988 and his M.D. in 1989. He served a surgical internship in 1989, a surgical junior residency in 1990, and his urology residency in 1991, before being named to the faculty as an instructor of urology in 1994. He was promoted to associate professor in 1995 and then to professor of urology in 1999. Before his appointment as the David Hall McConnell Professor and Chair, Dr. Partin was the Bernard L. Schwartz Distinguished Professor of Urologic Oncology.

The author of more than 350 scientific papers, he is also editor-in-chief of the journal Urology; editor of the leading urology textbook, Campbell-Walsh Textbook of Urology; associate editor of Prostate Cancer and Prostatic Diseases; and associate editor of Urology Reviews. Dr. Partin also serves on the editorial boards of the Journal of Andrology, Urology Research and Treatment, Current Urology Reports, Clinical Prostate Cancer, and the British Journal of Urology.
What are the goals of prostate cancer surgery?

Surgery still remains the #1 choice for men who have prostate cancer that is localized to the prostate. For surgeons, the issue has always been threefold, and is focused on achieving what I like to call the trifecta:

1. Remove all cancer from the patient so he is cured.
3. Do not adversely affect sexual function.

Surgery has always been about the trifecta, and all of the advances and discoveries we have made with surgery for prostate cancer over the years have been focused on those three goals.

When it comes to surgery, are best results achieved with open surgery or with minimally-invasive procedures?

There are three ways to remove the prostate: One is the traditional operation through an open incision, while the others involve a laparoscope or robot. Here is the bottom line: It's the same operation done three different ways. To date, there has been no single randomized study to fully evaluate the key issues.

Our Hopkins experts have looked at all of the critical variables regarding the different surgical approaches, including blood loss, need for transfusion, pain, erectile dysfunction (ED), cancer cure, side effects related to the surgery, and return to work. We found no differences. We had originally thought that the margin rates—was there any cancer at the end of the gland?—were a bit higher after robotic procedures, but when we statistically corrected that for surgical experience by removing the “Wizard's” [Dr. Patrick C. Walsh] surgery patients from the data, there was no difference found between open and minimally invasive procedures.

How can you counsel a man to look at all of the options for prostate cancer therapy when robotic surgery is so heavily marketed as the best choice?

It's not hard. I sit down with the patient and explain the marketing and advertising behind robotic prostate procedures and how they often help sway patient decisions. I also explain the fact that right here at Hopkins, where we are on the front lines in cancer treatment, there does not appear to be any difference between the open and robotic procedures. Speaking for the Hopkins surgeons who perform both open and robotic prostatectomies, we don't care which procedure a patient ultimately picks. For us, it's a matter of going to Room 6 or Room 18 to do the surgery. One operation takes a little over an hour to perform the other a little over two and a half hours. The end results are similar.  (Text continues on page 21.)
Before you decide on a treatment for your prostate cancer, it’s helpful to know how likely it is that your cancer has spread. The Partin tables, printed below, can help predict whether the cancer is confined to your prostate or has invaded the adjacent tissue, seminal vesicles, or lymph nodes.

These tables were developed by Johns Hopkins urologists Alan W. Partin, M.D., Ph.D., and Patrick C. Walsh, M.D., and were recently updated using data from 5,730 men treated for prostate cancer between 2000 and 2005. Using a man’s prostate-specific antigen (PSA) level, biopsy Gleason score, and estimated clinical stage, the likelihood (expressed as a percentage) that the cancer has spread can be calculated. (Final staging is based on the pathologist’s examination of tissue removed during radical prostatectomy.)

To use the Partin tables, you need to know the estimated clinical stage of your cancer (T1c or T2a, b, or c—see page 20), your PSA level, and your Gleason score. Use your clinical stage to find the table that applies to you. Next, find the PSA range that includes your PSA level. Then move across the row to find the column with your Gleason score. The four numbers listed in the column represent (as a percentage) the likelihood that your cancer is confined to the prostate or has spread to nearby tissues (extraprostatic extension), the seminal vesicles, or the lymph nodes.

As an example, a man who has a stage T2a tumor, a PSA level of 11 ng/mL, and a Gleason score of 5 has a 54% chance that his cancer is confined to the prostate, a 41% chance that it has spread to adjacent tissue, a 3% chance of seminal vesicle involvement, and a 1% chance of lymph node involvement. You can also calculate your score online using the calculator found at http://urology.jhu.edu/prostate/partintables.php.

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### Clinical Stage T2a

*(palpable, <½ of one lobe)*

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### Clinical Stage T2b

*(palpable, <½ of one lobe)*

or **T2c** *(palpable, both lobes)*

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<th>PSA Range (ng/mL)</th>
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Adapted from *Urology*, June 2007, pp.1095-1101.
### Understanding the TNM Cancer Staging System

The TNM (tumor, nodes, metastasis) staging system is used to describe a cancer’s clinical stage, or how far it has spread. The system assigns a T number (T1 to T4) to describe the extent of the tumor as felt during a digital rectal exam (DRE). The N number (N0 to N1) indicates whether the cancer has spread to any lymph nodes, and the M number (M0 to M1) indicates the presence or absence of metastasis (spread to distant sites). The T and M designations are divided into sub-categories (designated a, b, and c) that provide further detail on the extent of the cancer.

The TNM staging system is used in the Partin tables (see pages 18-19) to help determine appropriate prostate cancer treatment options.

<table>
<thead>
<tr>
<th>TNM</th>
<th>Description</th>
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</table>
| **T1** | Tumor cannot be felt during DRE or seen with diagnostic imaging  
• T1a: Tumor found incidentally during surgery for benign prostatic hyperplasia (BPH) and is present in less than 5% of removed tissue  
• T1b: Tumor found incidentally during BPH surgery but involves more than 5% of removed tissue  
• T1c: Tumor found during needle biopsy for elevated PSA |
| **T2** | Tumor can be felt during DRE but is believed to be confined to the gland  
• T2a: Tumor involves one half or less of one side of the prostate  
• T2b: Tumor involves more than one half of one side but not both sides  
• T2c: Tumor involves both sides of the prostate |
| **T3** | Tumor extends through the prostate capsule and may involve the seminal vesicles  
• T3a: Tumor extends through the capsule but does not involve the seminal vesicles  
• T3b: Tumor has spread to the seminal vesicles |
| **T4** | Tumor has invaded adjacent structures (other than the seminal vesicles), such as the bladder neck, rectum, or pelvic wall |
| **N0** | Cancer has not spread to any lymph nodes |
| **N1** | Cancer has spread to one or more regional lymph nodes (nodes in the pelvic region) |
| **M0** | No distant metastasis |
| **M1** | Distant metastasis  
• M1a: Cancer has spread to distant lymph nodes  
• M1b: Cancer has spread to the bones  
• M1c: Cancer has spread to other organs, with or without bone involvement |

Source: National Cancer Institute.
Some surgeons advertise the fact that they can do a robotic assisted prostatectomy in 90 minutes. Is that possible? If a surgeon says the procedure takes 90 minutes, then it comes down to the definition of “surgery.” These surgeons are only counting the time that they are sitting at the robotic console and operating on the patient. However, at Hopkins we start the clock when the patient is first wheeled into surgery and stop it when he arrives in the recovery room. This takes into account all the extra set-up time necessary to prepare the patient for surgery, and not just the time the doctor spends actually removing the prostate.

**How can a man choose between a surgeon who performs the open procedure and one who uses a robot or laparoscope?**

Here is what I tell all prospective patients: You don’t want to bring a plumber into your home to do electrical work. If your surgeon says he feels confident that he is going to provide the best operation for you with a certain technique—open, laparoscopic, or robotic—and you like that surgeon, you should choose him for your surgery.

**If Alan Partin were diagnosed with organ-confined prostate cancer and needed to receive treatment, what would he choose?**

I would seek out the doctor who has best experience and the best data concerning his cancer cure rates, continence rates, and maintenance of erectile function. I would then ask him what he felt would be the most appropriate operation for me.
A n ongoing and simmering debate in the prostate world has to do with whether or not to treat a prostate cancer that is low-grade and detected early. Some believe that it should be treated immediately to eliminate all chance of possible metastatic development. A growing number of doctors and patients, however, believe that a low-grade cancer detected early is more likely to never cause problems and is only a concern because it has been detected and brought to the attention of the patient.

Physicians know that most men over age 60 years harbor some cancerous cells in the prostate, and that many of the small cancers within the prostate can be detected using current biopsy techniques, even in men with low PSA levels (less than 4 ng/ml). Nevertheless, most of these small cancers will not cause harm during the lifetime of the patient. From birth to age 90 years, there is an approximate 17% chance of being diagnosed with prostate cancer, and a 3% chance of dying of the disease. It’s evident that older men are more likely to die with prostate cancer than from the disease. Therefore, deferring treatment may actually be the best approach for the carefully selected individual who is thought to have an early cancer.

However, how long do you defer? How can you identify the lucky man whose prostate cancer does no harm? And how can you determine which unlucky man has a cancer that will lie indolent for years, but then suddenly start to grow, metastasize, and ultimately prove fatal? These are the million-dollar questions that prostate researchers continue to grapple with. At this point, they still can’t accurately predict who has a cancer that will remain small and harmless, nor can they tell who has a cancer that will grow very rapidly, spread quickly out of the prostate, and move to nearby bone, forever immune from curative treatment.

Prostate cancer has a long, protracted course in most men. Today, in the United States, with widespread PSA screening of men who are free of any noticeable symptoms, prostate cancer is being detected at an extremely early point in the natural history of the disease. Based on studies of non-screened detected cancer, most of the cancers discovered today by PSA are of low to moderate risk and unlikely to result in death from prostate cancer if left untreated for 15 years.

Yet, most men today—even those whose age gives them a life expectancy of less than 15 to 20 years—undergo treatment for their prostate cancer at the time of detection, even though
the disease might have been so insignificant that the risks of treatment far surpass the risk posed by the cancer. For the most part, the reason this is done is that men and their doctors have no assurances that the cancer will not one day become significant and lethal.

Nevertheless, proactive surveillance (it has also been called active surveillance and expectant management) is an acceptable alternative for select older men who want to carefully monitor the disease rather than undergoing immediate treatment. I get the distinct impression that more and more people with prostate cancer are beginning to step back and make a more measured assessment of their cancer instead of automatically reacting with, “I am going to treat this cancer immediately.” Men today are more educated about prostate cancer. They recognize that we are over detecting small tumors that may never cause harm and they are beginning to understand that not all cancers need to be treated immediately.

Even though some men may have curable disease, they are opting for proactive surveillance instead of treatment, watching and monitoring instead of opting for surgery or radiation. These men are choosing to live with an uncertain future while still maintaining a high quality of life, free from any side effects of cancer surgery or radiation.

Q. What is the goal of a well-designed proactive surveillance program?

A. The goal of a proactive surveillance program is to avoid unnecessary treatment in men who harbor a prostate cancer that is not likely to progress during their remaining years of life. There are two important prerequisites for a successful proactive surveillance program:

- The ability to determine whether or not your cancer has a low probability of progression, and whether an proactive surveillance program would likely be safe for you to follow.

- A monitoring or follow-up plan that allows identification of disease progression at a time when cure is still possible.

Before we go further, it is important that you understand the difference between proactive surveillance with palliative intent (treat the symptoms if the disease becomes metastatic) as opposed to proactive surveillance with curative intent (careful monitoring with curative treatment before the disease becomes incurable).

In the past, proactive surveillance with the intention to give palliative treatment when there were signs of disease progression was often initiated for two reasons:

- In the pre-PSA era (before 1990) when we lacked a method of detecting prostate cancer early, most cancers were detected at a locally advanced or distant stage when the ability to cure the disease was quite limited.
• In the past, the side effects of local treatment (surgery and radiation) were hard to justify for a disease that was already too advanced to cure.

Today, with extensive PSA screening and wide area biopsy sampling, it is now possible to detect prostate cancers—on average—a decade earlier than in the era when screening was just being implemented. Many of these cancers will not progress during the remaining years of an individual’s life. Thus, a policy of proactive surveillance with curative intent would be rational if men with a low risk of disease progression could be identified, and careful monitoring of these men could identify disease progression during the window of curability.

I believe that both of these goals are achievable today. I also believe that proactive surveillance with curative intent will become a more popular option within the urological community (and among patients) as more information becomes available about the natural history of the prostate cancers that are being detected today with PSA screening.

Q. **Who are the best candidates for a program of proactive surveillance?**

A. If you are considering proactive surveillance, you should first study all other options carefully before choosing the therapy you think is best for you.

A man thinking about proactive surveillance should understand that it entails close monitoring by a physician. At Johns Hopkins, we generally monitor men with regular PSA measurements, digital rectal exams, and an annual biopsy. Proactive surveillance also requires that a person be able to live with the idea of the cancer, and not be overcome by the anxiety produced by the need for careful monitoring.

At Johns Hopkins, we use the following criteria for our ongoing proactive surveillance study, understanding that while we believe that spread to an incurable stage is unlikely during monitoring, it is possible.

**Criterion #1: Age (Life Expectancy) or Length of Follow-Up**

In a landmark Swedish study in the *Journal of the American Medical Association*, Dr. Jan-Erik Johansson, from University Hospital in Orebro, described the results of one of the longest studies ever of early prostate cancer. In that study, the length of follow-up was a strong predictor of death from prostate cancer. While the risk of death from prostate cancer remained stable for the first 15 years, between 15 and 20 years the risk of death from prostate cancer tripled. Thus, older men and/or those with significant illnesses (comorbidity) are less likely to experience disease progression and death from prostate cancer since they have fewer remaining years at risk (follow-up) when compared to younger men.

*At Johns Hopkins, we have generally discouraged men under the age of 65 who are otherwise healthy from pursuing proactive surveillance, although some younger men choose this approach.*
**Criterion #2: Cancer State (Extent of Disease)**

With the emphasis on early detection, most cancers detected today are non-palpable (stage T1c—cannot be felt during a digital rectal exam) or localized palpable (T2). While there is no proof that proactive surveillance is safer for men with non-palpable cancers when compared to those with palpable disease, the Johns Hopkins approach has been to select only those men with stage T1c cancer as appropriate candidates for proactive surveillance with curative intent, since—on average—tumor volumes are smaller among men with non-palpable cancer.

*We believe that proactive surveillance for non-palpable cancers is safer than for those that can be felt on examination.*

**Criterion #3: Needle Biopsy Findings**

**Cancer Grade.** The Gleason score is a way to classify the grade of cancer, based on how it looks under the microscope. Today most prostate cancers are detected on prostate needle biopsy and are not given Gleason scores below 5. One can think of lower grade cancers, therefore, as Gleason 5 and 6; higher-grade cancers fall into the Gleason 7-10 range. In multiple studies evaluating proactive surveillance for prostate cancer, grade is the strongest predictor of progression of disease and death from prostate cancer. One study reported that when compared to patients with low-grade cancers, men with high-grade cancers had a 16-to 47-fold greater risk of prostate cancer death without treatment.

*We have considered only those men with low-grade cancers (Gleason 6 or less) as appropriate candidates for our proactive surveillance study.*

**Extent of Cancer in Needle Biopsy.** Multiple studies have shown that the extent of the cancer (e.g., percentage of cancer in each core, total number of cores with cancer) on needle biopsy is a surrogate for the extent of cancer in the final pathological specimen after radical prostatectomy. Dr. Jonathan Epstein, Professor of Pathology, Urology, and Oncology at Johns Hopkins, is internationally recognized as the world’s expert in prostate cancer pathology. He has demonstrated that in men who underwent sextant (six core) biopsies, the finding of no more than 50% involvement of any core with cancer, and no more than two cores involved with cancer, were criteria predictive of small volume disease when used together with PSA density (PSA divided by prostate volume).

Perineural invasion (PNI)—the microscopic infiltration of cancer cells around nerves within the prostate—on needle biopsy has been shown to be associated with a greater likelihood that cancer has moved out of the prostate gland, but is not clearly associated with a higher risk of PSA failure after surgery.

*Nevertheless, at Johns Hopkins, men with PNI are not considered ideal candidates for proactive surveillance (expectant management) and are encouraged to undergo definitive therapy by choosing surgery or radiation.*
**Criterion #4: PSA Results**

PSA Density (PSAD). PSA density—the PSA score divided by the volume of the prostate, as determined by transrectal ultrasound—is a surrogate for disease extent, since men with PSA levels out of proportion to prostate volume are more likely to have prostate cancers that are not small volume. Dr. Epstein demonstrated that men with a PSA density of 0.1 ng/ml or less were more likely to have small volume prostate cancer.

Thus, PSAD is used together with the needle biopsy findings as one criterion for selecting patients who are candidates for proactive surveillance at Johns Hopkins.

**Percentage of Free PSA (fPSA).** This is PSA not chemically bound to proteins in the bloodstream. The higher your fPSA—25% or higher is considered a good score—the more likely you are free of cancer. Some investigators have noted a correlation between a lower percentage of fPSA and more aggressive cancers (higher grade and higher stage). While we have also noted that men with a lower percentage of fPSA have a greater likelihood of disease progression without treatment, the overlap in fPSA levels between those men who do and do not experience progression without treatment is too great to use fPSA on an individual basis for selection of men for proactive surveillance.

We are not enthusiastic about men with fPSA levels below 10% entering the proactive surveillance program at Johns Hopkins, and these men are generally encouraged to pursue definitive treatment.

**PSA Velocity (PSAV).** This is the rate of change in PSA from year to year. Dr. Anthony D’Amico, the highly regarded prostate cancer expert from Harvard Medical School, recently demonstrated that men with a PSA velocity of 2.0 ng/ml per year in the year preceding surgery had an increased risk of prostate cancer death after surgery (median follow-up five years). Thus, men such as these, who had micrometastatic disease at the time of surgery, may not be ideal candidates for proactive surveillance if the physician believes that local treatment would improve survival.

It is likely that future studies will demonstrate that PSA velocities lower than 2 ng/ml per year are predictive of death from prostate cancer. It seems intuitive that men with a higher PSAV would be more likely to harbor more extensive cancer, but the variability in PSA between measurements due to BPH and prostate inflammation makes it difficult to interpret PSAV for an individual man—especially in the short term.

*In my opinion, the current lack of knowledge about PSAV precludes the routine use of this variable to select men with prostate cancer who can be safely managed expectantly.*
Q. Is it difficult to find men who meet all the Johns Hopkins proactive surveillance criteria?

A. No. Many men are now choosing the proactive surveillance approach over immediate treatment. About 15% of newly diagnosed men meet the criteria for our proactive surveillance program than now has enrolled over 800 men over the past 15 years. Of men who met all the criteria for inclusion in our program, 20% chose not to enter because of other illnesses and/or personal preferences.

Q. If a man chooses proactive surveillance, should he make any dietary changes?

A. Most men ask what they should be doing in terms of dietary changes to help prevent progression of their cancer.

In a study of prostate cancer risk among twins, scientists have attributed 42% of prostate cancer cases to inheritance and the remainder to environmental factors. Based on epidemiological studies, in which researchers use food diaries, diet recalls, or questionnaires to closely examine what people eat, it’s now believed that diet is one of the most important environmental or lifestyle factors that can influence cancer rates of many organs. The problem is that we haven’t been able to specifically identify which components of the diet have the most effect—is it things we eat or things we don’t eat?

We do know, for example, that death rates from prostate cancer in Asian countries, where the diet is lower in animal and dairy fat and higher in vegetables compared to the west, are four times lower than they are for the United States. In the United States, diets are typically rich in animal fats and meats and lacking in fruits and vegetables. In addition, Americans eat meats that are cooked at high temperatures (charred) and this produces substances called heterocyclic amines, which are carcinogenic.

There are several possible reasons why people in Asian countries such as Japan and China are far less likely than Westerners to die of cancer of the prostate. Some believe there are important genetic differences between ethnic groups, and that this difference in cancer rates could be specifically related to our genes. Interestingly, though, when people migrate from Japan to the United States, their rates of prostate cancer and the rates in subsequent generations rise markedly. Since genetic makeup is unchanged, the increase in risk is likely related to environmental factors such as diet and lifestyle.

When it comes to nutrition, what I tell patients is that a diet that limits animal and dairy fat and protein, and that emphasizes a wide variety of fruits and vegetables, is thought to be a healthful diet with respect to reducing cancer rates, and also healthful with respect to heart disease.
There are dozens of free articles on the topic of nutrition and cancer in *CA, A Cancer Journal for Clinicians*, published for the American Cancer Society. The articles can be found on the CA website (http://caonline.amcancersoc.org). Type in the word “nutrition” in the search box to access the articles.

**Q. Have some men in the Hopkins proactive surveillance study eventually left to receive curative treatment?**

**A.** In our study, approximately 1 in 3 men will undergo curative treatment for their prostate cancer because a follow up biopsy revealed either higher-grade cancer or more extensive disease. This finding seems to be universal in all proactive surveillance programs in the United States and in other countries.

The important caveat is that although one could say these men had disease progression, the unfavorable biopsy findings may actually have been present when the men were initially diagnosed with cancer. The problem is that we just might have missed the disease with the original biopsy. For this reason we now recommend a repeat biopsy (confirmation biopsy) after diagnosis for those men who we believe have small volume cancers, to confirm that the original biopsy did not underestimate the disease extent.

In addition to the men who progressed, another 5% opted out of the study after three years, on average; many changed their minds and chose instead to have curative treatment even though their disease had not progressed since they entered the study.

**Q. By choosing to follow a proactive surveillance plan, is a man losing the window of opportunity for cure?**

**A.** The risk of proactive surveillance is that the cancer could escape from the prostate gland undetected and spread, leaving the man with no opportunity to try other curative treatments. We don’t believe men are losing the window of opportunity for cure, however. Furthermore, we believe that over a 20-year period that the man who enters our program (older and more carefully selected) has about a 5% chance of a prostate cancer death and a more than 60% chance of death from another cause.

**Q. When should a man stop his proactive surveillance and consider curative treatment for his prostate cancer?**

**A.** There are several important triggers we look for in our proactive surveillance study participants that would be reason to consider curative treatment. PSA changes are not used to trigger curative intervention but may trigger earlier prostate biopsies. When a man has one of the following triggers, however, we will strongly urge him to stop the proactive surveillance and opt for surgery or radiation to treat his prostate cancer:
1. Change in digital rectal exam findings.
2. Unfavorable pathology (high grade cancer, more than two cores with cancer, more than 50% involvement of any core with cancer) on the annual surveillance biopsy of the prostate suggesting that small volume disease is no longer present.
3. Presence of perineural invasion on needle biopsy of the prostate.

**Q. How can a man enroll in the Johns Hopkins Proactive Surveillance Study?**

**A.** This ongoing study, which is institutionally approved, is open to consider men who have low risk prostate cancer (stage T1c, PSA below 10 ng/ml, and Gleason score of 6 or less). To enroll, contact my office at 410-955-0351.
Radical prostatectomy surgery removes the entire prostate gland, along with the seminal vesicles and some surrounding tissue. It is the only treatment for localized prostate cancer (cancer confined to the prostate) that has been proven to reduce deaths from the disease when compared with no treatment. Radical prostatectomy offers the possibility of a cure only if the cancer has not spread to the lymph nodes in the pelvis or to other parts of the body. As a result, when the risk of spread is high, some surgeons perform a laparoscopic lymph node biopsy before the planned prostatectomy; others sample the lymph nodes at the time of surgery and discontinue the operation if the cancer has spread. Because PSA testing is widespread, today it is uncommon to find cancer that has spread to the lymph nodes at the time of diagnosis.

Radical prostatectomy was developed at Johns Hopkins at the beginning of the twentieth century. The operation was not popular at first because of the high rate of erectile dysfunction (ED) and urinary incontinence associated with the procedure. But in the early 1980s, Johns Hopkins urologist Patrick Walsh, M.D., developed a new approach to the operation. He devised a “road map” that allows surgeons to remove the prostate with less risk of damaging the nerves and tissues that are essential for erections and urinary control.

This anatomic approach has reduced the risk of severe incontinence to 1 to 3% and the risk of mild incontinence to around 5% to 10%. The risk of ED varies according to the patient’s age, the quality of his erections before surgery, and the surgeon’s skill at performing the procedure. The majority of men who have good-quality erections before surgery and a skillfully performed operation have return of erectile function. Full recovery can take more than a year in some instances, however. When ED does occur after surgery, it usually can be treated successfully with a variety of medications. The nerve-sparing radical retropubic prostatectomy can preserve sexual function, improve urinary continence, and decrease cancer-specific mortality.

**Surgical Details**

Nerve-sparing radical retropubic prostatectomy usually begins with a vertical incision in the abdomen—just above the pubic area. (In rare cases, some surgeons make the incision in
Choosing the Right Treatment for Prostate Cancer

The perineum, which is located between the scrotum and rectum; this approach is called a perineal prostatectomy—see page 36.) If appropriate, samples of tissue from the pelvic lymph nodes may be removed and tested for signs of cancer.

To minimize bleeding, which can obscure the surgeon’s view and increase the risk of complications, the surgeon then ties off and divides the group of veins that lie atop the prostate and urethra. Next, the surgeon divides the urethra, taking care to avoid the urethral sphincter muscles in order to preserve urinary continence.

At this point, the “nerve-sparing” aspect of the procedure begins. The tiny nerve bundles on either side of the prostate are required to produce an erection. The prostate is delicately separated from these nerves, leaving them intact (unless the cancer is suspected to have spread to these nerves, in which case they will be removed with deliberate precision).
The surgeon then dissects out the seminal vesicles beneath the bladder and separates the prostate from bladder neck (the junction between the bladder and the prostate) removing the entire gland.

Finally, the bladder neck is shaped to match the urethra and reconnected to it. A Foley catheter is inserted through the urethra to drain urine from the bladder. The catheter is left in place for about one week to allow the rebuilt urinary tract to heal.

For men found to have cancer confined to the prostate (stage T2) that is not high grade, the chance of a detectable PSA level indicating residual cancer 10 years after treatment is around 10%. A detectable PSA (biochemical recurrence) indicates the presence of residual prostate cancer months to years before the cancer would be visible on a CT or bone scans.

Patients and doctors alike ask me a variety of questions about surgery for organ-confined prostate cancer. To follow are some of the most frequently asked questions about the surgery, choosing a surgeon, post-treatment quality of life, sources of support, and more.

Q. When you have a consult with a potential surgical patient, do you place more emphasis on the doctor’s skill, or on the particular procedure that will be used?

A. If they have decided on surgery, I tell them that their most important consideration should be finding a surgeon who is deeply interested in prostate cancer, and who has spent a considerable amount of time learning about the disease and how to treat it. This should be a doctor who performs prostatectomies with some frequency. That is far more important than focusing on whether the surgeon uses a scalpel, robot, or laparoscope to remove the prostate.

At this point, we really have no meaningful data indicating that one approach versus another is going to result in a better outcome.

Bottom line: Find someone who does this surgery all the time. If you feel that you can develop a relationship with this physician, and you have confidence in your surgeon’s skills, you will ultimately be satisfied with the outcome.

Virtually everyone who has this operation experiences some impact on his quality of life. However, I have found that patients who have less than perfect outcomes—those who dribble a little urine when they cough or have less than perfect erections—are nonetheless happy with the results if their physicians truly care about them, answer all of their questions, and counsel them on their concerns.

Q. How can you find out if a doctor is competent and caring?

A. Doctors have reputations. You can’t be a non-caring physician for very long before word gets out about your attitude or skills.
The figures are disquieting: It’s now estimated that 25% of American surgeons performing radical prostatectomy surgery perform only one procedure a year, with 80% of surgeons performing 10 or fewer. Nationally, only 2% of surgeons perform more than 50 procedures per year.

When it comes to prostate cancer surgery, experience does count—a lot. According to a study published recently in the Journal of the National Cancer Institute, prostate cancer patients treated by highly experienced surgeons are much more likely to be cancer-free five years after surgery than patients treated by surgeons with less experience.

Several studies have examined the relationship between surgical experience and patient outcomes. However, it is often unclear whether the findings are related to differences in surgical technique or to differences in clinical variables or tumor characteristics. In one study, however, authored by Andrew Vickers, Ph.D., Associate Attending Research Methodologist, Memorial Sloan-Kettering Cancer Center in New York, the investigators made a statistical adjustment for cancer severity. In this way differences among surgeons were likely to reflect differences in their technique rather than just differences in the patients they saw.

The researchers analyzed the cancer outcomes of 7,765 prostate cancer patients who were treated with radical prostatectomy by one of 72 surgeons at four major American medical centers over a 16-year (1987-2003) period. Sophisticated statistical models were used to evaluate the link between the total number of prostatectomies performed by the surgeon prior to each patient’s operation and biochemical recurrence of prostate cancer. Recurrence was defined as a rising PSA level of more than 0.4 ng/mL.

The results after five years:
- The risk of recurrence was 18% for patients treated by surgeons who had performed 10 operations.
- The risk of recurrence was 11% for patients treated by surgeons who had performed 250 operations.

This means that patients treated by inexperienced surgeons were nearly 70% more likely to have a recurrence of their prostate cancer than those who were treated by surgeons with greater experience. In other words, 1 out of every 14 patients treated by an inexperienced surgeon will have a recurrence.

The results were described in terms of a learning curve, which showed a dramatic improvement in cancer control with increasing surgical experience up to 250 prior operations; however, there was no large change in recurrence rates with additional surgical experience.

“Our results provide support for what other studies have implied—that good technique is learned and increased volume leads to improved outcomes,” says Dr. Vickers.
Q. Is it okay to ask a doctor if you may speak to some of his patients about their surgical experience?

A. Of course. I actively encourage it with my patients. Back in 1993, I had a patient from Greece in his forties who was absolutely terrified at the prospect of surgery. I had never in my life met a patient who was this fearful. He was shaking and so scared that I actually thought he might have to be put on suicide watch. It finally dawned on me that the one thing that would help him most was to speak to someone who had already gone through the operation. I phoned a patient I had operated on the week before and he readily agreed to speak to this man.

Following the surgery, the patient readily admitted that nothing meant more to him than speaking to someone who had the surgery. It’s the only thing that could have calmed him down and allowed him to go through with it. It was at that point that I decided to ask all of my surgical patients to leave their contact information if they would be willing to speak to potential patients in the future. I now give prospective patients a 19-page list of contacts spanning the past 17 years. This list includes each patient’s age, occupation, and home and work phone numbers. I don’t know whether these men have had perfect outcomes or not. The only thing I am certain about is that they will relay their experiences about the surgery and about me, which in turn will give the prospective patient a realistic expectation of the whole experience.

Q. Is the volume of surgeries the single best indicator of a surgeon’s abilities?

A. It’s not totally clear. There are surgeons who can do thousands of prostatectomies and still not be very good at it. Then there are those who have done hundreds and are extremely gifted surgeons. That said, I would not want someone to operate on me if he had only done 50 or so procedures. I would seek out a doctor with a stellar reputation who had hundreds, at least, and preferably a top doctor who had done thousand of surgeries.

Q. Regarding regular surgery versus robotic or laparoscopic procedures, what are the advantages of the surgeon’s being able to feel the prostate with his hands when performing a radical prostatectomy?

A. Tactile feedback is not about feeling a node or bump on the prostate but about sensing consistency of tissues, of understanding the adherence and integrity of those tissues. Surgery is all about being able to separate one tissue from another, and they don’t all separate that easily. If there is cancer infiltrating into a section of tissue, it can make two tissues adhere to each other. If the surgeon doesn’t get a sense of that, he could tear two contiguous tissues, or the prostate itself. Tearing the prostate can leave prostate tissue behind and this can lead to a detectable PSA and another treatment at some time in the future.
Robotic surgeons will tell you that they can see the tissue as they operate and over time they develop a special “feel” that alerts them to tissue adherence, indicated by how the robotic arm reacts when they move it. Perhaps very talented robotic surgeons can indeed do this.

Q. What are the possible complications of open surgery for prostate cancer?

A. Rare complications of radical prostatectomy at the time of surgery include damage to the rectum or ureter (the tube carrying urine to the bladder from the kidneys) and the surgical and anesthetic risks that accompany any operation. Postoperatively, narrowing of the urethra (urethral stricture) by scar formation can cause a decrease in the force of the urinary stream or cause urinary retention. This is most likely to occur between one and three months after surgery.

Q. How long does it take to perform an open prostatectomy?

A. Last week I had a surgery that took an hour. The man was not large and he had a wide pelvis, plus a venous anatomy that was favorable, so the surgery went very smoothly. On average, however, my surgeries take about 90 minutes from beginning to end. There are certain factors, such as patient anatomy and weight that can affect surgical time. In general, a “pear-shaped” man—someone who carries most of his body fat around his hips, thighs, and buttocks—will pose the most difficulty, as will the obese patient.

While weight is a factor, I have operated on obese patients and the operation was relatively easy, while some operations on slender patients have proven particularly challenging. That’s because consistency of tissue is also a consideration. Some people have naturally stiffer or stickier tissue than others, which makes it more difficult to work with. Some have more veins overlying the prostate, which may cause more bleeding and this can also add time to the operation.

Pelvis size is also a consideration. A man’s pelvis is not as wide as a woman’s and it is harder to get in and operate whether laparoscopically or open. A man with a small pelvis and a prostate that is tucked deep underneath the pubic bone can present certain obstacles for the surgeon, whether the prostatectomy is performed open or with robotic assistance.

Q. What is the usual time frame from check-in to checkout for an open prostate surgery patient at Johns Hopkins?

A. The patient typically comes in the early morning and then leaves late the following day.
Edward James Wright, M.D.
Director of Neurourology and Chief of Urology at Johns Hopkins Bayview Medical Center

When Johns Hopkins surgeon Dr. Hugh Hampton Young pioneered the radical prostatectomy in 1904, he removed the prostate through a small incision in the perineum, the small area between the anus and the scrotum. He did this because of the advantages offered by this approach: Less bleeding and better access to the prostate, which is located just beneath the perineum.

This surgical approach remained the standard for many years because of its clear benefits: cancer outcomes were very good; it was a relatively minimally invasive procedure; blood loss was not excessive; the return to continence was fast; and recovery and return to activities of daily living were rapid. The major drawback to the perineal radical prostatectomy: It is extremely difficult to preserve erectile function when the surgery is performed through the perineum.

Following the introduction of the nerve-sparing radical prostatectomy by Dr. Patrick Walsh in the early 1980s, many surgeons abandoned the perineal approach and adopted this innovative technique in which the prostate is approached through a large incision made in the abdomen. With that said, the perineal approach still can benefit a specific patient population. Any man who does not stand to benefit from nerve sparing is an ideal candidate. A morbidly obese patient is also ideal: When it is unfeasible to operate using

**Q.** When the patient lives far from Johns Hopkins, what do you do about catheter removal?

**A.** For the past several years, we have been letting out-of-town patients take out their own catheters, if they so choose. We instruct them how to do it and also have a nurse available to guide them through it on the phone. Otherwise, they can have a local urologist or family doctor assist them.

**Q.** When can a patient return to work after an open prostate procedure?

**A.** I tell patients that while the catheter is in place, they are better off working from home. Once the catheter comes out, most men tell me they are back at work in an office setting about 15 days after surgery.

**Q.** When does post-surgical PSA testing begin?

**A.** After radical prostatectomy, PSA testing is performed to evaluate the success of the

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**THE PERINEAL APPROACH TO PROSTATECTOMY**

Edward James Wright, M.D.
Director of Neurourology and Chief of Urology at Johns Hopkins Bayview Medical Center

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the trans-abdominal approach because of the patient’s extreme girth, the perineal approach makes the procedure much easier to perform. Finally, men who have had kidney transplants or any type of abdominal wall reconstruction would benefit from the perineal approach if a surgeon were leery about going through the abdomen to reach the prostate.

When compared to the other radical prostatectomy approaches, the oncology outcomes and continence rates of perineal approach are comparable. Recovery from perineal prostatectomy is quicker. Patients reliably go home after breakfast the morning after the procedure; some doctors actually perform these surgeries as outpatient procedures. The surgery is associated with the quickest return to normal activities of any prostate surgery. When questioned afterwards, some men admit that they didn’t even feel that they had surgery.

I liken this surgery to building a ship in a bottle: with little space to operate in, it can be really challenging. Moreover, if not done properly, it can cause a variety of rectal injuries, including the creation of a fistula between the urethra and rectum. This injury will cause the mixing of stool with urine, a complication that needs to be corrected with additional surgery.

Therefore, if you decide to explore the perineal radical prostatectomy as an option, you need to find a doctor who is familiar with performing the procedure—a challenge, since there are not many surgeons who practice it. But it is offered at some hospitals and institutions, including here at the Brady Urological Institute at Johns Hopkins.
Q. What makes the prostate cancer program at the Brady Urological Institute at Johns Hopkins such a national standout?

A. For starters, although we perform more prostate surgeries than most institutions in the country, we are not a “mill.” Our focus is on patient care, with one doctor working with one patient. It’s not uncommon at other large centers for one surgeon to have two or three surgical rooms going at the same time: A surgeon will do a critical part of the prostate surgery in one room and then walk to the next room to perform a critical part of the procedure on another patient, leaving it to other doctors to finish up the surgeries.

If you hear some patient brag that his surgeon is doing 8 to 12 prostatectomies a week, that is a good indication that the surgeon is not spending a whole lot of time in the operating room with the patient or with any follow-up care. It’s hard to do that many surgeries and provide any personalized care. That is not the approach at Johns Hopkins. That’s just not part of our culture, and it’s part of the reason that we have such an outstanding reputation.
Robotic-Assisted Radical Prostatectomy

Mohamad E. Allaf, M.D.

Technology has long been a part of medicine, and prostate surgery is an outstanding example of how technology is making positive inroads. The introduction of the da Vinci robot more than a decade ago has taken the radical prostatectomy to a new level, allowing the surgeon to perform the operation with great precision and ease. Most major medical centers nationwide, and community hospitals as well, have da Vinci robots. Manufactured by Intuitive Surgical Corporation of Sunnyvale, California, these high-tech, big-ticket medical devices ($1.5 million, plus annual servicing and upgrades of more than $100,000) were first approved by the FDA in 2000 for use in surgical procedures.

Think of them not as the futuristic robots of Hollywood films but rather as high-tech mechanical “helping hands” that move precisely at the command of the surgeon. Many men now choose the robotic prostatectomy because they want a minimally invasive procedure that guarantees cancer cure, ensures minimal trauma, and allows them to get back to work quickly. With the robot-assisted surgery and its less invasive nature, many patients are ready to return to their regular schedules in a little more than two weeks.

Surgical Procedure

Before a robotic-assisted radical prostatectomy can begin, members of the surgical team first have to prep the patient. After the patient is anesthetized, his abdomen is inflated with carbon dioxide gas to expand the abdominal area and make it easy to manipulate the robotic arms within the body. Through “keyhole” incisions, six small tubes are placed in the abdomen through which the robotic arms, camera, and other laparoscopic tools can be inserted during the surgery. Once all this is taken care of, the robot

The surgeon sits down behind the highly sophisticated da Vinci console, which is situated a few yards from the operating table. Slipping on his finger controls, he looks into the eyepieces, which provides a stunningly clear 3-D view inside the patient’s abdomen, at twelve-fold magnification. Cables snake along the floor from the console to the mechanical parts of the da Vinci; its 18-inch robotic arms are positioned directly over the patient. Assistants direct these arms through the tubes leading inside the patient’s abdomen, and the surgery begins.
As the surgeon peers into the monitors, the robotic arms replicate the movements he makes with his fingers, wrists, and foot controls. Another surgeon or a physician’s assistant manipulates laparoscopic tools in the patient, assisting as the surgeon controlling the robot as it dissects and cuts away tissue to free the prostate from the bladder. Highly trained surgical nurses are also part of the team; they prepare the miniature tools and sutures that are inserted and removed from the patient’s abdomen during the course of surgery.

The million-dollar robot rechecks the position of the surgical instruments 1,500 times a second as the surgeon delicately cuts tissue. Great use is made of the robotic arms, with their mechanical “hands” that revolve a full 360 degrees within the body: they are used not only to cut tissue, but to stop bleeding and grasp tissue, lymph nodes, and seminal vesicles over the course of the prostatectomy procedure. The camera inside the abdomen sends back highly detailed color images to the surgeon’s console, providing a detailed view of delicate structures surrounding the prostate gland (nerves, blood vessels, and muscles), thus allowing for optimal preservation of these vital structures.

When the cancerous prostate gland is finally detached from the bladder and urethra, it is placed in a small plastic bag that is removed at the end of the operation by slightly extending the incision at the patient’s navel. The surgeon finishes his work by manipulating the robotic arms to suture the bladder and urethra to restore continuity of the urinary tract.

Just as in laparoscopic and open radical prostatectomy, a Foley catheter is placed through the penis to drain the bladder and allow healing of the bladder-urethra connection. A small drain is placed around the surgical site, the tube exiting one of the keyhole incisions, and the patient is then prepared to go to the recovery room. Up and walking early the next day, patients are typically discharged that afternoon.

Proponents of robotic-assisted laparoscopic radical prostatectomy firmly believe that this minimally invasive form of nerve-sparing surgery not only offers results comparable to those achieved with the traditional open procedure performed with a scalpel, but also leads to faster recovery with fewer complications for the patient.

*Now offered in hundreds of hospitals nationwide, the robot-assisted radical prostatectomy, which is performed through multiple small incisions, can potentially result in quicker recovery, less postsurgical pain, and a quicker return to everyday activities. To follow are the questions I am most frequently asked by patients and doctors about the procedure.*

**Q.** When it comes to prostate surgery, is the robotic-assisted procedure better than the traditional open surgical procedure?

**A.** For me, the most important factor for treating prostate cancer is the surgeon you choose and not the approach that is taken to remove the prostate. Whether it’s an open, laparoscopic, or robotic procedure, the underlying principles and goals of the surgery are all the same.
Prostate surgery is only going to be as good as the surgeon who performs it. If you have a surgeon who is inexperienced, then your outcomes following surgery may be suboptimal regardless of which method you choose. Likewise, in experienced hands, excellent and comparable outcomes can be achieved regardless of surgical approach, whether it is open, laparoscopic, or robotic-assisted prostate surgery.
Choosing the Right Treatment for Prostate Cancer

robotic-assisted. Now, if you want to know if one procedure is better than the other, the fact is that no one can say, simply because we don’t have any good studies comparing one procedure to another. Yes, there are studies from robotic surgeons showing excellent results, and there are also studies from open surgeons showing great results.

We know that blood loss is likely to be less with robotic procedure, but beyond that, nothing has come out in the scientific literature to indicate that one is superior to the other when performed by experienced doctors at high-volume medical centers. What I tell prospective patients is that I don’t see any difference between open and robotic prostatectomies. Therefore, the goal of each patient is to find a surgeon who can achieve good results with the surgical approach with which he/she is most comfortable.

Q. Since a doctor needs to perform many procedures to gain experience with a surgical robot, how many are needed for absolute competence in a prostate procedure?

A. There is a definite learning curve for robotic-assisted surgery just as there is for open surgery. While that number is variable when it comes to robotic prostatectomies, you really want someone who has performed at least 150 procedures. This is probably a doctor who does at least two robotic-assisted procedures a week.

Q. What makes the prostate cancer program at Johns Hopkins different from other academic centers?

A. Drawing on exceptionally brilliant and dedicated people, and our outstanding accomplishments in the research field, the Brady Urological Institute is the international leader in urology and for the past 20 consecutive years has been named the #1 urology department by U.S. News & World Report. Whether it’s developing a new therapy, fine-tuning an improved surgical technique, discovering a cure for a disease, or seeking better ways to educate patients, every time we set out to do something—through careful observation, study, and detailed research—we are envisioning how improvements can be made.

Our team is a multidisciplinary one, drawing on all areas related to prostate cancer—be it the best surgeons, the most caring nurses, and accomplished pathologists, to name a few. Optimal care starts with an excellent surgeon but it is only complete with an all-star team such as the one that we have at Johns Hopkins.

When it comes to minimally invasive surgery, we have been using a robot here since 2001. We were one of the first institutions in the country to have the robot, and Johns Hopkins scientists were involved in the earliest studies related to this technology. More important, we are not merely satisfied with offering robotic surgery, but we are constantly looking for ways to improve upon the status quo. For example, we are now involved with some exciting projects to enhance the capabilities of our two new “SI” model robots, which are even more sophisticated than the original.
In an effort to further improve the surgical outcomes of the da Vinci robot prostatectomy, Hopkins experts are trying to determine whether the introduction of the TRUS Robot, a special robot (created by Dan Stoianovici, Ph.D., Professor and Director of the URobotics Program at Johns Hopkins, and his team) handling a transrectal ultrasound probe (a special device inserted through the rectum that creates pictures of the internal organs using sound waves), can enhance viewing of the prostate and adjacent blood vessels for the surgeon.

“Last year, we tried the tandem robot approach in a limited feasibility study,” says Misop Han, M.D., an Associate Professor of Urology and Oncology at the Brady Urological Institute, and an expert in all forms of prostate surgery. “The study showed that the da Vinci robot and the TRUS Robot can be used safely and concurrently during radical prostatectomy. From the data using the TRUS Robot, we were able to generate impressive 3-dimensional reconstruction images of the prostate gland. Then, using a Doppler ultrasound, we could visualize the blood vessels around the prostate gland. We believe that they correspond to the blood vessels of the neurovascular bundles that are responsible for penile erections.”

“ln theory, this dual robot approach will offer enhanced visualization and help the surgeon avoid the neurovascular bundle as he or she removes the prostate. Our hope is that this will result in better nerve-sparing, and consequently improved sexual potency preservation after radical prostatectomy.”

A new clinical trial that will eventually enroll 60 patients over the next two years has already started at Johns Hopkins. The goal is to test the feasibility and capabilities of the tandem robot approach. If you are considering robot-assisted radical prostatectomy and you would like to participate in this trial, please contact Dr. Han at 410-502-7454 or mhan1@jhmi.edu for further information.
Working together, surgeon Misop Han, M.D. and Dan Stoianovici, Ph.D., Professor of Urology and Mechanical Engineering, are now testing a robot designed at Johns Hopkins that can be used along with the da Vinci to transmit ultrasound images of the prostate to the surgeon as he operates (see page 43).

Another ongoing collaborative project involves technology known as ultrasound elastography. My hope is that this will eventually help the robotic surgeon develop “feel” during surgery. The open surgeon’s skill comes from years of experience, understanding where key veins, nerves, and other structures are. He relies on a headlight and powerful loupes (magnifying eyeglasses) to see everything clearly as he operates. He also depends on the “feel” of the tissues, as transmitted by his fingers.

Since we don’t have tactile feedback with a robot—we can’t feel with our fingers—I always say that we robotic surgeons make up for it with our improved visualization, and we use visual cues to make our decisions. We can also tell if some tissue is hardened or adherent based on how it reacts when we move it with a robotic arm. That all comes from the expertise of the robotic surgeon, which is one reason that it takes 150 cases or so for a robotic surgeon to achieve a high level of competence when performing prostate surgery.

Given that the robot does not have tactile feedback, one of the ideas we have at Brady is to replicate human touch through the use of ultrasound elastography. An advanced form of ultrasound, this technology helps the surgeon know where tissue is harder or more dense. Elastography imaging is noninvasive, relatively inexpensive, and does not expose the patient to radiation while giving the surgeon real-time information regarding the tissues on which he is operating.

Since cancerous tissue may be stiffer than normal tissue, elastography could help us make better intraoperative decisions. My collaborations with Emad Boctor, Ph.D., an engineer in the division of Medical Imaging Physics at Johns Hopkins, have resulted in encouraging preclinical results. Once we have completed our testing, our hope is to be able to integrate a measuring device into one of the robotic arms so we can “feel” for hardness of prostatic tissue as we operate with the robot.

Q. What is the greatest benefit of robotic prostatectomy for you as a physician?

A. I would have to say it’s the dexterity and precision that I can achieve with the robot, no matter what the anatomy of the patient is like. Because the prostate sits deep in the pelvis underneath the pubic bone, it can be challenging with open surgery—especially in overweight patients—to get the exact angle you need. With the robot, however, you have seamless access to every area.

With the sophisticated “wristed” technology located at the tips of the tiny robotic instruments, I am able to work in the abdomen just as if I had my hands in the patient’s body. I can easily turn the various cutting devices and dissecting instruments up and down, side to side, and in and out
with this robotic technology. The ability to move the robotic arms 360 degrees in all directions allows me to dissect with more ease—and with absolutely no tremor in the instruments.

**Q. What are the potential risks and complications of a robotic-assisted prostatectomy?**

**A.** Although the robot-assisted radical prostatectomy procedure has proven very safe, any surgical procedure involves risks and potential complications. The safety and complication rates are similar when compared to the open surgery. Potential risks may include:

**Bleeding:** Blood loss during this procedure is relatively low compared to open surgery, and it is not necessary to donate your own blood prior to surgery.

**Infection:** All patients are treated with intravenous antibiotics before surgery to decrease the risk of infection within the urinary tract or at the incision sites.

**Adjacent tissue/organ injury:** Although uncommon, possible injury to surrounding tissue and organs including the rectum and ureter may occur. Transient injury to nerves or muscles can also occur related to patient positioning during the operation but these are exceedingly rare.

**Hernia:** Wound separation and hernia formation are rare following robotic surgery given the size of the incisions and the fact that these are closed under direct vision. Some patients, such as those with diabetes or those taking steroid medications, can heal poorly and are at possible higher risk for developing a hernia somewhere down the road. As a precaution, I advise my patients not to exert themselves or do any heavy lifting for four weeks after surgery.

**Conversion to open surgery:** The surgical procedure may require conversion to a pure laparoscopic procedure (performed without the robotic system) or even to the standard open operation if extreme difficulty is encountered during the robotic procedure (a mechanical failure, for example). While rare, it is important to choose a center where surgeons are familiar with all approaches to prostate surgery.

**Urinary incontinence:** As in open surgery, urinary incontinence can occur following robotic prostatectomy; it often improves over time with the use of Kegel exercises, which help strengthen the urinary sphincter muscle.

**Erectile dysfunction:** As in open surgery, a nerve-sparing technique is attempted during robotic dissection of the prostate gland in appropriate candidates. The return of erectile function following radical prostatectomy is a function of the age of the patient, his degree of preoperative sexual function, the technical precision of the nerve-sparing technique, and how much time has elapsed since the surgery.
Urethrovesical anastomotic leakage: There can be small urinary leakage at the connection between the bladder and urethra following both open and robotic prostatectomy; this often resolves without further intervention within a few days to a week. The urinary catheter will remain in place until the leakage has stopped.

Q. How long is hospitalization following the robot-assisted prostatectomy?

A. At Johns Hopkins, the length of hospital stay following a robotic procedure is one to two days for most patients.

Q. What is the post-operative pain level after a prostatectomy performed with a robot?

A. While patients are given a prescription for narcotic pain medication, most transition to extra strength Tylenol shortly after being discharged from the hospital. Some patients may experience minor transient shoulder pain related to the carbon dioxide gas used to inflate the abdomen during the surgery. Bladder spasms are commonly experienced as a moderate cramping sensation in the lower abdomen or bladder and are quite common after prostatectomy. These spasms are usually transient and will normally decrease over time. If they are severe, medications can be prescribed to ease the spasms. Transient nausea, usually related to the anesthesia, may be experienced during the first 24 hours following surgery. Medication is available to treat persistent nausea.

Q. How long will a catheter be required following a robotic procedure?

A. You can expect to have a urinary catheter (Foley) draining your bladder for approximately one to two weeks after the surgery. The device is inserted while the patient is still in the operating room under anesthesia. In addition, a pelvic drain is placed to drain the pelvic space around the bladder-urethra anastomosis. This drain is usually removed prior to discharge form the hospital.

Most men will have some initial difficulty with urinary control at the time the catheter is removed. Therefore, it's advisable to have a small supply of insert pads that can be purchased at any pharmacy. Once your catheter is removed, it is recommended that you avoid caffeine, alcohol, and excessive fluid intake for one to two months to minimize incontinence.

Q. Once home from the hospital, when can a patient resume normal activities?

A. At Johns Hopkins, we urge our robotic-assisted prostatectomy patients to adhere to the following guidelines regarding activity, toileting, medication, and bathing:

Activity: Your physical activity is to be restricted, especially during the first two weeks home. During this time, use the following guidelines:
• Take six to eight separate short walks a day to prevent blood clots from forming in the legs or pneumonia in the lungs.
• Climbing stairs is permitted if necessary but should be taken slowly. Climbing stairs is otherwise not a necessary activity in terms of exercise.
• No lifting heavy objects (anything heavier than 10 pounds).
• No driving for at least one week following surgery, and you should limit long car trips, even as a passenger. On longer rides, you should get out and walk around every hour to prevent blood clots from forming in your legs.
• No strenuous exercise for four to six weeks. Following this, patients can return to their normal activities.

Eating: You may return to your normal diet immediately upon discharge from surgery. However, it’s a good idea to eat foods that are relatively low in fiber, such as white rice, soups, and pasta, because your intestines may take up to a week to recover from the surgery and anesthesia. Because the lining of your bladder and urethra will be raw after surgery, you may find that alcohol, spicy foods, and caffeinated drinks cause some irritation or a feeling of needing to void despite the fact that the catheter is emptying your bladder.

If these foods don’t bother you, however, there is no reason not to consume them in moderation. It’s important to keep your urine flowing freely. Drink plenty of fluids (8 to 10 glasses) during the day. The type of fluid (except alcohol) is not as important as the amount, but plain water is best.

Bowels: It should take two to four weeks for your bowels to return to normal after the surgery, although pain medications can cause constipation and therefore should be discontinued as soon as possible. The rectum and the prostate are next to each other, so any very large and hard stools that require straining to pass can cause bleeding in the urine. Use a mild laxative (e.g., Milk of Magnesia) or stool softener (e.g., Colace) if needed, and call your doctor if you’re having problems.

Medication: You should resume your pre-surgery medications unless told not to. We recommend staying off aspirin or aspirin-containing products until after the catheter comes out and at the discretion of your surgeon. Your doctor will probably give you a prescription for narcotic pain pills for incisional discomfort. Once back at home following robotic prostatectomy, most men rely only on extra-strength Tylenol and do not require narcotic pain medication. You will also be given a prescription for an antibiotic (currently we prescribe Ciprofloxacin) to take around the time the catheter comes out. Typically, it will be a three-day course of antibiotics, which you will start the day before your catheter is to be removed.

Bathing: You may shower once you’re at home. If your wound sites get wet, they must be patted dry. Tub baths can soak your incisions; they are not recommended in the first two weeks after surgery. You will have adhesive strips across your incisions, and these will probably fall off on their own; if they don’t, you can remove them in five to seven days.
LAPAROSCOPIC RADICAL PROSTATECTOMY

Christian P. Pavlovich, M.D.

In 1989, the first laparoscopic cholecystectomy (removal of the gallbladder) was successfully completed; the surgeon used miniature tools attached to long rods, manipulating them through very small “keyhole” incisions instead of the 10-inch abdominal incision required for conventional surgery. The smaller incisions offered cosmetic advantages (the wounds heal with almost no visible scar), and many experts felt that there would be less blood loss and a quicker return to normal activities.

Since then, there has been a decided move to perform all types of surgeries utilizing minimally invasive laparoscopic techniques, and it wasn’t long before many urologic surgeons began to explore the approach, developing laparoscopic skills initially targeted toward the upper urinary tract, specifically the kidney and ureter.

Laparoscopy (from the Greek words lapara, or flank, and skopion, a means of viewing something) is a type of surgical procedure in which small incisions are made and plastic tubes (ports) are inserted into them to keep the channel open so that tools—including surgical instruments and the viewing tube (laparoscope) with its mini-camera—can be inserted. With the abdomen inflated slightly with carbon dioxide, organs can be pushed out of the way for access and better vision, allowing the surgeon to work while watching an external video monitor that shows exactly what’s going on in the patient’s body.

The tools can be manipulated to make necessary repairs, just as if the abdomen had been cut open the old-fashioned way. Minimally-invasive surgery has evolved over the years since its first use in gallbladder, liver, and kidney procedures, and the technique is now applied to radical prostatectomy at Johns Hopkins and other American institutions.

Laparoscopic prostatectomy was first performed by William W. Schuessler, M.D., at Southeast Baptist Hospital in San Antonio, Texas, in 1991, and was later refined and popularized in France in the late 1990s. In the 2000s, the da Vinci robot was applied to laparoscopic radical prostatectomy, allowing the control of several of the laparoscopic instruments remotely and offering 3-D visualization. The surgery is typically performed through four or five 1-centimeter “keyhole” incisions (each about the size of a dime) made across the mid-abdomen. Through these entry points, the surgeon uses fine laparoscopic instruments to precisely dissect the prostate gland, seminal vesicles, and vasa deferentia from the urethra and bladder.
A remotely-controlled stabilizing arm is used to control the telescopic lens that goes into the body. This high-powered lens is attached to a camera that projects images onto a video monitor. Although depth perception is lost because the images are displayed on a two-dimensional screen, this projection provides the surgeon with excellent visualization and details of the prostate gland and the surrounding neurovascular structures, allowing for precise removal of the prostate and suturing of blood vessels.

The advent of high-definition video and larger flat screen monitors that can be manipulated onto the operative field has greatly enhanced the optics of pelvic laparoscopy. Although it is performed laparoscopically, the surgery adheres to the same anatomic principals of the nerve-sparing open surgery perfected by Dr. Patrick Walsh, but without the surgeon’s hands ever entering the patient’s body.

Once the prostate gland is free from the bladder, rectum, and urethra, it is placed in a small plastic bag and is later removed by extending one of the keyhole incisions to accommodate it. The bladder is carefully sewn back to the urethra, using laparoscopic suturing techniques inside the body, to restore continuity of the urinary tract while maintaining as much healthy tissue as possible at the urethra and bladder outlet.

Finally, a Foley catheter is placed through the penis to drain the bladder and allow healing of the bladder-urethra connection. In addition, a small drain is placed around the surgical site, exiting one of the keyhole incisions.

Here are the questions I’m most frequently asked on the topic of radical prostatectomy performed minimally invasively—laparoscopically or robotically.

Q. When you meet with prospective patients, which procedure do you offer them?

A. Surgeons typically recommend what they do best. If I were asked what I do best, what I prefer, or what I think is the best procedure for prostate cancer in my hands, I will say laparoscopy. To date, I have done about 1,000 radical prostatectomies, using the open procedure, traditional laparoscopy, or a da Vinci robot. However, the majority of my work has been done with a laparoscope.

The laparoscopic radical prostatectomy program at Johns Hopkins was initiated in 2001. I routinely perform four laparoscopic prostatectomy procedures per week and currently use the da Vinci robot for about half of my cases.

Traditional laparoscopic prostatectomy without the use of a robot is a surgical art that is slowly being lost because of the relative ease of learning how to perform the surgery with a robot. In addition, with no industry support behind traditional laparoscopy, fewer surgeons are learning how to operate on the prostate with a laparoscope. That said, there are definite advantages to this approach.
Q. Who are the best candidates for a minimally invasive laparoscopic radical prostatectomy?

A. Most men who are considered candidates for open surgery are also good candidates for a minimally invasive approach with the laparoscope. Patients with a history of prior abdominal and/or pelvic surgery, large prostate glands (i.e., over 100 grams), or morbid obesity are often more challenging. However, these conditions are not contraindications to laparoscopy, and in my opinion patients with them are often better treated can be treated laparoscopically because I am able to place laparoscopic instruments outside of the abdominal cavity and into the space in front of the bladder, thus avoiding prior surgical incision sites, internal scars (adhesions), and the area where most men carry their excess fatty tissue. Staying out of the abdomen minimizes surgical risks to abdominal organs and the risk of postoperative adhesions, and allows for speedier return of bowel function postoperatively.

Q. What are the advantages of the laparoscopic approach to prostate surgery?

A. I find that this surgical approach offers a reasonable level of tactile feedback, which allows me to feel the prostate as I am working on it, while at the same time, allowing excellent visualization and minimal blood loss. The tactile feedback one gets using laparoscopic instruments is similar to that one might get using chopsticks, or a knife and fork—you can feel the difference between soft and hard tissue.

Moreover, when I am tying a knot with my laparoscopic hand-held instruments, I can get a good feel for the tension I am applying; the tools are an extension of my hands. However,
when I tie a knot using a da Vinci robot, it’s easier to tear a stitch, not tie it tight enough, or tie it too tightly since only visual cues are afforded the surgeon. There is no subjective feeling of tightness or knot strength because I am looking at a screen and watching the knot come together rather than feeling it and seeing it come together. It takes many cases to gain true proficiency with the da Vinci where one can confidently operate solely using visual cues.

**Q. Is there blood loss with a laparoscopic procedure for prostate cancer?**

**A.** When performing laparoscopic or robotic surgery for prostate cancer, I have not transfused a patient with any kind of blood product since 2003. That is probably some kind of national record. When the procedure is done properly, you just don’t encounter bleeding. Patients benefit because they are not going home anemic nor being asked to donate blood for themselves preoperatively, saving time and money.

**Q. How long does a laparoscopic radical prostatectomy take to complete?**

**A.** I am not after speed records. When I operate, I typically perform two surgeries a day, and my average surgical time is somewhere between one hour and thirty minutes and two hours and thirty minutes. The duration of the operation does vary based on a variety of factors, including a patient’s weight, and the size and shape of their prostate and adjacent organs.

**Q. How long is hospitalization following a laparoscopic radical prostatectomy?**

**A.** Hospitalization usually lasts one day with minimally invasive laparoscopic techniques, including laparoscopic and robot-assisted radical prostatectomy. Patients are able to walk the night of their surgery under their own power and are almost always ready to go home 24 hours after surgery.

**Q. How long will a patient require a bladder catheter following a laparoscopic radical prostatectomy?**

**A.** Removal of the catheter is dependent on a surgeon’s particular preference. In general, however, because of the excellent visualization offered by minimally-invasive techniques, a water-tight connection between the bladder and urethra can be achieved in most cases, allowing for safe and relatively early removal of the bladder catheter. In my practice, I leave a catheter in for approximately one week.

**Q. When can a patient return to normal activities following a laparoscopic radical prostatectomy?**

**A.** In general, most patients can return to desk work in two weeks, and to full activities by three to four weeks after surgery.
Q. What are the chances of urinary incontinence following a laparoscopic radical prostatectomy?

A. Most men experience at least some degree of urinary stress incontinence following any form of radical prostatectomy, including laparoscopic prostatectomy, typically when sneezing or coughing. This generally improves with time and with adherence to a routine of Kegel exercises. Within 6 to 12 weeks, the vast majority of men, particularly those in their 40s and 50s, have recovered urinary control. Older men have a slightly more protracted course, but nevertheless the vast majority recovers control within two to three months.

Q. What are the chances of a patient developing erectile dysfunction following a laparoscopic radical prostatectomy?

A. The return of erectile function is perhaps the most difficult outcome measure to predict. Many factors are involved in the return to sexual function following surgery, including:

- Age of the patient
- The quality of a man’s erection before surgery
- Having an active sexual partner
- The time since surgery was performed
- Whether one or both nerve bundles were spared during surgery

I am able to spare both nerve bundles, or at least a portion of both nerve bundles, in the vast majority of patients. I have found that judicious nerve-sparing or partial nerve-sparing does not lead to a higher rate of positive cancer margins, but on the other hand it does correlate both with recovery of erectile function and even to some degree of urinary control. Therefore, it is important in most men to try to preserve as much neurovascular tissue as possible unless cancer control considerations dictate otherwise.

I reassure patients that it often takes 6 to 18 months to regain optimal erectile function, and I recommend they resume an active sexual lifestyle as early as possible. I prescribe ED medicines like Viagra and Cialis for use as needed. My patients in their 40s and 50s tend to recover erectile function over time, some earlier than others. Patients of mine in their 60s and 70s generally have more difficulty, however, and typically only 50% to 70% recover functional erections two years after nerve-sparing laparoscopic radical prostatectomy.
TREATING PROSTATE CANCER WITH RADIATION THERAPY

On the pages that follow, some of the most respected medical specialists in radiation oncology at Johns Hopkins provide detailed, authoritative answers to the most frequently asked questions about the use of radiation for treating prostate cancer. Their expert advice will help guide you through all of the options and steps you will be facing when making your prostate cancer treatment decision.

Radiation therapy for prostate cancer has been available for almost a century—but you wouldn’t have wanted any part of the early therapies. The concept of treating prostate cancer with radiation was certainly innovative, but the results were far from acceptable. Thankfully, much has changed over the past decade.

Hugh Hampton Young, M.D., the extraordinary Johns Hopkins physician who on April 7, 1904 performed the first radical prostatectomy—one of the major surgical breakthroughs of the twentieth century—also experimented early on with radiation therapy as a means of eradicating prostate cancer.

Dr. Young placed high-intensity radium directly in the tissue surrounding the prostate, urethra, bladder, and rectum. Writing in the Journal of Urology, Dr. Young noted that radiation could shrink the prostate, and that the treatment produced definite cellular death. While his novel procedure was primitive and not completely successful in eradicating the cancer, the concept of killing cancer cells with radioactivity was certainly a sound one. It was now left to others to improve upon the technology, making it safer and more effective.

Achieving those goals has taken quite some time, in part because the initial low-energy radiation treatments were so ineffective and the side effects so devastating. It has taken more than half a century of slow, steady advances to reach a point where carefully calibrated doses of external beam radiation can be used to effectively kill prostate cancer cells and do so with minimal damage to the healthy urethra, rectum, and bladder.

Tremendous improvements have been made in external radiation therapy and the LINAC (linear accelerator) machine that delivers the beams of high-energy photons. Equipment capable of delivering radiation has been made even more powerful, and also more precise, thanks to the development of technologies that combine the latest in computer and imaging capabilities.
The integration of the latest technologies offers huge benefits to the prostate cancer patient that will truly improve his quality of life and increase the likelihood of cure.

Currently there are several types of radiation therapies in use: external beam radiation, with its various iterations, and brachytherapy, or internal radiation therapy.

**External Beam Radiation Therapy**

This treatment involves aiming high-energy beams precisely at the prostate from outside the body in an effort to shrink and ultimately destroy cancer cells. It is a treatment option for men with localized prostate cancer (stages T1 and T2) or locally advanced disease (stage T3). Although no randomized trial has directly compared radical prostatectomy and radiation, available evidence suggests that for men with cancer confined to the prostate, either approach offers the patient a good chance of being cancer free five to ten years after treatment.

Moreover, studies have shown that conventional-dose external beam radiation therapy coupled with hormonal therapy may prolong survival in men at increased risk for prostate cancer recurrence when compared with radiation alone. External beam radiation therapy is also used as a palliative treatment.

For a man with prostate cancer that has spread to the bones, radiation therapy can reduce pain and lessen the likelihood of bone fractures. It can also reduce neurological symptoms resulting from spinal cord compression when cancer has spread to the spine. Radiation oncologists have made a number of improvements in external beam radiation therapy in an attempt to increase cure rates and reduce the risk of complications. These improvements include three-dimensional conformal radiation therapy (3DCRT), intensity modulated radiation therapy (IMRT), and image-guided radiation therapy (IGRT).

**3DCRT (Three-dimensional conformal radiation therapy)**

Three-dimensional conformal radiation therapy (3DCRT) increases the potential of the external beam by maximizing the dose of radiation to the tumor while minimizing risk of damage to nearby tissue. This prostate cancer therapy was introduced in the U.S. in the late 1980s at the University of Michigan in Ann Arbor, Memorial Sloan Kettering Cancer Center in New York, and the Fox Chase Cancer Center in Philadelphia. This type of radiation delivery system, which uses a special computer program to plot radiation dosages, was revolutionary, and represented the most important technological advance in radiation oncology over the previous decade. No longer did medical physicists have to spend days performing extensive calculations in order to determine the course of radiation treatment for a particular patient. A computer now did the work, not only speeding up the planning process but also increasing precision in delivering the radioactive dose.
3DCRT precisely directs radiation energy into the body. With the advances in CAT (computer assisted tomography) scans and the ability to integrate information gained from these scans, oncologists were able to see both the prostate cancer and normal tissue in three dimensions, which was not feasible before. The radiation beams could be more accurately aimed to hit the cancer and avoid an even greater percentage of the healthy surrounding tissues. This allowed the use of higher radiation doses and led to decreased damage to the rectum, bladder, and large intestine—the sites that typically had been damaged with less precise equipment.

Conventional external beam radiation uses large, square beams. Formerly, the best that could be done was to focus the beam on the general location of the prostate. The treatment would deliver large and uniformly shaped radiation to the gland itself, but because of the shape and size of the beam, it would often also inflict unnecessary irradiation on nearby normal tissues.

The development of 3D CRT represented a huge improvement in radiation therapy. Each patient’s prostate is of unique size and shape. Each individual has a different extent of cancer, and in each man’s body, the nearby normal organs (bladder and bowel) are uniquely situated. The beauty of conformal radiation is that it can accurately determine this unique anatomy and then deliver radiation exactly where the individual patient needs it. Whereas conventional external beam therapy treated all prostates with the same big uniform beams, conformal radiation treats a round prostate with round beams and a sausage-shaped prostate with sausage-shaped beams.

**IMRT (Intensity-modulated radiation therapy)**

The next advance in delivering radiation—aided by even more sophisticated computer software and computer-controlled mechanical parts—was intensity-modulated radiation therapy, or IMRT. Relying on computer software to determine the orientation, number, and intensity of the radiation beams, IMRT is even more precise than 3DCRT.

What is so innovative about IMRT is that we can modulate the intensity of each beam during the therapy with a multileaf collimator. (This is a shutter-like attachment at the end of a linear accelerator that filters the radioactive rays; the longer a leaf stays open, the stronger the dose of radiation.) Using IMRT, we can treat specific portions of the prostate with higher or lower dosages in an infinite number of patterns.

With over 100 digital CT scans taken in a matter of minutes to create a 3-dimensional picture of the prostate tumor, we can now sculpt the dose of radiation even more precisely, delivering extremely high doses of radiation to within a millimeter of a cancer site. This maximizes the dose delivered to the thickest part of the tumor and minimizes the dose that affects the nearby healthy tissues of the bladder and rectum. The result is a higher cure rate and fewer side effects.
We always recommend that men considering radiation therapy for prostate cancer choose a facility that at least offers therapy using this advanced IMRT equipment.

**IGRT (Image-Guided Radiation Therapy)**

Radiation therapy for prostate cancer continues to evolve, and a lot of time and effort is being spent on research and development. We have recently entered into a new era of image-guided radiation therapy, or IGRT. Some refer to it as ART, which is short for adaptive radiotherapy, since the patient can be moved (adapted) so his anatomy is realigned and radiation correctly hits the target at every treatment session. Treatment can also be adapted if the patient loses weight, for example, which results in changes in anatomy and position.

<table>
<thead>
<tr>
<th>COST OF TREATING PROSTATE CANCER</th>
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<tr>
<td>According to the American Cancer Society, more than 217,000 men will be diagnosed with prostate cancer in the United States this year, and 30,000 will die. It's estimated that $3 billion will be spent on treatment for this cancer, the second most common cancer in men. Here is a breakdown compiled by Daniella Perlroth, M.D. from Stanford University of the comparative costs for treating prostate cancer over a two-year period:</td>
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<tr>
<td>Active surveillance .......................................................... $2,436</td>
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<tr>
<td>Radical prostatectomy ...................................................... $23,000</td>
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<td>Brachytherapy .................................................................. $29,000</td>
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<tr>
<td>IMRT .............................................................................. $50,000</td>
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<tr>
<td>Proton beam therapy ....................................................... $100,000</td>
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IGRT uses daily computed tomography (CT) scanning to create three-dimensional images that pinpoint the exact size and location of the tumor just before treatment. This information is then transmitted to a computer and allows doctors to compare the current image with earlier images taken the day before. During IGRT, doctors continually compare these images to see if the treatment area needs to be adjusted. Radiation specialists use IGRT to deliver more radiation to the tumor, ultimately leading to higher cure rate.

A good way to think about the differences between IMRT and IGRT is that IMRT allows the high-dose region to be individually shaped to “fit” the prostate, while IGRT enables the doctor...
to direct that high dose of radiation precisely to the intended location that day. Both therapies are used to achieve the best outcome with the least toxicity.

**Internal Radiation: Brachytherapy**

In brachytherapy, another type of radiation treatment for prostate cancer, 80 to 120 radioactive seeds (tiny metal pellets) are implanted directly into the prostate under ultrasound guidance. For several months, they emit a highly concentrated radiation dose. The pellets remain harmlessly in the body after their radioactive energy is spent.

The side effects of brachytherapy are similar to those of external beam radiation therapy—urinary and bowel problems—but these complications may occur more often with brachytherapy. Men with bothersome lower urinary tract symptoms are more likely to have worsening of these symptoms after brachytherapy when compared with other treatments. In addition, the radioactive seeds can migrate (rarely) to other parts of the body, such as the lungs, although research suggests that seed migration has no negative consequences.

A refinement of brachytherapy is high-dose-rate brachytherapy, in which radioactive pellets are delivered to the prostate via 25 hollow plastic needles. Over a 24- to 48-hour period, radioactive pellets are placed in the needles and then removed.

Available research suggests that outcomes are similar among men treated with either high-dose-rate brachytherapy or traditional brachytherapy. However, men treated with the newer technique experienced less urinary frequency, incontinence, blood in the urine, and rectal pain.

For more details about brachytherapy, please go to page 72.

There are other types of external and internal radiotherapy that are being used for treating prostate cancer. For information on proton-beam therapy, HIFU, CyberKnife, and cryotherapy, please go to page 68.

**Radiation Side Effects**

The complications of radiation therapy are primarily adverse effects on the urinary tract and bowel. These effects usually disappear days to weeks after treatment is completed.

The risk of long-term urinary complications, such as blood in the urine, bladder problems, or narrowing of the urethra, is about 8%. The risk of long-term rectal complications, such as rectal inflammation (prostates), bleeding, ulceration, narrowing, and chronic diarrhea, is about
A recent study reported that men who are treated with radiation therapy for prostate cancer have a higher risk of developing rectal cancer and should be monitored for the disease.

With radiation therapy, the risk of erectile dysfunction (ED) becomes more likely with time. In an analysis from the Prostate Cancer Outcomes study, 63% of men treated with radiotherapy had ED five years after the procedure. Younger men and those with normal sexual function before radiation therapy are the most likely to maintain potency, just as with surgery.

A post-radiation PSA level greater than 0.5 to 1 ng/mol strongly suggests that some cancer remains; rising PSA levels after radiation therapy are evidence of disease progression. If cancer recurs after radiation therapy, but there is no evidence of metastasis, some patients may benefit from removal of the prostate or from cryotherapy. Hormone therapy is used to treat recurrent disease at distant sites.

The following are the questions about radiation therapy that the experts at Johns Hopkins are most frequently asked by patients they counsel, and their answers to those questions.

Q. Who is the ideal prostate cancer patient for radiation therapy?

A. Anyone with prostate cancer is a candidate, no matter what his or her cancer diagnosis. The best candidates are men who are otherwise healthy and can benefit from definitive therapy. They should have an expected lifespan of at least 10 years, and be willing and able to come for therapy for six to nine weeks.

Most of the men we treat for prostate cancer at Johns Hopkins are in their 60s, whereas other centers around the country generally recommend radiation only for men in their 70s. Radiotherapy is not only for older men. This therapy can be effectively applied to men with prostate cancer at any age.

Surgery has typically been recommended for younger prostate cancer patients, those under the age of 70, with radiation reserved for the older man. There has been a sense in the prostate world that if a man has many more years to live, there is an intrinsic value in removing a cancerous organ so it can never regenerate more cancer cells. However, there is no data to support that contention—only a generalized gut instinct within the medical community. Younger men can greatly benefit from either radiation therapy or surgery for prostate cancer.

Since brachytherapy has a narrower selection criterion, there are two things radiation oncologists look at when considering possible candidates. First, they need to know the aggressiveness of the cancer. Brachytherapy works best for men with low- and intermediate-risk cancer. They should have PSAs less than 20 and a Gleason of 7 or less, and no higher than stage T2 cancer. Even though some experts say there is a role for brachytherapy for high-risk patients, these men are not ideal.
The ideal candidate also has prostate gland volume under 60 cc. Since the radioactive seeds can worsen urinary symptoms, the patient should not have preexisting urinary conditions, such as frequency, weak stream, or incomplete emptying.

**Q. How does radiation therapy actually kill cancer cells?**

**A.** The physics and biology of high-energy X-ray beams are now fairly well understood. Normal cells divide and replace themselves in an orderly process, keeping the body healthy and repairing structures as needed. However, cancer occurs when the cells lose the ability to control their own growth. They begin multiplying quickly, forming clumps called tumors, sometimes spreading to nearby tissues and organs as well as other parts of the body.

The classic theory of how radiation kills cells is that the radiation goes through the cancer cell, causing the formation of free radicals. These are molecules or atoms with a free electron that makes them react easily with other molecules. These molecules eventually cause the cell’s DNA to break into several pieces. Once their DNA is broken, the cells are eventually unable to divide naturally, so they die. The more modern thinking about radiation’s killing power is that, yes, radiation goes through the cells, damaging the DNA, but it also sends out a message to the cells that they are injured and therefore should undergo programmed cell death, known as apoptosis.

The mechanism by which radiation actually works to kill cancer may be a combination of these two concepts. That said, the actual dose of radiation that is delivered to cancer cells has a lot to do with who is cured of their cancer and who isn’t. High doses of radiation kill these cells or prevent cancerous cells from growing and dividing by damaging the DNA and chromosomes in the nuclei of the cells, causing the tumor to shrink and eventually die.

**Q. How are dosages for external radiation therapy patients determined?**

**A.** Your radiation oncologist and his team of specialists will determine the right dose of radiation for you based on the size of the tumor, the grade and stage of the tumor, and the proximity of the tumor to healthy tissue.

The best way to deliver radiation for treating prostate cancer is in increments, or fractions. Too much radiation at one time can cause irreversible damage to surrounding healthy tissue. Therefore, radiation doses are spread out over a period of several weeks, allowing the healthy noncancerous tissue a chance to heal after each treatment. Daily treatment lasts just a few minutes, and is typically repeated five times a week for seven to eight weeks.

Radiation is measured in units called Gy (pronounced “gray”), named for English physicist Louis Harold Gray. A man with prostate cancer is usually treated with a minimum total dose of 75 Gy, sometimes as high as 80 Gy, depending on the equipment. With IMRT and IGRT, the usual radiation dose is about 2 Gy per day over the course of the multi-week treatment.
period. Overall, it appears that everyone—low- and high-risk patients—benefits from higher dosages of radiation.

**Q. What are the problems associated with radiotherapy in the treatment of prostate cancer?**

**A.** Irradiation experts can guarantee the eradication of any cancer in the prostate if they can deliver enough radiation to the tumor. Saturation with one or several large blasts of radiation can certainly kill cancer, but it also kills healthy tissue adjacent to the tumor and can lead to very unpleasant side effects. However, delivering treatment in smaller bursts of energy, spread out over time, has proven to be the best way to kill prostate cancer and reduce side effects.

Most prostate cancer radiation patients today have few or no side effects from the therapy. Still, some have problems, ranging from urination difficulties to extreme rectal pain. We don't know why some men have these side effects and others don't. Why is it that one man's rectum or bladder tolerates the radiation without consequence while another man suffers severe side effects? We don't know, but with the advent of stem cell research and genomics, we are getting closer to coming up with the answers.

**Q. How difficult is it to deliver radiation to the prostate gland compared to other body parts?**

**A.** The prostate is relatively easy to irradiate because it is almost spherical. What makes it difficult, however, is that right next to the prostate are the rectum and bladder. Those structures demand critical evaluation during the treatment planning stage and their volume must be measured. The radiation oncologist must determine what portion of the rectum is actually near the prostate, and what percentage of the total dose of radiation it can receive without raising the risk of side effects. The same important questions have to be answered about the bladder.

In the world of radiation medicine, just about anyone can treat the prostate. However, calculating how the radiation should best be delivered to maximize radiation dose to the prostate, while also understanding the amount of radiation the other organs can tolerate on a daily basis, takes a large and talented radiation team, and they must give each case their focused attention. The challenges for the team are understanding the locations of the other organs—primarily the rectum—and being sure that they can clearly control the dose of radiation to the prostate. Accomplishing these things requires expertise that can be acquired only through years of study and practice.

**Q. What are the risks involved with radiation therapy for prostate cancer?**

**A.** There is the possibility that the radiation will not kill all the cancer cells, leading to an eventual recurrence of prostate cancer.
**Q.** How would you guide a patient in selecting external-beam radiation therapy, brachytherapy, or radical prostatectomy as a cancer therapy?

**A.** Johns Hopkins is not just a surgical center for prostate cancer; it is a multifaceted prostate cancer treatment facility. Patients with prostate cancer who come to Hopkins will hear about all the options we have, including external beam radiation treatment, brachytherapy, surgery (open, robotic, laparoscopic), and our active surveillance option, where no aggressive therapy is offered to patients who are monitored regularly over the year(s). Men with all stages of prostate disease are candidates for radiation therapy.

External beam has the broadest indications and eligibility criteria for patients with prostate cancer. For brachytherapy, the eligibility and indications narrow somewhat. Patients should not have a high degree of urinary symptoms, because that can lead to obstruction (temporary) after the treatment, with a negative impact on quality of life. We have reports of people with severe obstructive symptoms following brachytherapy needing to use a Foley catheter for several weeks.

There are two major considerations in selecting a treatment for prostate cancer. The first one concerns the patient’s particular tumor indices. We want to know the extent and aggressiveness of the disease, as measured by the current PSA level—and where it was a year ago. This will give us a sense of the pace of the disease. The Gleason score and clinical exam findings also play major roles; a very low Gleason score—6 or lower—means the cancer is probably very slow growing.

Also, in terms of the biopsy, how many biopsies were performed? What percentage of the biopsy cores actually had cancer cells?

When it comes to how many cores should be taken in a biopsy, a recent Journal of Urology study reports that 12 cores are optimal. Although 6 are an absolute minimum, we prefer to see between 10 and 16 cores taken during a biopsy. Now that doctors can inject the rectal wall with a local anesthetic prior to a biopsy, it is not at all an uncomfortable procedure for the patient.

**Q.** What are other factors that must be considered in making a treatment decision?

**A.** A patient’s overall health status must be considered. Diabetes and coronary artery disease put a man at higher risk for developing side effects from radiation therapy. Since he already has disease in the small vessels of the body, the addition of radiation will put him at slightly elevated risk of rectal bleeding and can also influence his ability to heal following radiation treatment.
Q. What happens during an external radiation therapy session?

A. You could compare an external radiation therapy session to getting a full-mouth x-ray from your dentist. The treatment is painless; the radiation is directed to your tumor from a machine located outside of your body. Several steps are needed to before you reach this point, however.

To ensure a high level of accuracy in delivering radiation to the prostate, the patient is first fitted with a custom-designed pelvic immobilization device. This will ensure that the man is in the same position when he lies on the treatment table for each daily session. When he is properly positioned, the radiation can be delivered exactly to its intended destination.

A CT scan is then performed with the patient in his immobilization device. The prostate gland is identified in three dimensions so treatment beams may eventually be directed at the prostate from multiple directions. Each beam is specifically shaped by the radiation physicists and other members of the team who help plan the radiation doses so that it conforms to the shape of the target as seen from any particular beam direction. Conformal therapy is thus fine-tuning the beam to the shape and size of the target while including a 5- to 10-mm margin of normal tissue around the prostate for safety purposes. When a patient comes in for his daily therapy, he simply lies on the treatment table for several minutes while his personalized dose of radiation is delivered.

Q. What is your definition of success with external radiation therapy?

A. PSA testing is the touchstone for determining success with radiation therapy. The tests are given every 3 to 6 months for the first several years after treatment. We want PSA to go under 1 ng/mol and stay there. If the PSA stays there for several consecutive measurements, then PSA is tested every 6 to 12 months. After several years of stable PSA levels, testing may be recommended on an annual basis.

Q. What’s your definition of a treatment failure for radiation therapy?

A. PSA should drop after radiation therapy—and this includes both external and internal radiation—although in many cases it may never become undetectable. This, however, does not mean that the cancer isn’t gone or that it is recurring.

Treatment failure, which means that the cancer has come back, is based on what is known as the Phoenix consensus. This is a definition of cancer recurrence following radiation therapy that was recently decided upon by radiation experts who met at a conference in Phoenix, Arizona.

According to the experts, treatment failure (they call it biochemical failure) is based on PSA nadir (the lowest PSA value ever obtained after radiotherapy, which could take upwards of 12 to 18 months to achieve) plus 2 ng/mol.
Here’s an example of the Phoenix definition of cancer recurrence following radiotherapy: The patient (PSA: 5.2 ng; Gleason 6 at diagnosis) had external radiation and his PSA eventually dropped to 0.5 ng/dL after 16 months, stayed at that level for three years, and then started to gradually rise. Using the Phoenix definition for failure, cancer recurrence would be noted when the PSA level reached 2.5 ng/mol.

Q. After five years of steady PSA readings, can a patient who has had radiation therapy for his prostate cancer feel that he is cured?

A. Five years is a good milestone, and if a patient makes it to five years, that’s a good sign. However, seven to eight years is a better marker of success. The risk of recurrence is certainly lower beyond that point.

Q. What happens if prostate cancer comes back?

A. Fighting prostate cancer once it has returned is an enormous battle, pitting you and your physicians against a lethal onslaught. Therefore, first and foremost, you have to take total control of your health and learn all you can about the upcoming battle, as well as all the possible battle scenarios you may be confronted with in the coming years. Possible treatment strategies include:

- Active surveillance in which PSA tests are given regularly and charted
- External beam therapy to control the cancer
- Hormonal therapy to stop the androgen supply to the cancer cells
- Joining a clinical trial with an investigational drug

Q. Is there a benefit in adding hormone therapy to radiation therapy in the treatment of prostate cancer?

A. It’s thought that the addition of hormone therapy to radiation therapy will kill or weaken additional cancer cells, bolstering the overall killing effect of the radiation and increasing survival possibilities.

With the Partin tables (see page 18), a contemporary method of stratifying patients into “low-risk,” “intermediate-risk,” and “high-risk” groups for tumor recurrence has been achieved. Not surprisingly, the likelihood of disease recurrence between such groups varies dramatically following unimodal therapy (radiation only or surgery only). Patients at low risk, intermediate risk, and high risk have a likelihood of biochemical recurrence at five years of approximately less than 30%, 40–50%, and 65–75%, respectively. For patients with intermediate- and high-risk disease, improved therapeutic approaches are needed.

Given the responsiveness of metastatic cancer to androgen suppression therapy using special hormone medications, many investigators have integrated such an approach into the manage-
Researchers from Fox Chase Cancer Center reported at an annual meeting of the American Society for Radiation Oncology that radiation therapy alone can reduce prostate specific antigen (PSA) levels below detectable amounts in prostate cancer patients. More importantly, patients who have an undetectable level of PSA after therapy have less chance of biochemical failure than other patients and a good chance of being cured.

“With high quality radiation—whether it is from an implant or external beam—it is possible to get really low PSAs,” says Eric M. Horwitz, M.D., acting chairman and clinical director of radiation oncology at Fox Chase. “And if you do, you have a really good chance of being cured.”

Prostate cancer patients have several options for therapy, including radiation or surgery. After radical prostatectomy surgery, patients are expected to have an undetectable PSA because the entire prostate has been removed. However, patients treated with radiation alone may still have viable prostate tissue after treatment because the radiation beam is narrowly focused on the tumor. Therefore, radiation oncologists have not expected their patients to have the same very low PSA scores as surgical patients.

What’s new, according to the researchers, is that that expectation appears to be changing. “We used to tell our patients that they wouldn’t have an undetectable or really low PSA, but we are seeing that some do,” Dr. Horwitz says.

To find out whether a very low PSA score predicts a better clinical outcome, Dr. Horwitz and his colleagues examined patient records for 1,330 men with prostate cancer who were treated with radiation therapy alone at Fox Chase between 1989 and 2005. Their findings:

- The 154 men who had undetectable PSA after therapy were 59% less likely to have biochemical failure than men who had detectable PSA after therapy.
- There were also trends for reductions in the risk of local or distant recurrence and in cancer-specific death.

According to Dr. Horowitz, physicians should no longer be surprised when they see radiation-treated patients achieve such low PSA levels. With better radiation techniques, such as three-dimensional conformal radiotherapy (3DCRT), which was developed at Fox Chase, and intensity-modulated radiation therapy (IMRT), radiation oncologists regularly deliver higher doses to the tumor bed than they were able to in the past. Patients experience fewer side effects with these techniques, despite the increased radiation dose.
ment of men with nonmetastatic disease in combination with radiation therapy in an attempt to improve treatment outcome.

For high-risk patients, there is definitely value in adding hormonal therapy. No one will debate that. However, for intermediate-risk patients, it is an area of great controversy. In the past, we thought hormone therapy was benign, but it’s becoming clear that it’s far from benign. Hormone-suppressing drugs can trigger undesirable side effects, such as weight gain, fatigue, breast growth, loss of libido, erectile dysfunction, anemia, and “hot flashes,” a sudden and uncontrollable rush of heat to the face, chest, and back that can last for minutes or hours.

For some men, hormone use can also lead to the bone-thinning disease of osteoporosis, and impaired mental function. Also, there is recent evidence that hormonal therapy can lead to increased risk of cardiac death. Therefore, for most patients with intermediate-risk disease, many doctors will not prescribe hormone therapy.

**Q. What is the impact of external radiation on sexual function?**

**A.** Contrary to what many men think or have been told by their doctor(s), radiation can take a gradual toll on a man’s ability to achieve an erection; the problem may occur several years after the procedure. There are many reasons for this. It could be a result of damage to the small blood vessels that control erection, damage to the penile bulb, which sits just below the lower portion of the prostate (and thus was inadvertently treated), or a combination of both.

Based on study results, the good news is that drugs such as Viagra, Cialis, and Levitra can offer help for at least half of the men who develop these erection problems after radiation therapy.

**Q. Since Johns Hopkins has a variety of machines for providing external radiation therapy, how do you choose which one to use?**

**A.** There are not drastic differences between machines used for treating prostate cancer. Although the various machines from different companies do have different capabilities that impact other cancer sites, for prostate cancer they pretty much all do an excellent job. Too many patients give too much weight to the particular machine or the technology rather than the expertise of the doctor, the treatment team, their years of experience, and the excellence of the hospital or cancer center.

**Q. How do I find the best treatment facility for radiation therapy for prostate cancer?**

**A.** Just as not all hospitals are alike, the same goes for radiation therapy centers. Since it’s very hard for a consumer to assess what makes a good radiation team, one critical factor, which applies across many disciplines in medicine, is patient volume. Find out how many
choosing the right treatment for prostate cancer

prostate cancer patients the hospital or cancer center treats annually. If you see they have managed hundreds of prostate cases, that’s a good sign.

Caveat emptor: Some hospitals and cancer centers funnel patients to a particular radiotherapy treatment because they have more expertise in that therapy or they are motivated by other factors to have most of their patients treated with that one type of treatment. As a prospective patient, you need to hear a balanced range of all prostate cancer treatment options in order to make an informed decision.

It’s a very good sign if you hear about all treatment options and why you would or would not be a good candidate for each. On the other hand, if you only hear about one option, it’s time to look for another center. If your doctor has recommended radiation therapy for you, it pays—as it does in all areas of medical treatment—to be an informed consumer. Getting answers to the following four questions can help you make the best choice.

1. How many patients with prostate cancer are treated daily at the hospital/radiation center?

Radiation therapy, like surgery, is technically demanding and operator dependent. For the most part, you will be better served at a high-volume facility that treats your kind of cancer. Hospitals that do a greater number of the same procedures achieve better outcomes for their patients. For a common cancer, such as prostate cancer, look for a center that treats 30 to 40 prostate cancer patients a day with IMRT.

2. Does the facility use IMRT and “real time localization” to keep patients in the exact same position for each treatment?

The position of glands and organs within the body varies daily and is affected by normal movement. Daily ultrasound or CT scans done in the treatment room immediately before radiation delivery can track these positional changes so that the affected area can be properly targeted by IMRT, which is the preferable way to employ it.

3. Are the medical specialists who will be involved in my care board certified?

Specialists in several related areas make up the team in charge of radiation therapy, and professional boards should certify them all. The key team member is the radiation oncologist, a highly-trained cancer specialist who decides if you should be treated, and what oncologic modality should be used (surgery, chemotherapy, or radiation therapy). If radiation is needed, this specialist decides what area specifically needs to be treated and with what dose. The radiation oncologist must also decide how to best protect adjacent normal tissues. This specialist must understand when it is best to combine surgery with radiation, or chemotherapy with radiation, and must be skilled in both externally applied radiation therapy techniques and in the implantation of radioactive sources (brachytherapy).
The oncologist also directs medical radiation physicists, who are responsible for developing and directing quality control programs for equipment and procedures. A medical physicist not only makes sure the equipment works properly, but also takes precise measurement of radiation beam characteristics and performs other safety tests on a regular basis. Radiation dosimetrists carefully calculate the dose of radiation to make sure the tumor gets enough radiation. Dosimetrists develop a number of treatment plans to destroy the tumor while sparing the normal tissues. They work with the radiation oncologist and medical physicist to choose the treatment plan that is just right for the patient.

4. Am I able to travel to and stay at a radiation treatment site that is far from my home?

There are distinct differences between radiation therapy provided by general community facilities and large academic centers. Some very good community facilities deliver excellent contemporary care. But, for the most part, the technology required to deliver high doses of radiation and the support necessary to use that technology to the fullest in not always readily available at most community facilities. While treatment away from home may be inconvenient, the time required is relatively short, usually six to eight weeks.
Proton Beam Therapy

Proton beam therapy (PBT) is an increasingly popular form of external radiation treatment that promises fewer side effects. However, only a few centers offer it, and some experts don’t believe it’s superior to other advanced radiation treatments. Here’s what you need to know.

Since standard radiation therapy is delivered by x-rays, which deposit energy on entering and exiting the body, both the cancer cells and some surrounding healthy tissue are exposed to radiation. However, PBT is unique because it uses protons (small subatomic particles) instead of x-rays to treat cancer. While conventional x-rays tend to “spread” like the light from a flashlight, in PBT most of the proton energy is released at the end of a narrow proton beam, so only a small area of healthy tissue between the skin and the tumor is exposed.

Despite its benefits, some experts argue that PBT isn’t necessary because of the now widespread use of intensity-modulated radiotherapy (IMRT). IMRT radiation is broken up into thousands of tiny beams that enter the body from many angles and intersect at the tumor. Much like PBT, IMRT also allows very precise aim, resulting in a higher radiation dose to the tumor and a lower dose to surrounding tissue. This precision has made it a great tool for treating rare cancers in hard-to-reach places like the spine, brain, and eye, and to use on infants who cannot withstand much radiation.

No clinical trials directly compare PBT and IMRT. But IMRT is less expensive than PBT (see page 56), and some experts argue that no data indicate PBT is more effective than IMRT, even at higher doses. The Centers for Medicare and Medicaid Services reviewed all the evidence surrounding PBT and decided to continue covering the cost of this expensive treatment for prostate cancer because it has proven benefits, despite the lack of direct evidence from clinical trials comparing PBT and IMRT.

It should be noted that there is a strong monetary incentive for offering PBT for prostate cancer patients. Medicare offers a generous reimbursement of more than $30,000 for a course of treatment, which is more than double the fee for conventional radiotherapy.

While PBT is superior to older forms of radiation and is at least as effective as IMRT, only 1% of prostate cancer patients receive it. The reason? The proton accelerator that provides the radiation is the size of a football field and costs $100 to $200 million to build. Nationwide, there are only five PBT facilities (although more are being built). Most men who get PBT are under age 65 and have localized, low to intermediate-grade prostate cancer. In the few centers that offer PBT, space for these patients is limited: PBT treats other types of cancer, too, and priority is given to children and patients with rare, inoperable tumors or other conditions that can’t be treated any other way. Therefore, more than half of patients who apply for PBT are turned away.

This situation is changing, though, as many proton centers are under pressure to treat increasing numbers of people with common cancers to turn a profit and repay investors. Many centers are connected to special hotel/spa facilities where people receiving PBT can opt to stay.
sive marketing and positive word of mouth from enthusiastic patients, this costly radiation treatment is gaining in popularity—even though it doesn’t have the positive long-term results that men with prostate cancer should be looking for.

Proton Beam Therapy Centers: Proton beam therapy centers can be found in each major region of the United States. Additionally, four new centers are under construction and one is in the planning stages.

- Midwest Proton Radiotherapy Institute at Indiana University Bloomington, IN (812) 349-5074 www.mpri.org
- University of Florida Proton Therapy Institute Jacksonville, FL (877) 686-6009 www.floridaproton.org
- University of Texas MD Anderson Cancer Center Houston, TX (877) 636-6789 www.mdanderson.org
- Francis H. Burr Proton Therapy Center at Massachusetts General Hospital Boston, MA (617) 726-0923 www.massgeneral.org/radiation oncology/BurrProtonCenter.aspx
- James M. Slater, M.D. Proton Treatment and Research Center at Loma Linda University Medical Center Loma Linda, CA (800) PROTONS (776-8667) www.protons.com

Cryotherapy

Also known as cryoablation, cryotherapy is a treatment that kills cancer cells by freezing them. In the procedure, thin needles (cryoprobes) are inserted through the perineum (the area between the scrotum and anus) and into the prostate. Needle placement is guided with an ultrasound probe placed in the rectum. Freezing gases drop the temperature of the cryoprobes to about -40° C. The extremely low temperatures create ice balls that freeze the entire prostate and some of the nearby tissue. Warm saline is circulated through the urethra and bladder to protect them from the freezing temperatures.

Cryotherapy may be an option for men whose cancer is contained within the prostate, and it is sometimes used when radiation therapy has failed to destroy the cancer. The risk of erectile dysfunction is high with cryoaablation, and its long-term effectiveness is less certain than that of surgery or radiation therapy.

HIFU

High-intensity focused ultrasound, or HIFU (pronounced HIGH-foo), is a promising technology for noninvasive tumor ablation and its potential clinical impact is indeed significant. Image-guided HIFU procedures could permit the ablation of tumors (not only in the prostate, but also in the liver and lung) and each procedure, which heats cancerous tumors to near-boiling temperatures, could be carried out without the need for surgery or an incision. This form of treatment has the possibility to minimize side effects—incontinence and erectile dysfunction—and improve quality of life, while offering a rapid recovery and return to daily activities.

There are currently two HIFU devices for the treatment of prostate cancer: Sonablate (Indianapolis, IN) and Ablatherm (EDAP, Lyon France). Although both devices are approved in Europe, Mexico, Canada, and the Far East, they are only available in the

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OTHER FORMS OF RADIATION THERAPY (CONTINUED)

U.S. for prostate cancer treatment as part of ongoing Phase III trials to access their safety and efficacy.

HIFU treatment with the Ablatherm device is straightforward and there is typically no hospital stay required. After receiving a spinal or epidural anesthesia, as well as intravenous sedation, the patient is placed on his right-hand side—a safety precaution to prevent any bubbling in the fluid surrounding the treatment probe that could end up between the HIFU treatment crystal and the prostate, muting its overall effectiveness.

The small probe—encased in a latex balloon filled with cooling liquid—is placed eight inches into the rectum. This helps maintain a cool temperature in the rectal wall during the therapy. Using ultrasound, the urologist then locates the parts of the prostate he wishes to treat. Pressing a button emits a computer-controlled beam of high-intensity focused ultrasound, raising the temperature at the desired (focal) point in the prostate to 85°C to 100°C for three seconds. The beam heats up a portion of tissue equal to about the size of a few grains of rice stacked end to end, leading to eventual tissue death. By repeating the process 400 to 600 times as the probe is moved around the prostate, it is possible to destroy most of the prostate tissue.

Depending on the size of the prostate, treatment takes anywhere from one to three hours. For best results, prostates should be 40 cc or smaller. Larger glands can be treated after being reduced in size by pretreatment with short-term hormonal therapy or a TURP. A few weeks following treatment, when most of the ablated tissue has sloughed off, the prostate glands shrinks considerably and it is often difficult to find the prostate during a digital rectal exam.

Cancer cure rates are the primary consideration in any prostate therapy, whether it entails surgery, radiation, or high frequency sound waves. Since HIFU is such a new therapy for prostate cancer, and the pool of treated patients is relatively small, there is not a rich source of data to draw upon. A five-year follow-up study from urologists at the University of Regensburg in Germany was published in the journal Urology (High-Intensity Focused Ultrasound for the Treatment of Localized Prostate Cancer: 5-year Experience ) in 2004. From the pool of 137 patients, the doctors reported that 93% had negative biopsies following HIFU therapy for prostate cancer; 87% of all patients had constant PSA levels of less than 1 ng/ml; and only two patients had PSA levels that surpassed 4 ng/ml. However, you would find the same PSA results if you did a TURP on a patient with prostate cancer—and the cancer would still be there.

While HIFU is a technology that has promise, and several centers in Europe have used it and achieved varying results with many patients, there still have not been many scientific publications on clinical outcomes. We are in the dark about how effective this treatment is long term.

CyberKnife

Approved by the FDA in 1992, CyberKnife is a piece of linear accelerator equipment that uses different instruments to deliver high-
energy photons to a cancer site on a robotic arm, while an image guidance system allows the tumors’ location to be tracked in real time to make sure the radiation is directed exactly to the tumor site.

Due to the way it delivers radiation, this device falls into an equipment group called stereotactic body radiotherapy (SBRT). Even though CyberKnife is heavily marketed as being more precise than other methods or radiotherapy, that is not true. Several manufacturers have machines that are as precise and even better in certain circumstances.

CyberKnife has nonetheless created a lot of interest in the prostate cancer community because of the convenience factor. Treatments are given with a maximum of five doses, compared with the 40+ doses over the course of eight weeks that it takes with other technologies. This has certainly played a large part in the decision-making process of the more than 3,000 men with prostate cancer who have opted for the procedure over the last six years—even though there is no long-term evidence that this therapy adequately controls cancer or that side effects won't emerge at a later date.

There is also a catch with the five-treatment convenience factor: Prostate cancer patients get a higher dose per day than conventional radiation with CyberKnife, not because of capabilities of the CyberKnife but because of reimbursements given from Medicare. Medicare officials decided that CyberKnife fell under the banner of SBRT and this has a special billing code where the therapy must be offered in five treatments or less in order for owners of the $5 million machine to receive reimbursement for treatment.

People who operate CyberKnife facilities then decided they would try to treat prostate cancer the same way they used the device to treat brain cancer: with five treatments or less.

There has been debate in the medical community as to whether or not shortening the course of radiation would be beneficial in improving the cure rates of prostate cancer. The concern has been that shortening treatment times and giving more radiation at each session could create a risk for delayed side effects. This can include urination issues that appear six to eight years after the procedure.

Finally, the long-term curative potential of prostate cancer with SBRT in general, and the CyberKnife in particular, is still not known. On the other hand, radical prostatectomy has a large body of long-term data indicating a high cure rate, for localized prostate cancer, as does IMRT and brachytherapy. ASTRO, the American Society for Radiation Oncology, issued a report last year on emerging technologies and called stereotactic body radiotherapy (SBRT) promising but not well proven. They said, “While favorable data exist from several SBRT studies with small patient numbers and short follow-up, the American Society for Radiation Oncology (ASTRO) recommends that these treatments be performed under Institutional Review Board (IRB)-approved clinical trials until the data matures.”
A growing number of men with prostate cancer are choosing a form of internal radiation therapy known as brachytherapy. In brachytherapy (pronounced “BRAKE-ee-therapy”), radiation oncologists insert dozens of radioactive rice-size pellets, or “seeds,” into the gland in an effort to destroy all cancerous cells. Each seed releases its radiation over time in a very small area (about the size of the top of a pencil eraser), killing all cancer cells nearby. These implants, which lose their radioactivity within a few months, are generally left in the patient’s body permanently but do not cause any untoward side effects by remaining in the prostate.

Brachytherapy is by no means a new medical procedure. Back in the early part of the twentieth century, doctors utilized brachytherapy to treat prostate cancer, but because they had no great success, the procedure quickly fell out of favor. The technique was not widely used to treat prostate cancer until the 1980s, when improvements in medical technology made it more effective. In particular, transrectal ultrasound guidance technology permitted doctors to implant the radioactive seeds with greater precision.

The following are the questions most frequently asked about brachytherapy by patients at Johns Hopkins, and our answers to those questions.

**Q.** What is the appeal of brachytherapy?

**A.** For the patient, convenience is certainly an important element. When compared to a radical prostatectomy (having to use a catheter for one to two weeks) or external radiation therapy (radiation needs to be administered several times a week for six to eight weeks), the two-hour seed implantation procedure seems appealingly convenient.

**Q.** Who is the ideal brachytherapy patient?

**A.** Based on our current data, here’s what can be said: He has low-risk prostate cancer. “Low-
risk” refers to an early cancer stage that is either non-palpable or presents as a small nodule on one side, classified as T1 or T2a. The ideal candidate for brachytherapy also has a PSA below 10 ng/mL and a Gleason score of 6 or less. He is in good overall health and has a probable lifespan of 10 to 15 years.

Q. **Is brachytherapy a good option for a patient with high-risk prostate cancer?**

A. High risk refers to the patient with an advanced stage—a large palpable mass on both sides or beyond the prostate; or a PSA of 20 ng/mL or more; or a Gleason score of 8 or more. We don’t treat those patients with brachytherapy. The risk of disease being outside the confines of the prostate gland is high, and the brachytherapy may not benefit this patient.

For the true high-risk patient, we give high-dose external beam radiation therapy plus a course of hormonal therapy. By contrast, for the low-risk patient we recommend brachytherapy alone, or else surgery.

For the intermediate-risk patient, we may recommend brachytherapy plus external beam radiation, depending which side of intermediate risk the man is on. Intermediate refers to a stage of T2b—a nodule on one side of prostate; or PSA of 10–20 ng/mL; or a Gleason score of 7.

Q. **What comes first in a combination radiation therapy protocol for the intermediate-risk patient: brachytherapy or external beam radiation therapy?**

A. More and more evidence is suggesting that patients with intermediate risk, especially the more favorable intermediate risk (Gleason 3 + 4 with a few cores involved and a low PSA, in the low teens), will do well with brachytherapy alone, and we treat them that way.

For those patients with more aggressive-appearing intermediate-risk disease, we will offer a combination of external beam and seeds, or standard high-dose external beam without seeds. When it comes to dual radiation therapy, Hopkins experts have found that by placing the seeds first, they can then modify external beam therapy based on how well the patient tolerates the seeds, and the distribution of the seeds within the prostate.

Q. **What type of brachytherapy “seeds” do you use?**

A. We favor palladium-103 seeds, which are about the length of a grain of rice and about the width of a mechanical pencil lead. The palladium isotope releases its energy much faster and the radiation source is much stronger than iodine-125 seeds, the other type of seed that can be used. With palladium-103, you need fewer seeds to attain the full dose of radiation within the prostate.

Since the seeds are radioactive, we place some restrictions on the patient in terms of interactions with children and pregnant family members. Since we do use the quicker-acting palla-
Ch o o s i n g Th e Ri g h T TRe at m e n T Fo r Pr o s T a t e Ca n c e r

dium seeds, we find that our patients like the fact that in two months the palladium is generally all decayed, whereas you may have to wait six to eight months with the iodine seeds for complete decay.

Q. How many seeds are needed in a brachytherapy treatment for prostate cancer?

A. That all depends on the size and contour of the prostate gland and the location of the tumor. For a smaller gland, we might use 60 seeds, while a larger gland may need close to 100.

Q. Do the seeds kill cancer cells?

A. Not only do the seeds kill cancer cells within the prostate, but they also seem to wipe out the vast majority of all PSA-producing cells, including normal prostate tissue. In the past, when people gave lower doses of radiation with external beam, it was not uncommon to see PSA levels around 1.5 ng/mL as the nadir.

Nowadays, it’s not uncommon to see undetectable PSA levels after external beam radiation or seed treatment. No one is saying PSA has to reach undetectable levels in order to effect a cure; We definitely see patients who have a PSA of 0.4 ng/mL that stays that way for years. But when you see someone who goes to undetectable PSA levels with radiation, you realize that not only has the treatment killed the prostate cancer, it has destroyed all the prostate tissue.

CANCER FREE AT FIVE YEARS: GOOD NEWS

A recent study form New York researchers has reported that prostate cancer patients who receive brachytherapy and remain free of disease for five years or greater are unlikely to have a recurrence at 10 years. In the study published in the International Journal of Radiation Oncology *Biology* *Physics*, researchers at The Mount Sinai Medical Center Departments of Radiation Oncology and Urology followed 742 prostate cancer patients who were treated with brachytherapy alone, brachytherapy and hormonal therapy, or combined brachytherapy and external beam radiotherapy (EBRT) between 1991 and 2002. None of these patients had recurred during their first five years post-treatment. Also, none of the study participants developed metastatic disease or died from prostate cancer.

The researchers found that the PSA level taken at five years was an indicator of how well a patient would do in the future and the overall chance of being cancer free at 10 years was 97%. With improvements in brachytherapy technology, the researchers believe that late failure rates will continue to decrease, making prostate brachytherapy alone and combined with hormonal therapy and/or EBRT an increasingly attractive treatment option.
Q. What is a cold spot and how is it treated?

A. You have to understand that each radioactive seed releases radiation within a confined area, with all of the seeds contributing radiation to the overall implant. Cold spots are areas of unintentional, inadvertent under-dosing. These spots may develop because of movement of the seeds caused by bleeding within the prostate; the seeds may also eventually settle with gravity, moving out of their intended place in the gland.

If a cold spot is found at the time of re-examination the day after the procedure, it can easily be filled in with a follow-up treatment. This is not something we have to do often, but it has been done on occasion.

Q. What is considered a success in terms of PSA measurement after radiation therapy?

A. We generally would like to see the PSA of our patients go to 0.5 ng/mL or less. There are data showing that patients with PSA who reach this level have a better prognosis than patients who reach 1.0 ng/mL and that those patients are better off than those who reach 1.5 ng/mL.

Q. What is PSA “bounce”?

A. Following radiation treatment, PSA falls, but for some men it may actually start to go back up—a “bounce”—before going back down again. While it is certainly scary for a man to see his PSA rising, this scenario is not uncommon, and it does not mean that the cancer has recurred. PSA bounce occurs in almost 25% of men undergoing radiation treatment. For some unknown reason, those who are generally at risk are in their 50s. Bounce can be caused by sexual activity, which is the most common cause; rectal bleeding causes bounce, as do bike riding, horseback riding, cystoscopy, and colonoscopy. We tell patients not to be scared when bounce occurs, and we will see them every three to six months after the procedure. We want to be the one to take PSA and discuss their history to be sure that if there is an issue, we can define exactly what it is.

Q. Is erectile hardness maintained with brachytherapy?

A. It is important that men be asked prior to any procedure exactly what their erection capabilities are. We have patients fill out the International Index of Erectile Function (IIEF). The beauty of this questionnaire is that it is specifically designed to assess a man’s current level of erectile function, getting precise answers in five key domains—erectile function, sexual desire, orgasmic function, intercourse satisfaction, and overall satisfaction. Translated now into more than 20 languages and used worldwide, the questionnaire is an excellent way to assess not only a man’s personal level of erectile dysfunction (ED), but also the extent to which it affects his overall sex life. (Text continues on page 78.)
**BRACHYTHERAPY STEP BY STEP**

**One week prior to the implant.** Patients should stop taking aspirin or ibuprofen. If the patient is taking any anticoagulants or other medication that may cause bleeding, the anesthesiologist or the doctor who prescribed the drugs will give him specific instructions on when to stop taking them.

**On the day before the implant.** You may want to have a light snack before going to bed (toast, crackers, or soup) because you cannot have anything to eat or drink after midnight. By 8 p.m., the patient should also use a Fleet enema to cleanse the colon.

**On the day of the implant.** If you must take any of your regular medications, you should do so with only a small sip of water. For your safety, you should be prepared to stay in the hospital overnight while the anesthesia effect wears off. Bring your toothbrush, slippers, a change of underwear, and comfortable clothing to wear home. Bring your shaving equipment if you wish to shave prior to discharge.

You will change into a hospital gown. You then will be asked to get on a gurney to start getting ready for anesthesia and for the implant procedure. This entails measuring your vital signs and getting an intravenous line inserted. You may get some medication to relax you at this time.

You will be wheeled into the procedure room. Prior to being given anesthesia, you will undergo scans to determine the best position for you to be in. Once this is done, you will be given your anesthesia. The catheter will not be inserted into your penis until you are asleep.

During the procedure, needles loaded with palladium-103 seeds are inserted through the skin of your perineum (the area between the scrotum and the rectum). The needles are removed after it is determined that the seeds are in the appropriate place. On average, 15 to 25 needles and 70 to 120 seeds are used. The entire procedure takes approximately two to four hours.

**Immediately after the implant.** After you awaken, the first thing you may experience is a sensation in your bladder as if you have to urinate. This is from the catheter, which is still in place. Any urine that is in your bladder will drain into a collection bag on the side of your bed. Some individuals experience nausea after anesthesia. Medications that help control nausea will be offered.

When you have fully awakened from anesthesia and your vital signs are stable, you will be moved to a hospital room. You will continue to receive medication for nausea if you need it. If your stomach feels up to it, you may receive a light meal for supper. You will be encouraged to drink fluids as you can tolerate them.

**The day after the implant.** The Foley catheter will be removed. Most men are able to urinate within 8 hours after the catheter is out. Occasionally patients have some swelling from the procedure that prevents them from passing urine. In that case, the catheter is reinserted and you will go home with the catheter. It is removed after a week.

Most men are feeling well the next morning and can eat a normal breakfast. You may have some soreness in the area where the needles were inserted. The soreness is usually relieved with Tylenol.
A CT scan and an x-ray will be taken to note seed positioning.

**Urination**
You may experience some burning on urination because of irritation to the urethra. This may last for several weeks after the implant. Try to drink at least 8 glasses of non-caffeinated liquids per day. The prescription drug Pyridium will help relieve the urinary burning. You should take this as prescribed. The antibiotic levofloxacin will be prescribed to help prevent a urinary tract infection. The drug Flomax is prescribed to improve the force of your urinary stream.

You may see small amounts of blood in your urine. This is normal. However, if you are passing large clots or are unable to pass urine you should go to an emergency room for evaluation. In the unlikely event that you pass a seed with your urine, flush the toilet as you would normally do. Do not attempt to retrieve a seed. Notify your doctor.

**Bowel Movements**
It is important to move your bowels a day or two after the procedure. If constipation should occur, you may take prune juice, Metamucil (one tablespoon once or twice a day), or a laxative such as Milk of Magnesia (two tablespoons), Citrate of Magnesia (one bottle), or Senokot (two tablets). A Fleet enema may be used if oral agents are not effective.

**Skin Care**
You may have some swelling in the perineum (the area between your testicles and your rectum) where the needles containing the radioactive seeds were placed. There may be some bruising and tenderness as well. You may take Tylenol—one to two tablets every four to six hours—as needed for discomfort. Sitz baths or tub baths once or twice daily will be soothing and will help keep the area clean.

**Daily Activities**
After general anesthesia, it takes time for your reflexes to return to normal. You may not be able to react as quickly as you normally would. Do not drive or operate heavy machinery for two days after the procedure. Full activity, including work, may be resumed on the third day after the implant. The doctor should approve any strenuous physical activity during the first week. A small percentage of men experience leg cramps one to two weeks post-procedure.

Because of the radiation the seeds emit, children should not sit on your lap for more than 30 to 60 minutes for the first two weeks. Pregnant (or possibly pregnant) women should also avoid prolonged close contact (within 12 inches for 6 uninterrupted hours) with you for two days after the implant. At a distance of 6 feet, there is no limit to the length of time anyone can be with you.

**Sexual Relations**
You may resume sexual intercourse two weeks after the implant. Your semen may be dark brown or black in color. This is normal and is caused by minor bleeding that may have occurred during the implant. Mild

*continued on following page*
It’s estimated that upwards of 20% of men will experience some ED in the years following treatment. Five years after brachytherapy, all men will say their erection capability has changed. That is because of the effect of the radiation itself, and also because of age. The good news is that if men are offered Viagra, Cialis, or Levitra, 80 to 90% will report similar sexual function as they had at baseline, or better.

**Q. Why does sexual function typically decline after radiation therapy?**

**A.** The time scale over which you see radiation-induced ED is a period of years, not months, and it has to do with scarring. We cannot identify the actual area that is scarred and triggering the erectile dysfunction. Some experts believe it is the neurovascular bundle that is damaged, while some say it is the penile bulb. Some believe that both are damaged by the radiation.

**Q. When can a man resume normal activities of daily living after undergoing brachytherapy?**

**A.** If a man has brachytherapy alone, typically the catheter comes out the night of the procedure or the next day. In the vast majority of patients, 90% or so, the catheter stays out and they can get back to normal activity in days, or a week at most.

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### BRACHYTHERAPY STEP BY STEP (CONTINUED)

<table>
<thead>
<tr>
<th>Pain on ejaculation can occur the first few times. Although the chance of passing a seed in your ejaculate is highly unlikely, you should use a condom for the first two weeks after resuming intercourse.</th>
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</thead>
<tbody>
<tr>
<td><strong>FOLLOW-UP</strong></td>
</tr>
<tr>
<td>You will see your doctor shortly after the procedure. At this visit, your medications will be adjusted. You will be followed at three months, then every six months for two years, and then annually. These visits include a rectal examination of your prostate and a PSA level. You should refrain from sexual activity, bicycling, horseback riding, and jet skiing for one week prior to having your blood drawn for your PSA test. It is important to note that your PSA level can “bounce” during the first one to four years following the implant. The doctor will talk more about this at your follow-up visits.</td>
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**Call your doctor if you experience:**
- Burning on urination that persists beyond the first week, or difficulty passing urine at any time.
- Temperature greater than 101°F during the first two weeks after your implant.
- Increasing pain or bleeding in the perineal area.

Rare symptoms to look for after six months and up to five years following the implant:
- Urinary obstruction. Go to the emergency room.
- Rectal bleeding. Call your doctor immediately.
Q. When can sexual activity be resumed after brachytherapy?

A. We tell patients to wait one to two weeks before ejaculation because of inflammation of the urethra.

Q. Does where you receive your brachytherapy treatment make a difference in prostate cancer outcome?

A. We believe that where you receive your brachytherapy makes a difference in outcome, but it’s hard to find clinical data to support this. We also believe that you can expect fewer side effects when a top expert performs your brachytherapy. In addition, when brachytherapy is performed at a center of excellence, if any problems develop—before, during, or after the procedure—the oncologist can draw upon the immediate assistance of a whole cadre of experts at the hospital to help. You cannot expect this level of expertise and assistance at smaller facilities that do not perform as many brachytherapy procedures.

Q. What is high-dose brachytherapy?

A. Think of high-dose-rate brachytherapy as temporary brachytherapy. This form of radiation therapy involves placing 18 to 25 plastic catheters into the prostate, and then giving a series of brief computer-controlled high-energy radiation treatments through the catheters. Depending on whether the patient has low-, intermediate-, or high-risk cancer, the computer is programmed to determine how long the single radioactive iridium-192 seed remains in each of the catheters. This ensures that different parts of the prostate receive adequate radiation doses, and that the rectum and urethra will be spared. Over the next 24 hours (in which the patient remains hospitalized), the procedure is typically repeated twice. Since this type of brachytherapy is performed quickly, there is no radiation exposure to anyone who comes close to you once you leave the hospital. Results appear to be comparable to standard brachytherapy.
If you’re like most sexually active men facing surgery for prostate cancer, one of your greatest concerns is whether you’ll be able to have sexual intercourse after the operation. While nerve-sparing surgery—in which a skilled surgeon preserves the cavernous nerves necessary to achieve a natural erection—has significantly improved the likelihood that you will regain erectile function, it might take a while. For the 60 to 85% of men who do regain sexual function, the average wait is about 18 months. For some men, it can take two years or longer for adequate erections to return. But new research suggests that waiting for nature to take its course may actually make recovery of natural erectile function more difficult. These findings are the basis of a novel strategy called erection rehabilitation, in which erections are induced with medication several times a week in the hopes of hastening and increasing the odds of a return of sexual potency.

What’s Behind ED After Radical Prostatectomy?

Even an expertly performed nerve-sparing procedure causes some degree of trauma to the cavernous nerves. Located on either side of the prostate, these nerves supply electrical impulses to the corpora cavernosa, the two chambers in the penis that fill with blood to create an erection. The source of the surgical trauma is unclear. But researchers speculate that it could result from stretching the nerves as the prostate is removed; application of heat during cauterization; reduced blood flow during efforts to control surgical bleeding; or inflammation in response to the surgery. The trauma may cause degeneration of nerve fibers and loss of nerve connections to the corpora cavernosa. This, in turn, can lead to deterioration and shrinkage of the spongy tissue within the chambers. When these changes occur, blood may leak from the chambers, preventing you from developing or maintaining an erection.

Use It or Lose It?

The premise behind erection rehab is that achieving erections soon after surgery may help prevent tissue damage and restore normal sexual function sooner. One theory is that when the penis remains flaccid for many months (because the corpora cavernosa
are not filling with oxygen-rich blood), the lack of oxygen damages the spongy tissue. Oxygen-deprived tissue overproduces collagen (the main structural protein found in connective tissue).

Over time, the excess collagen causes thickening and scarring of tissue within the corpora cavernosa. In contrast, a substance called prostaglandin E1 (PGE1)—which is produced in the presence of adequate oxygen—decreases collagen production and promotes healthy tissue. The pharmaceutical form of PGE1, alprostadil, is available as an injectable drug (Caverject, Edex) or as an intraurethral suppository (MUSE), and has been used for years to treat erectile dysfunction.

Alprostadil increases blood flow to the penis, producing an erection even when the cavernous nerves have been damaged or removed. One erection rehab strategy involves self-injecting alprostadil into the corpora cavernosa three times a week, starting four weeks after prostatectomy. The first report that early injection of alprostadil promotes a faster recovery of spontaneous (natural, unassisted) erections came from Italian researchers in 1997.

In a preliminary study, reported in The Journal of Urology, they found that eight of twelve men who began using the injections one month after nerve-sparing radical prostatectomy achieved spontaneous erections adequate for intercourse within six months, compared with only three of fifteen men who didn’t use the injections. Similarly, the use of intraurethral alprostadil shortly after a radical prostatectomy for six months shortened the recovery time needed to regain erectile function. Some evidence suggests that early use of a vacuum pump also could help. A study in BJU International reports that using a vacuum pump one month after a radical prostatectomy produced earlier sexual function in men who had undergone nerve-sparing or non-nerve-sparing radical prostatectomy.

Of late, the oral ED drugs—sildenafil (Viagra), vardenafil (Levitra), and tadalafil (Cialis)—have become the erection rehab strategy of choice because they are noninvasive, convenient, and well tolerated. Although these drugs tend to be less effective in men who have undergone radical prostatectomy, early use appears to offer some benefit. Results from a recent randomized controlled trial in the Journal of Sexual Medicine show that men who took Viagra shortly after a radical prostatectomy each night for nine months had significantly greater improvement in erectile function than men who took a placebo, and much of the improvement was seen within the first four months of treatment.

Researchers aren’t completely sure why early use of the ED drug appears effective, but they speculate that the improvement is related, at least in part, to increased corporal oxygenation. Some doctors recommend that men who inject alprostadil three times a week also take an oral ED medication on the other days. This strategy may enable the men to use a lower dose of alprostadil.
The bottom line: No single treatment is effective for every man. You may need to experiment to find a method that works for you. No matter which method you use, the best results occur when rehabilitation is started within one to two months of surgery, and many doctors evaluate patients for a rehab program as soon as the catheter is removed.

Is Erection Rehab for You?

If you didn’t have ED before surgery and your doctor feels it’s safe for you to take an oral ED drug or use alprostadil, you’re likely a candidate for erection rehab. However, if you didn’t have a nerve-sparing operation, or if you have diabetes or cardiovascular disease, you may not respond as well as a healthy man. In addition, you’ll need to stick with the regimen exactly as prescribed to get the best results.

For some men, the cost of oral medications may be a concern because insurance coverage may be limited. Some plans will pay for four pills a month, with additional doses costing $10 a pill or more. If you find you’re limited by your insurance plan, consider asking your doctor to write a letter of medical necessity to the insurance carrier to increase the monthly allotment of medications.
WHEN PROSTATE CANCER HAS ADVANCED

Prostate cancer is highly curable when diagnosed early, before it spreads beyond the prostate gland. More men than ever before are being identified and treated at this early stage thanks to regular screening with a digital rectal exam (DRE) and a blood test for prostate-specific antigen (PSA), the enzyme that is usually elevated in the blood of men with prostate cancer. The men diagnosed with prostate cancer still within the prostate can be treated with surgery or radiation therapy, and the cure rates are superior.

Still, there are men who are diagnosed too late—the cancer has already extended beyond the prostate or the prostate cancer has recurred after therapy—and neither surgery or radiation therapy can offer a cure. For this group of men, two options remain: hormonal therapy and chemotherapy.

Hormonal Therapy

Hormonal therapy—also called hormone or androgen deprivation, or hormonal or androgen ablation—is effective at turning off the body’s supply of male hormones, which prostate cells need to grow and develop. The medications used for advanced prostate cancer include LHRH agonists, female hormones, and antiandrogens. An orchiectomy, an outpatient procedure to remove the two testicles, can also produce a rapid decline in hormone levels.

Not having a hormone supply can set back proliferation of prostate cancer cells for years. Unfortunately, it is not a lethal blow because prostate cancer is heterogeneous, which means it’s actually made of a variety of cells. Some of the cells are resistant to a hormone treatment that targets only one kind of cell and they continue to grow in the absence of male hormones. These are called androgen-independent or androgen-insensitive cell. Cancer that seems to defy hormonal therapy altogether is called hormone-refractory disease.

Hormonal therapy is very effective in causing a remission, improvement in pain, and reduction in tumor mass and PSA levels for some time. Sadly, at some time most patients eventually develop resistance to the treatments and the cancer begins to grow again.

If you want to attack cancer aggressively, don’t pin your hopes just on hormones. As
Chemosensitivity of the tumor and PSA begin to rise yet again after a course of therapy, consider chemotherapy or else enrolling in a clinical trial aimed at killing cancer cells that hormones can't touch.

Chemotherapy

Chemotherapy, or drug therapy, is used to kill cancer cells in organs or in the blood while attempting to limit the damage to normal cells. Chemotherapy is useful in fighting cancer that cannot be easily detected or treated with surgery or radiation therapy and has now moved on from the original site to other parts of the body (metastasis).

More than three decades ago, chemotherapy was tried in an effort to delay the progression of advanced prostate cancer, but the results were extremely disappointing. This was due in great part to the fact that the drugs being used were not designed for prostate cancer. The therapy was offered to men who had failed all other treatments. These patients were already suffering from pain and weakness, and chemotherapy was their last chance at survival.

Thankfully, we are now in a new era. With Taxotere, which was approved by the U.S. Food and Drug Administration in 2004, we have a drug that has show it not only improves the patient’s quality of life by reducing pain, but can also extend the life of the advanced prostate cancer patient.

Taxotere is a drug in the taxoid class of chemotherapeutic agents that inhibits cancer cell division by inhibiting the effects of Bcl-2, a protein that is thought to prevent cancer cells from dying. The drug essentially “freezes” the cell's internal skeleton, which is comprised of microtubules. These are hollow tubular structures composed of the protein tubulin that help maintain the shape and movement of a living cell and the transport of material within it. These microtubules assemble and disassemble during a cell cycle. What Taxotere does so well is promote their assembly but then prevents their disassembly, preventing many cancer cells from dividing, resulting in cancer cell death. Once exposed to the Taxotere, these cancer cells do die.

With its reproducible evidence of cancer-fighting activity, Taxotere has now defined a new standard for chemotherapy treatment for advanced prostate cancer. In at least 50% of the patients who use the drug, half will get a remission of some duration. In the studies, the men who received Taxotere-based therapy lived, on average, about three months longer when compared to men who received the old drug combination of prednisone (a corticosteroid) and the cancer medication Novantrone (mitoxantrone), which was approved by the FDA in 1996 as a treatment for the pain of metastatic prostate cancer. With a survival benefit over standard treatments now proven, the use of Taxotere marks the first giant step in the battle against advanced prostate cancer.
Taxotere, like hormonal therapy, kills a significant number of cancer cells, but not all of them. The population of cells that is not killed—depending on how severely these cells are stressed—may take either a short or a long time to finally return. Decreases in PSA are an important indicator that the drug is working.

The success of Taxotere dramatically points out that researchers are getting much better at anticipating the next move that androgen-independent prostate cancer cells will make. Thanks to the creation of bioengineered antibodies 30 years ago, and the deciphering of the human genome, researchers have been painstakingly working on a generation of targeted biological drugs that they hope will deliver the death blow directly to specific molecules, genes, or proteins that cause the cancer while cleverly avoiding nearby healthy tissue. The past decade’s tremendous advances in research methods and biotechnology have led to a variety of drugs that are now leaving the laboratory for testing on human subjects with advanced prostate cancer.

These experimental drugs offer oncologists alternative ways to help prostate cancer patients. Moreover, when one of the new drugs or drug combinations stops working, there will be a wider selection of other drugs with which to replace it to continue battling the cancer. Many in the prostate cancer research community believe that as these drugs become more effective, less toxic, and improve the quality of life of patients, advanced prostate cancer will one day become a chronic yet manageable disease—similar in treatment strategy to rheumatoid arthritis or diabetes—with a routine of daily medications, lifestyle modification, and regular checkups.

Research is now aimed at developing novel chemotherapeutic agents to destroy the aberrant cells as they replicate. We are not giving up in our quest to develop these drugs. More drugs than we ever imagined are now being developed and tested for prostate cancer. In addition, some drugs approved for other tumor types are being tested on prostate patients as well.

Although progress has been sluggish—that is the nature of good science—please understand that the prostate cancer research community is committed to finding solutions.
Here you will find dozens of prostate terms, organized and cross-referenced for your convenience. If a word used in a definition is in *italics*, that word has its own entry.

The terms are those most often used by urologists in describing prostate disorders.

**A**

**Ablation:** Removal, elimination. For example, hormonal ablation means eliminating the androgens (male hormones) that nourish prostate cancer.

**Acid phosphatase:** An enzyme (such as prostate-specific antigen) that is secreted by the prostate gland. Elevated levels may indicate something is wrong with the prostate.

**Acute bacterial prostatitis:** A form of prostatitis associated with urinary tract infections. The ailment comes on quickly, accompanied by fever, pain in the perineum (area between the scrotum and rectum) and lower urinary tract symptoms that demand prompt medical attention.

**Adenocarcinoma:** A cancer originating in glandular tissue. Prostate cancer is classified as adenocarcinoma of the prostate.

**Adjuvant:** An additional treatment used to increase the effectiveness of the primary therapy given concurrently or after the primary treatment. Hormonal therapy is often given concurrently with radiation therapy as an adjuvant therapy.

**Adrenal androgens:** Weak male hormones made by the adrenal glands. They include androtenedione, dehydroepiandrosterone (DHEA), and dehydroepiandrosterone sulfate (DHEAS). Their overall effect on the prostate is controversial. Most (95 percent) of the testosterone in the blood comes from the testicles.

**Agonist:** A drug that triggers an action by a cell, another drug, or a hormone.

**Alpha blockers:** Medications, originally designed to treat hypertension, that act on the prostate by relaxing smooth muscle tissue within the prostate and at the bladder neck. Used to treat lower urinary tract symptoms in men with BPH.

**5-alpha reductase:** An enzyme in the prostate that converts testosterone to DHT.

**5-alpha reductase inhibitors:** Medications that block the formation of DHT by blocking the enzyme 5-alpha reductase, causing the prostate to shrink by about 20-30 percent. These drugs are used to treat lower urinary tract symptoms in men with BPH.

**Analgesic:** Painkiller.

**Analog:** A synthetic drug that can mimic one of the body’s natural signaling molecules.

**Anal stricture:** Tight scar tissue that can interfere with a bowel movement.

**Androgen:** A substance with male hormone activity, such as testosterone.

**Androgen ablation therapy:** A treatment designed to inhibit the body’s production of androgens (male hormones) or block the action of the androgen.

**Androgen-dependent, or -sensitive cells:** Prostate cancer cells that are dependent on male hormones for survival. These cells undergo apoptosis (cell death) when the hormones that nourish them are shut off.

**Androgen-independent, or -insensitive cells:** Prostate cancer cells that are not dependent on male hormones and therefore do not respond to hormone-blocking therapy by undergoing apoptosis.
Angiogenesis: The body’s process of forming new blood vessels. Some anti-cancer drugs called angiogenesis inhibitors work by blocking angiogenesis, thus preventing blood from reaching and nourishing a tumor. Although the tumor may not die, its growth may be slowed or stopped.

Antiandrogens: Drugs such as bicalutamide and flutamide used in hormone therapy to treat prostate cancer. These drugs block or neutralize the effects of testosterone and DHT on prostate cancer cells by preventing testosterone and DHT from binding to the androgen receptor.

Anticholinergic drugs: A group of drugs that suppress bladder contractions. These medications may help some men with incontinence or overactive bladder.

Anti-metastatic drugs: Drugs that help prevent cancer from invading other cells or from developing new blood vessels (the process known as angiogenesis).

Apoptosis: Programmed cell death. The normal molecular mechanism that governs the life span of cells so that they die in a very organized fashion.

Artificial sphincter: A surgically-implanted device used to treat severe incontinence that has persisted for a year or longer and is not improving.

Asymptomatic: Experiencing no symptoms.

Atypical: A finding on a prostate biopsy meaning the cells do not look normal but are not necessarily cancerous.

Benign: Harmless; not cancerous.

Benign prostatic hyperplasia: See BPH.

Biochemical failure: Residual prostate cancer detected by a rising PSA after treatment.

Biopsy of the prostate: The removal of tissue from the prostate so it can be examined for the presence of cancer. This is performed using transrectal ultrasound (TRUS) guidance.

Bladder: The hollow, muscular reservoir that functions as a holding tank for urine.

Bladder neck: The junction between the bladder and the prostate.

Bladder neck contracture: Constriction of the bladder neck, generally by scar tissue. This can block urine flow.

Bladder stones: These may occur when urine in the bladder is concentrated and compounds (such as calcium and uric acid) crystallize.

Bone scan: Diagnostic image of the skeleton, used for detecting the spread of cancer to the bone through the use of radioactive tracers injected into the bloodstream.

Also called radionuclide scintigraphy.

“Bound” PSA: PSA molecules in the bloodstream that are chemically tied to proteins. Other PSA molecules without chemical ties are called “free.” If a man has a PSA test and most of the PSA is bound, the PSA elevation is more likely linked to cancer.

BPH: Benign prostatic hyperplasia, a non-cancerous condition of the prostate that is more common in older men. It results in a growth of prostate tissue around the urethra and an increase in the size of the prostate gland.

Brachytherapy: A form of radiation therapy in which radioactive pellets (“seeds”) are implanted into the prostate to deliver radiation directly to the tumor sites. Also called interstitial brachytherapy.

Capsule of the prostate: The outer wall of the gland.

Carcinoma: A malignant tumor made up chiefly of epithelial cells. See adenocarcinoma.

Castrate range: The level to which the body’s testosterone drops after orchiectomy. This is an important factor in monitoring hormone therapy, as certain drugs are judged by their ability to reduce testosterone to this range.
Castration: See orchiectomy.

Catheter: A tube used for drainage or irrigation, most commonly to drain urine out of the bladder.

CAT (CT) scan: See computed tomography.

CGy: Abbreviation for centigray; a unit of radiation equivalent to the older unit called a “rad.”

Chemical castration: The use of drugs to lower testosterone to the castrate range.

Chemotherapy: The treatment of cancer using chemicals to deter or stop the growth of cancer cells.

Chronic bacterial prostatitis: A form of prostatitis associated with urinary tract infections. Diagnosis is based on positive cultures that identify bacteria in the prostate, and an abundance of white blood cells in prostatic secretions. This illness may recur periodically after an initial acute episode.

Chronic prostatitis/chronic pelvic pain syndrome: The most mysterious category of prostatitis. The causes of symptoms are not known. In some men, the prostate may not even be the problem with pain coming from the lower back, pelvis, or rectum. This category has two subgroups-inflammatory and non-inflammatory, based on whether any white blood cells can be found in the prostatic fluid.

Clinical trial: A type of research study designed to test a new approach (prevention or treatment) to a disease in people. The study is overseen by the Institutional Review Board of the institution where the study is being carried out, or the Food and Drug Administration. There are typically three phases in the clinical trial that must be passed before a new drug or device is approved.

Combination therapy: A form of hormonal therapy that surgically or chemically blocks the production of testosterone by the testes, and involves the additional use of an anti-androgen to block the receptor sites from utilizing adrenal androgens.

“Complexed” PSA (cPSA): The same as bound PSA.

Computed tomography: The use of special x-ray equipment to obtain image data from different angles around the body together with computer processing of the information to render a cross-section of body tissues and organs. Also referred to as cross-sectional imaging or CT or CAT scan.

Conformal radiation therapy: A technique for delivering external-beam radiation precisely to a target (e.g., the prostate), while minimizing damage to nearby healthy tissue.

Corpora cavernosa: Spongy chambers in the penis that become engorged with blood during an erection.

Creatinine test: A blood test that helps check kidney function.

Cryotherapy: The use of liquid nitrogen probes to freeze tissues or organs (e.g., the prostate), causing cancer cells within the gland to rupture and die as they begin to thaw.

CT scan: A special imaging test. See computed tomography.

Cystometry: A urological test that measures bladder pressure and function using a pressure sensing catheter that is passed through the urethra into the bladder.

Cystoscope: An optical instrument consisting of a tiny lighted tube that is usually passed through the urethra into the bladder, allowing for inspection of the bladder, prostate, and urethra for abnormalities.

Cytokine: A chemical messenger protein released by white blood cells. Cytokines facilitate communication among immune system cells and between immune system cells and the rest of the body.

DES (diethylstilbestrol): A synthetic female hormone used until 1971 to prevent miscarriages, but taken off the market when it was found to cause birth defects. Now used in lower doses as a form of hormone.
therapy for men with advanced prostate cancer.

**DHT (dihydrotestosterone):** The most potent form of androgen in the prostate derived from conversion of testosterone by an enzyme known as 5-alpha reductase.

**Digital rectal examination (DRE):** An uncomfortable but not painful screening procedure in the urological examination during which the physician inserts a gloved, lubricated finger into the rectum to examine the prostate gland for enlargement, lumps, or hard areas.

**Diuretics:** Medications that alter water absorption by the kidney. These drugs cause the kidneys to absorb less water, so more of it leaves the body in the form of urine.

**“Dry” orgasm:** An orgasm that occurs without the expulsion of seminal fluid (ejaculation) either because seminal fluid is no longer produced (e.g., after surgical removal of the prostate and seminal vesicles for prostate cancer), or because the fluid travels backwards into the bladder (retrograde ejaculation) due to an abnormality or absence of the bladder neck. Surgery (e.g., TURP) and drugs can result in retrograde ejaculation.

**Ejaculate:** Seminal fluid produced by the prostate and seminal vesicles that transports sperm at the time of orgasm.

**Endothelin:** A family of proteins considered the most potent stimulants of blood vessel constriction. These proteins are thought to play an important role in the bone pain that results from metastatic prostate cancer.

**Epithelial cells:** Cells that line the lumen (inside) of glandular tissue like the prostate and are responsible for production of the secretory fluid produced by the gland (e.g., seminal fluid).

**Erectile dysfunction (ED):** An inability to obtain or maintain an erection suitable for penetration.

**Estrogens:** Female hormones. Estrogens can block the release of luteinizing hormone (LH)—the protein produced in the pituitary that signals the testicles to produce testosterone—and can lower testosterone to the castrate range. The main oral estrogen is DES (diethylstilbestrol).

**External-beam radiation therapy:** Treatment to kill cancerous tissue from outside the body by focusing a high-powered X-ray beam on the affected area a few minutes at a time, usually over the course of weeks.

**Flomax (tamsulosin):** A popular alpha-blocker drug used to treat lower urinary tract symptoms in men with BPH by relaxing prostate and bladder neck smooth muscle.

**Flutamide:** The generic name of Eulexin. An anti-androgen used to treat advanced prostate cancer.

**Foley catheter:** A catheter inserted through the urethra into the bladder where it is held in place with a tiny, inflated balloon. It drains urine from the bladder and can be used to irrigate the bladder free of blood clots.

**Fosamax (alendronate sodium):** A drug used to treat osteoporosis.

**Free prostate-specific antigen (PSA) test:** A blood test that measures how much PSA is not bound to blood proteins (free). The lower the percentage of free PSA the higher the chance that prostate cancer is present.

**Frozen sections:** A technique in which removed tissue from the body is frozen, cut into very thin slices, and stained for microscopic examination by a pathologist. Physicians sometimes use frozen sections to analyze tissues while surgery is taking place. Frozen sections are rarely used during prostate surgery today.

**FSH:** Follicle-stimulating hormone, made along with LH by the pituitary gland. FSH has its major effect on the testicular cells that make sperm; whereas LH acts on the cells that produce testosterone.

**Gene therapy:** A technique for correcting defective genes responsible for disease development by insert-
ing normal or genetically-altered genes into cells.

**Gleason score:** A method for grading the cellular differentiation of prostate cancer based on how it looks under the microscope. In general, well-differentiated cancers are less aggressive than poorly differentiated cancers. Prostate cancers are usually composed of cells with multiple grades from 1 to 5 with higher grades representing more poorly differentiated cells. A Gleason score is derived from combining the two most prevalent grades (1 to 5) within the tumor resulting in a score of 2 to 10 (e.g., 3 + 4 if the most prevalent grade was 3 and the second most prevalent grade was 4). Cells that are well-differentiated are given a low grade, ranging from 2 to 4. Moderately well-differentiated cells fall in the middle, with grades of 5 to 6. Poorly differentiated cells have high grades of 7 to 10.

**Gynecomastia:** Tenderness, pain, or swelling of the breasts in men. This is a treatable side effect of some forms of hormone therapy.

**Hematuria:** Blood in the urine.

**Hematuria:** Blood in the urine.

**Hereditary prostate cancer (HPC):** A term used to describe a family that is thought to have a heritable form of prostate cancer transmitted from generation to generation. A definition of HPC that is commonly used is the family in which prostate cancer is present in three first-degree relatives (a father or brothers)—or two first-degree relatives, if both developed it before age 55—or, if prostate cancer has occurred in three generations in the family (grandfather, father, son). The cancer can be inherited from either side of the family.

**Hormone-refractory prostate cancer:** *Metastatic* prostate cancer that is no longer responsive to hormonal therapy usually manifested by a rising PSA.

**Hormonal therapy:** A treatment that uses drugs to deprive the prostate of androgens. Some cancerous prostate cells are responsive to the therapy, others are not.

**Hot flash:** A side effect of some forms of hormonal therapy for prostate cancer that results in a sudden rush of warmth to the face, neck, and upper body, lasting anywhere from minutes to hours.

**Hyperplasia:** An increase in the number of cells in the prostate.

**Immunotherapy:** Treatments designed to maximize the ability of the immune system to fight cancer.

**Incontinence:** The involuntary loss of urinary control. Also called urinary incontinence.

**Insulin-like growth factors:** A class of proteins that promote cell proliferation and may influence the development of prostate cancer.

**Intensity modulated radiation therapy (IMRT):** The newest form of delivering external beam radiation that allows for more precise delivery of calculated radiation dosage to the selected target.

**Intermittent hormonal therapy:** An approach to hormonal therapy whereby PSA levels are used as a trigger to stop and start androgen ablation. When PSA levels begin to drop therapy is discontinued and initiated again when PSA levels begin to rise.

**Irritative lower urinary tract symptoms:** Bothersome symptoms including some or all of the following: Frequent urination that can occur both day and night (*nocturia*); a strong sense of urgency to urinate; inability to postpone urination; pain with urination.

**Isoflavones:** Natural compounds found in soy products that have been promoted as anticancer agents.

**Kegel exercises:** Special exercises to strengthen the pelvic floor muscles that help control urination.

**Kidneys:** The paired organs primarily responsible for making urine that helps the body dispose of the by-products of metabolism, the body’s mechanism for maintaining function of tissues.
L

Laparoscopy: A technique in which a tiny instrument containing a light and camera at one end is inserted into the body through a small incision. Used for a variety of surgical and diagnostic procedures, including radical prostatectomy.

Latent: Dormant.

LH (luteinizing hormone): A chemical substance transmitted by the pituitary gland that causes the testes to make testosterone.

LHRH (luteinizing hormone-releasing hormone): A chemical signal (protein) originating in the hypothalamus portion of the brain that causes the pituitary gland to make LH and FSH.

LHRH agonists: Synthetic versions of the body’s LHRH that can block pituitary production of LH and therefore, testosterone production.

Libido: Sex drive.

Localized prostate cancer: Cancer that is thought to be confined to the prostate gland, and therefore considered curable.

Lupron (leuprolide acetate): The brand name of an LHRH agonist used in hormone therapy.

Lymph node: A bean-shaped tissue found throughout the body that is part of the immune system. The lymph nodes trap foreign substances (e.g., bacteria) keeping them from spreading to other areas of the body.

M

Magnetic Resonance Imaging (MRI): A painless, non-invasive technique using equipment that produces strong magnetic fields to yield detailed three-dimensional images of internal body structures.

Malignant: Abnormal growth associated with the ability of cells within the tissue to spread beyond the organ of origin (become metastatic).

Medical castration: The use of medication to interfere with the manufacture or actions of testosterone.

Metastasis, metastases, metastatic: Cancer that has spread from the original tumor site and established itself elsewhere. Metastases is plural, and metastatic is the adjective form.

Middle lobe enlargement: Growth of prostate tissue that extends inside the bladder. When it enlarges, it can block the opening of the bladder like the cork in a bottle.

Morbidity: The rate at which disease occurs.

N

Nadir: The lowest point. When PSA is recorded over a period of time, the lowest number would be the nadir.

“Nerve-sparing” radical prostatectomy: The anatomical approach to radical retropubic prostatectomy, which includes important modifications to reduce blood loss, preserve urinary control, and preserve delicate nerves essential for erections.

Neurovascular bundles: Cordlike conduits located on the rectum beside the prostate that contain blood vessels and the microscopic nerves essential for erections.

Nitric oxide: A signaling molecule released by nerve endings during erection that allow the smooth muscle tissue in the penis to relax.

Nocturia: Frequent urination during the night.

Obstructive lower urinary tract symptoms: Includes weak urine flow; hesitancy in beginning urination; pushing or straining to start urine flow; intermittent urine stream; a sense of not being able to completely empty the bladder.

Oncology: The study and treatment of benign (non-cancerous) and malignant (cancerous) growths. An oncologist (surgical, radiation, or medical) is a specialist in the study of and treatment of cancerous tumors.

Orchiectomy: Surgical castration. A
form of hormone therapy involving removal of all or part of the testicles. This causes testosterone to fall to the castrate range.

Palliative: Treatment that makes symptoms better but not designed to treat the underlying cause of these symptoms.

Pathologist: A doctor who examines tissues removed from the body to help determine a diagnosis, stage, and prognosis of a disease process like cancer.

Penile implant: Mechanical prosthesis that enables a man with erectile dysfunction to have erections.

Perineum: The area between the rectum and the scrotum.

Perineural invasion: Prostate cancer in the spaces around the nerves within the prostate, not nerves outside the prostate (e.g., neurovascular bundles).

Peripheral zone: The area of the prostate contiguous with the rectum and where most prostate cancers arise.

Peyronie’s disease: An abnormal curvature of the penis due to an abnormal deposition of fibrous tissue in the elastic covering (tunica albuginea) surrounding the corporeal penile bodies (cavernosa). The cause is unknown.

Phosphodiesterase inhibitors: Vasoactive drugs such as Viagra, Levitra, and Cialis that can enhance the penile erectile response to stimulation.

Phytotherapy: The use of plant-derived substances to treat medical conditions such as benign prostatic hyperplasia (BPH).

PIN (prostatic intraepithelial neoplasia): Abnormal prostate epithelial cells found on biopsy that are believed to be precancerous.

Placebo: A non-active “pill or capsule” often given to subjects in a medical study that comprise the control group against which those taking the study drug are compared.

Proactive Surveillance: A management option for prostate cancer in which patients (usually older age) are monitored for the progression of cancer without undergoing active treatment (surgery, radiation, or hormonal therapy). Formerly called “watchful waiting” and “expectant management.”

Prostate membrane specific antigen (PMSA): A protein that is made by prostate cancer cells and expressed on the surface of the cells.

Pressure-flow studies: A test to monitor bladder pressure changes as a man urinates. See cystometry.

Proctitis: Inflammation of the lining of the rectum.

Prostate: A walnut-shaped gland about an inch and a half long that sits directly under the bladder. Its main function is to make part of the seminal fluid for sperm transport.

Prostate capsule: The outer covering of the prostate gland.

Prostate Specific Antigen (PSA): A protein made by both benign and cancerous prostate epithelial cells. The PSA test is a blood test that measures levels of PSA in the blood. An elevated reading indicates an abnormal condition of the prostate gland, either benign or malignant. The PSA test is the best tumor marker for the identification and monitoring of prostate cancer.

Prostatectomy: Surgical removal of all or part of the prostate gland. A simple prostatectomy removes the inner portion of the prostate to relieve obstruction from BPH; whereas a radical prostatectomy removes the entire prostate and seminal vesicles to treat prostate cancer.

Prostatic calculi: Tiny, generally harmless stones found in the prostate. When they become infected, as they often do in men with chronic bacterial prostatitis, they can cause a lingering infection.
Prostatitis: Inflammation of the prostate.

Proton-beam radiation: A form of external-beam radiation therapy that uses charged particles instead of electromagnetic waves to deliver ionizing radiation.

PSA: See prostate specific antigen.

PSA density: The PSA level divided by the volume of the prostate, as determined by transrectal ultrasound.

PSA velocity: The change in PSA between measurements divided by the elapsed time between the measurements.

Radiation therapy: Use of ionizing radiation to destroy cancer cells by damaging DNA within the cells. See external-beam radiation and interstitial brachytherapy.

Radical prostatectomy: A surgical procedure to remove the entire prostate gland and seminal vesicles to treat prostate cancer.

Recurrence: Evidence for residual prostate cancer following treatment usually manifested today as a rising PSA. Local recurrence indicates a return of the cancer in the pelvis either in the prostate or in the area of the prostate; whereas distant recurrence indicates the presence of disease beyond the pelvis in lymphatic tissues or bone.

Refractory: No longer responsive to therapy.

Resection: The surgical removal of tissue.

Retrograde ejaculation: See dry orgasm.

Retropubic prostatectomy: Surgical removal of all or part of the prostate gland through an incision in the lower abdomen above the pubic bone. Radical retropubic prostatectomy is removal of the prostate and seminal vesicles to treat cancer; and simple retropubic prostatectomy is removal of the inner portion of the prostate to treat enlargement causing urinary obstruction.

Reticular: No longer responsive to therapy.

“Salvage” therapy: Secondary treatment for recurrence of cancer.

Saw palmetto: An extract from the berries of the sabal palm growing in southeastern U.S. that can reduce lower urinary tract symptoms in some men.

Selenium: An essential mineral in the body that is part of antioxidant enzymes and necessary for normal function of the immune system. It is primarily found in plant foods and may play a role in prostate cancer prevention.

Semen: The fluid that transports sperm.

Semen vesicles: Glands that, like the prostate, support male reproduction by producing seminal fluid for transport and maintenance of sperm.

Sextant biopsy: A procedure in which six samples of cells are taken from the prostate, one each from the top, middle, and bottom of the gland, on the right and left sides. Sextant biopsies are now thought to be inadequate for diagnosing prostate cancer.

Spinal cord compression: The collapse of bone surrounding the spinal cord (vertebrae) due to destruction by metastatic cancer that can result in nerve damage and loss of motor and sensory body functions.

Sphincter: A circular muscle that contracts to close an orifice. The urethral sphincter closes the bladder outlet and contributes to urinary control.

Spot radiation: Localized external-beam radiation treatment designed to target one or several painful bone metastases. While it can relieve pain in treated sites, it cannot prevent new metastases from appearing in bone.

Stage of prostate cancer: The extent of the disease determined by physical examination, scans, and/or direct assessment of removed lymph nodes and prostate tissue that helps a physician determine the prognosis and appropriate treatment.
**Stress incontinence:** The involuntary leakage of urine during activities that increase pressure inside the abdomen (e.g., bending, laughing, exercising).

**Stricture:** Narrowing caused by scar tissue that can lead to blockage.

**Surgical castration:** Surgical removal of either the testicles (bilateral orchiectomy) or the contents of the testicles (subcapsular orchiectomy).

**Surgical margins:** The borders established when pathologists look at the edges of tissue that has been removed during surgery. If no cancer appears on these edges and the margins are “clear,” or “negative,” then there is a higher likelihood that all cancerous tissue was removed. However, if the margin is “positive,” there is a lower likelihood that all the cancer was removed.

**Testicles:** Paired male organs lying within the scrotum responsible for production of sperm and the male hormone testosterone. Hormones produced in the brain modulate testicular function.

**Testosterone:** The male hormone, or androgen, that is responsible for many male traits including libido (sexual drive), and the maintenance of prostate function. Lowering testosterone results in regression of prostate tissues including prostate cancer cells and is a major goal of hormone therapy used to treat prostate cancer.

**Thermal therapy (thermotherapy):** Using heat to destroy tissue. TransUrethral Microwave Thermotherapy (TUMT) and TransUrethral Needle Ablation (TUNA) are methods for transmitting heat to the prostate for the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia (BPH).

**Three-dimensional conformal radiation:** An approach to external-beam radiation therapy in which many X-ray beams, shaped to fit the target area, are focused on the prostate to deliver a high dose of radiation, with minimal damage to nearby healthy tissue.

**TNM system:** A system for describing the clinical stage of a cancerous tumor using T numbers (T1 to T4) to indicate whether the tumor can be felt or not and if it can be felt, the extent of the tumor. In addition, an N+ is used to indicate cancer that has spread to the lymph nodes and an M+ for cancer that has spread to other parts of the body.

**Transition zone:** The interior portion of prostate tissue surrounding the urethra that grows and enlarges in men with benign prostatic hyperplasia (BPH).

**Transrectal ultrasound (TRUS):** An examination of the prostate with a small probe placed in the rectum. The probe emits high-frequency sound waves aimed at the prostate that are used to construct images of the prostate gland and surrounding structures. TRUS is used by urologists and radiologists to determine the size of the prostate and direct the needle used in prostate biopsies.

**Transurethral incision of the prostate (TUI):** A benign prostatic hyperplasia (BPH) treatment in which one or two small incisions are made in the prostate with an electrical knife or laser. Decreasing the pressure the prostate exerts on the urethra alleviates symptoms of BPH.

**Transurethral microwave therapy (TUMT):** A benign prostatic hyperplasia (BPH) treatment that uses microwave energy to heat and destroy prostate tissue. The microwave energy is emitted form a catheter inserted in the urethra.

**Transurethral needle ablation (TUNA):** A benign prostatic hyperplasia (BPH) treatment in which prostate tissue is destroyed with heat delivered by low-energy radio waves through tiny needles at the
tip of a catheter inserted into the prostate through the urethra.

Transurethral resection of the prostate (TURP): A procedure used to treat lower urinary tract symptoms due to benign prostatic hyperplasia (BPH) in which prostate tissue is removed (resected) with an instrument that is passed through the urethra.

Tumor: An excessive accumulation of cells within an organ that occurs when the normal mechanisms controlling cell replacement are lost. Tumors that are benign do not have the ability to produce cells that spread beyond the organ of origin (become metastatic or metastasize); whereas malignant tumors possess the ability to metastasize.

Ureters: The conduits for transport of urine from the kidneys downward to the bladder.

Urethra: The tubular structure from the bladder that traverses the penis and carries urine from the bladder, and seminal fluid from the prostate and seminal vesicles out of the body.

Urethral sphincter: The muscular structure responsible for preventing urinary leakage.

Urethral stricture: Scar tissue that can block the urethra and prevent the normal passage of urine.

Urge incontinence: A sudden need to urinate accompanied by a bladder contraction, resulting in an involuntary loss of urine.

Uralysis: Microscopic examination of urine.

Urinary catheter: A thin, flexible tube that can be passed into the bladder through the urethra to allow the urinary tract to heal around it after surgery, or to monitor the output of urine.

Urinary retention: Inability to urinate either due to a blockage in the urinary tract, or inadequate contraction of the bladder or relaxation of the urinary sphincter.

Urodynamic studies: Tests that evaluate the pressures generated by the bladder to expel urine and the flow of urine in order to determine the cause of lower urinary tract dysfunction.

Urologist: A surgeon that specializes in the diagnosis and treatment of male and female urinary tract disease, and male reproductive disease.

UTI: Urinary tract infection. The presence of bacteria in the urinary tract that cause inflammation. The inflammation of the urinary tract can cause fever, pain, and lower urinary tract symptoms, such as frequency and urgency.

Vacuum erection device: A tubular device placed over the penis that creates a vacuum, drawing and trapping blood within the penis to produce an erection.

Vasodilator: A drug that allows the penis to become engorged with blood by widening the blood vessels. Used as a treatment for erectile dysfunction (ED).
Choosing The Right Treatment For Prostate Cancer

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**The Best Treatment Strategies for BPH**

Top specialists at Johns Hopkins’ renowned James Buchanan Brady Urological Institute present the latest thinking on managing benign prostatic hyperplasia (BPH), or enlarged prostate. This essential guide answers dozens of questions from patients searching for practical, no-nonsense advice on living with BPH. It covers current pharmacological therapies—and provides a thorough discussion of all the surgical options when medication no longer works, weighing the pros and cons of TUNA, TUMT, and TURP. Armed with the information in this guide, you’ll be able to meet with your own physician and make the right decisions in your quest for the best possible outcome.

**The Johns Hopkins Prostate Disorders Bulletin**

Written by Dr. Jacek L. Mostwin and his esteemed colleagues at the world-renowned James Buchanan Brady Urological Institute, the Johns Hopkins Prostate Disorders Bulletin is an indispensable quarterly journal for men with prostate cancer. It also covers other prostate health concerns, including benign prostatic hyperplasia (BPH) and prostatitis, and related concerns such as overactive bladder and erectile dysfunction. In in-depth reports from leading experts and summaries of critical research findings, the Bulletin goes far beyond the basics to inform you about the latest therapeutic treatments, advanced news of clinical trials, and new medications, plus detailed answers to subscribers’ concerns about all aspects of your prostate health. A subscription includes 5 FREE special reports.

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**Restoring Sexual Intimacy After Prostate Cancer Treatment**

Responding to a major concern shared by men facing surgery for prostate cancer, two leading experts at the James Buchanan Brady Urological Institute at Johns Hopkins provide the latest thinking on erection rehabilitation after radical prostatectomy. This in-depth report explores the full range of erectile dysfunction treatment options—effective oral medications, injection therapy, penile implants, and more. The report includes answers to dozens of real questions from patients on sexuality and prostate cancer.

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