THE CONRAD | PEARSON CLINIC
UROLOGY CENTER OF THE SOUTH

John R. Adams, Jr., M.D., F.A.C.S.
Ravi D. Chauhan, M.D., F.A.C.S.
Paul R. Eber, M.D., F.A.C.S.
Michael A. Granieri, M.D.
Robert S. Hollabaugh, Jr., M.D., F.A.C.S.
Thomas B. Shelton, M.D., F.A.C.S.
Matthew Sims, M.D.
Adam F. Stewart, M.D.
Val Y. Vogt, M.D., F.A.C.S., F.P.M.R.S.
Patrick J. Zielie, M.D.

Prostate Cancer

By Robert S. Hollabaugh, Jr. MD

Introduction

The prostate gland is a focus of medical concern for all men after age 40. Both benign and malignant conditions can affect the gland. Benign enlargement of the prostate (BPH) can cause urinary difficulties and will affect almost all men as they get older. Of even greater concern, 1 in 6 men will develop prostate cancer, making prostate cancer the second most common cancer and the second leading cause of cancer death in American men. The good news regarding prostate cancer is that most cases are diagnosed while the cancer is still confined to the prostate (localized or organ confined), and cancer found at this early stage usually has a high cure rate. According to recent data regarding all men with prostate cancer, the relative 5 year survival is nearly 100%, the relative 10 year survival is 91%, and the relative 15 year survival exceeds 76%. While many statistics surround prostate cancer, it is still comforting to know that most men who have prostate cancer do not die from it.

Screening and Detection

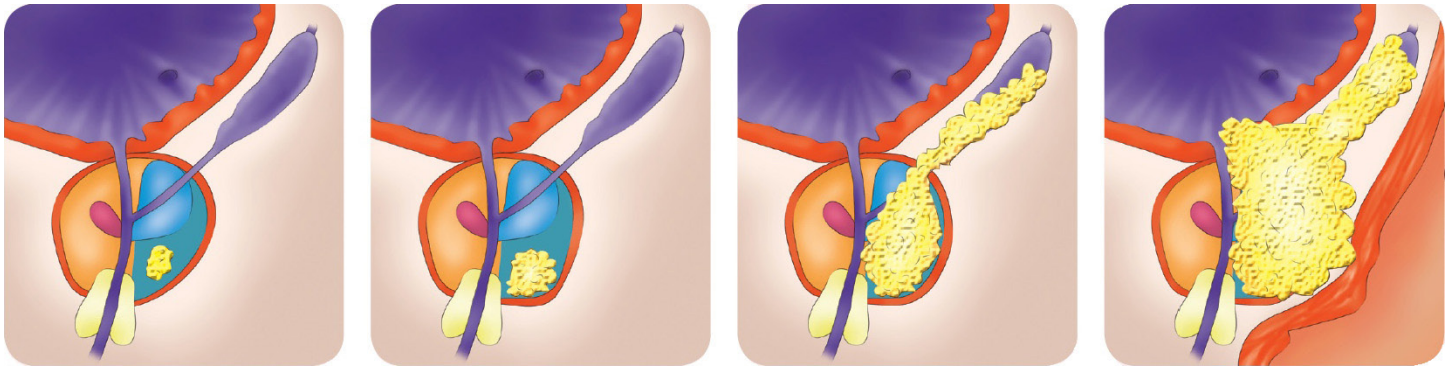
As with many cancers, the most important aspect of prostate cancer is early detection. If the cancer is caught early, before it can spread, then cure rates are excellent. Early detection is accomplished by regular screening- a **DRE (digital rectal exam)** and a blood test called **PSA (Prostate Specific Antigen)**. Both are recommended yearly after age 50. African Americans and patients with a family history of prostate cancer have a higher risk for developing prostate cancer, and screening is recommended to begin at age 40. Because early prostate cancer does not give any reliable signs or symptoms, annual screening is critical to detect it. If there is any abnormality in the PSA or in the rectal exam of the prostate, it is critical to determine whether or not cancer is present, as some findings may be due to other causes. For example, the PSA is notoriously affected by urinary infection. If the PSA is high in the midst of a urinary infection, then the infection should be treated and the PSA rechecked several weeks later before making decisions. Clearly not every abnormal PSA means cancer.

If suspicion of possible cancer persists, your urologist will recommend a **prostate biopsy**. This is performed in the office or surgery center and consists of a small needle poking the prostate thru the rectum under ultrasound guidance. It sounds a lot worse than it actually is, and generally feels about like a bee sting in the bottom. If done under anesthesia in the surgery center, you feel nothing except a mild ache in the rectum for an hour after you wake up. There is almost always mild blood in the urine and bowel movements for 2 days after the biopsy, and semen will remain stained for several weeks. Pathologists review the tissue samples and report the grade and stage of the cancer if present. The results of the biopsy are usually available one week later, and your urologist will go over these with you. If there is cancer, lots of information needs to be considered, and some additional tests may be ordered to further evaluate the extent of the cancer. **Early stage prostate cancer rarely spreads**. If it does, it preferentially metastasizes to the bones or lymph nodes. To assess these areas, bone scans and CT scans may be ordered; however, in many low risk cases these are not even necessary. In recent years, genomic assays that look at genetic markers in the cancer tissue have been developed that can give even more information predicting prostate cancer behavior. Based on all this information, your urologist will sit down with you, consider a variety of treatment options, and decide what is best for your particular situation. While the cancer specifics are very important, other factors such as an individual's medical history and personal preferences are also considered. Clearly there is no single treatment that is best for all situations.

Decision Making

Lots of different factors are used in deciding what course of treatment is best for each individual case of prostate

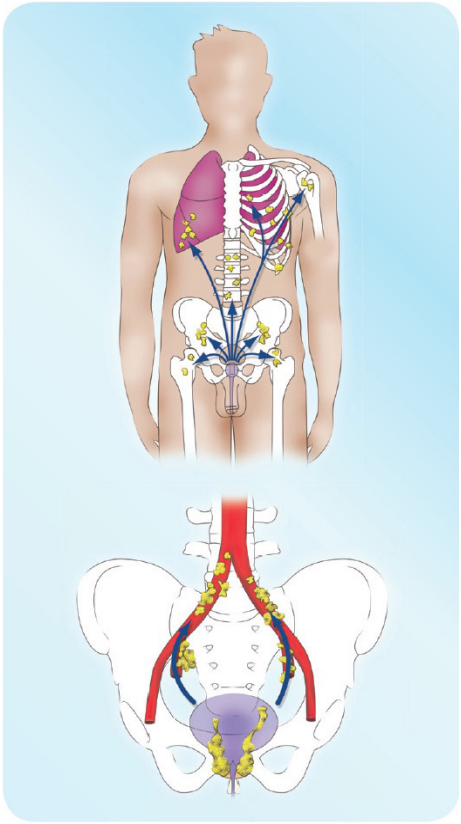
CANCER STAGES



STAGE 1 STAGE 2 STAGE 3 STAGE 4

cancer. The doctor's assessment of the extent of disease is perhaps the most important initial consideration. Using the patient's test results and statistics, your urologist will try to assess if the cancer is confined to the prostate or not. Organ-confined prostate cancer has lots of effective treatment options. If the cancer is not organ confined, the degree of spread needs to be determined. Whether the cancer is metastatic (widespread) or just locally advanced (spreading near but outside the prostate) will determine what options are available. Cases of metastatic prostate cancer usually rely on hormone deprivation therapy, immunotherapy, or chemotherapy regimens to target all of the areas where cancer has spread throughout the body. Merely treating the prostate gland would not be effective against cancer cells already spread beyond the prostate. In cases where the cancer is locally advanced but not widespread, combinations of treatments are likely to be needed. For example, even if surgery is unlikely to remove all of the cancer, a secondary boost of radiation to the periphery might be an effective adjunct in combination. Various combinations of primary and secondary therapies may be recommended depending on the overall assessment. In any case, statistics can shed light on the successes of treatment options in these various circumstances.

CANCER METASTATIC SITES



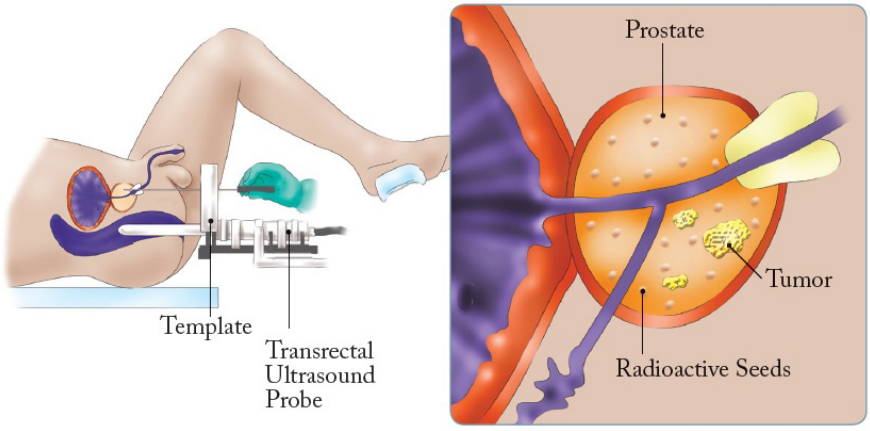
Traditionally, our link to predicting cancer behavior has been pathology. Pathologists diagnose cancer by looking at biopsy tissue under the microscope, and their visual assessment of certain features and peculiarities of the cancer cells enables prediction of the cancer's likely behavior. For prostate cancer, a **Gleason score** ranging from 2 to 10 is a numerical summary of the pathologist's findings. In recent years, cancer research has begun to look deeper into the cancer tissue, not just how it looks under the microscope, but deeper into its genetic makeup. Growing research has identified many specific genes related to cancer behavior, and we are now able to test cancer tissue for the presence, absence, amplification or reduction of gene products that correlate more closely than ever before with cancer behavior and prognosis. Being able to accurately predict a cancer's likely behavior, aggressive versus indolent, helps us more reliably make the proper treatment choice. **Genomic tests** like Prolaris and OncoType Dx are now widely used in our practice.

The chances of treatment failure or success can be assessed by categorizing prostate cancer with regard to Stage, PSA level, and Gleason Score. Patients with (1) Early Stage (T1 or T2a), (2) PSA less than 10 ng/dl, and (3) Gleason 2-6 are considered **"Low Risk"** for treatment failure. If any one of these three criteria is not met, then the patient is **"Moderate Risk."** If any two of the criteria are not met, then the patient is **"High Risk"** for failure. While there are many other methods for risk stratification, this one is fairly simple and lots of statistical data regarding treatment failure has been reported using this methodology.

Treatment Options

In deciding how to treat newly diagnosed prostate cancer, the first fork in the "decision tree" usually revolves around the decision of trying to either (1) cure

BRACHYTHERAPY PROBES



the cancer, or (2) control the cancer. With most cancers, the patient's main focus is on "cure", but in many cases "control" may be just as advantageous. In general, prostate cancer is a very slow growing cancer. It takes years, rather than days, for it to get to the problematic stages. Knowing this, we can safely take our time and consider the various options and understand the risks and benefits of each. Strategy matters with prostate cancer.

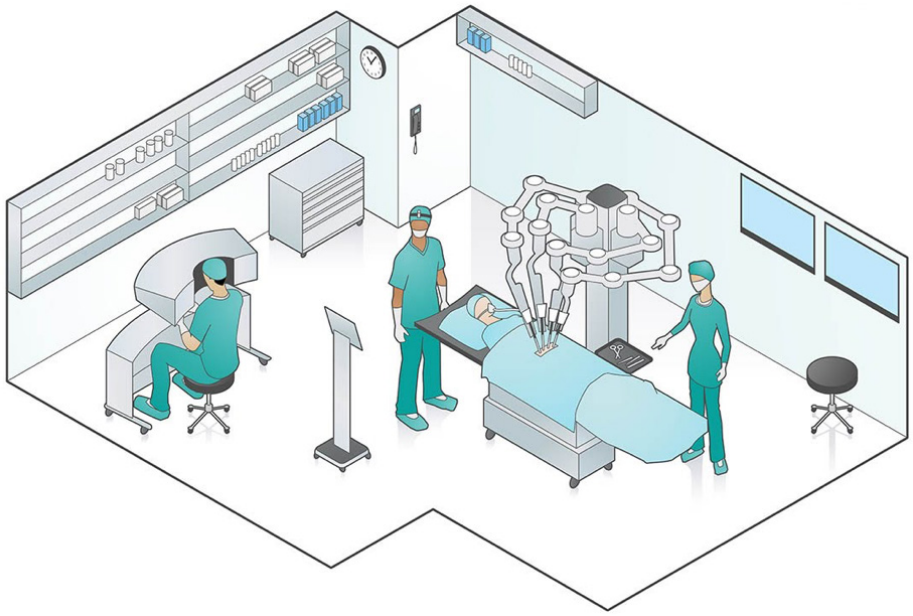
Many cases of low-risk prostate cancer are unlikely to progress or spread for many years. Knowing this, patients may elect for **Active Surveillance**, counting on the likelihood of minimal if any progression of the cancer for many years to come. While there is some risk in this, our current testing allows for pretty reliable assessment of a cancer's growth potential. Particularly if all parameters place the patient in a low-risk stratification, he may safely watch the cancer for many years, even decades. The surveillance plan calls for regular PSA monitoring (usually every 3 months) combined with either MRI or repeat biopsy every 12-24 months. As long as there is no hint of progression, the risks of aggressive treatments, particularly incontinence and erectile dysfunction, can safely be delayed or avoided altogether.

For many people definitive treatment is a priority, especially if their cancer has any higher risk features. For these patients, particularly if they are young or if they have a life expectancy of greater than 10 years, curative intervention is recommended. Curative treatment options include radical prostatectomy, radiation therapy, cryotherapy, and HiFU (high intensity focused ultrasound). For the elderly or those who have lots of medical problems, non-curative management options that control the cancer, but not cure it, may be reasonable options, allowing these individuals to live out their remaining life expectancy while avoiding both (1) complications of the cancer as well as (2) potentially risky cancer treatments. Non–curative management options include watchful waiting and androgen deprivation therapy.

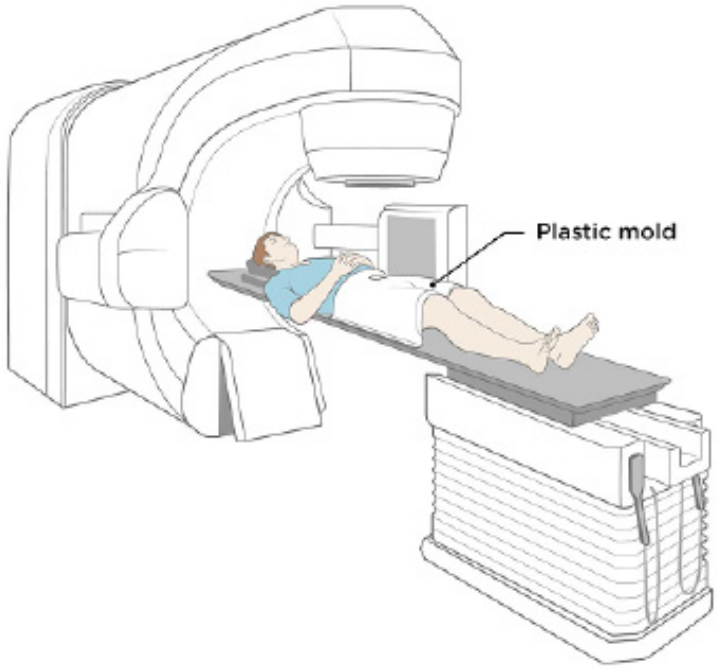
Radical Prostatectomy is perhaps the most well-known treatment for prostate cancer, and involves the surgical removal of the entire prostate gland. Traditionally, this surgery is performed thru an incision in the lower part of the abdomen allowing open access for the surgeon to remove the prostate. Many urologists still prefer to perform the operation this way and have excellent results. A modern enhancement of this operation is **Robotic Prostatectomy**, also called **da Vinci Prostatectomy**. Rather than a single abdominal incision, the robotic operation uses very small incisions where instruments and a camera are placed. Surgery offers excellent cancer control, especially with low risk stratification cases. Even so, studies have shown that residual cancer may exist in about 30% of cases which may require further treatments.

Not all cases of prostate cancer are best treated with radical surgery, and in fact, many cases need consideration for other

ROBOTIC DIAGRAM



IMRT



therapies. The extent of the cancer or the overall health of the patient will have a major role in determining the best of many other treatment options. **Radiation therapy**, like surgery, offers excellent rates of cure for localized prostate cancer. Radiation therapy is available in two broad categories: External Beam therapy and **Brachytherapy** (radioactive seed implantation). For Brachytherapy, radioactive seeds are placed in the prostate tissue using a computer generated model that allows for delivery of radiation dosing for a prescribed amount of time once implanted. The radioactive seeds are put in place using needle guides while the patient is under anesthesia. Each seed is about the size of a grain of rice, and do not have to be removed later. Usually about 70 seeds are placed, but that is determined by the actual size of the prostate. The procedure is performed in a hospital with patients usually going home within 24 hours. External beam radiation therapy has a favorable longstanding track record and continues to have technological upgrades. Currently, most external radiation therapy is delivered using **Intensity Modulated Radiation Therapy** (IMRT). IMRT uses computer models and CT scan technology to focus radiation dosing on the precise area of the prostate, avoiding radiation exposure to other nearby organs. Less exposure to neighboring organs means much less complications related to collateral radiation damage. The course of treatment is usually a 20 minute, daily regimen over a period of about 6 weeks (40-45 treatments); however, some centers can offer more abbreviated courses using a hypofractionation techniques (that need only 6-8 sessions). IMRT requires no anesthesia, and patients are usually at near normal activity levels throughout the course of therapy. Statistics for success rates treating prostate cancer vary with risk groups, but are very good in general. Comparing outcomes of radiation therapy to radical surgery for low risk cases, the cure rates are almost identical until about 10 years of follow-up. At 10 years, the cure rates for radiation begin to fail slightly. Much research is underway to evaluate these late failure rates. The controversy focuses on whether the failure is (1) a recurrence of the original cancer or (2) development of a new, unrelated cancerous area. If cancer reappears years after radiation treatment, a variety of options are still available to treat the ongoing cancer.

Many new variations of radiation therapy are now available and marketed under various names. **Cyberknife** is external XRT with adjustments in the radiation delivery that allow for treatment completion in just 6-8 sessions. **Proton**

Beam Therapy is the newest technology, using proton beam radiation as opposed to gamma radiation, and offers shorter treatment regimens and expectations of more precise radiation delivery.

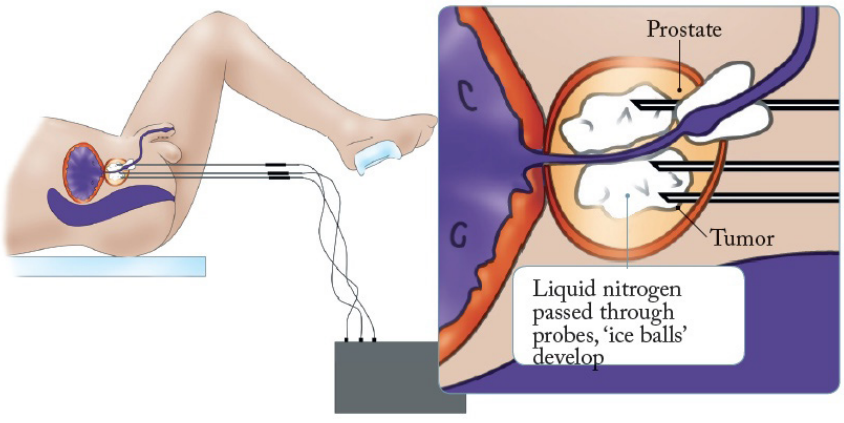
Two other treatment options with curative intent are **Cryotherapy** (freezing therapy of the prostate) and **HIFU** (high intensity focused ultrasound). Cryoablation of the prostate, also called Cryo, is usually performed in an outpatient setting, with patients going home within 24 hours. Under anesthesia, several needle-like probes are placed under the scrotum and into the prostate gland which allow for precise freezing of the prostate tissue. This freezing process destroys the cancer cells, and at the end of the procedure, the probes are removed. The newest application of Cryo is called **Focal Cryotherapy**, and involves treating only cancerous parts of the prostate, rather than the whole gland. This is still in its infancy as a treatment option, but offers promise of much fewer side effects. **HIFU** targets prostate cancer using a computer generated model that destroys prostate tissue using high intensity ultrasound waves. It can treat specific areas of cancer if architecturally distinct or treat the whole gland. It is done in a surgery center setting under full anesthesia. Neither Cryotherapy nor HIFU has nearly the amount of clinical research or outcomes data as does radiation or surgery in the treatment of prostate cancer. While each of these has its place in our prostate cancer armamentarium, the data supporting Cryo and HIFU is not nearly as robust as that of Robotic Prostatectomy or IMRT.

Watchful waiting is a management option designed for those individuals who may consider themselves too old or too ill for aggressive curative therapies. In many cases, prostate cancer is so slow growing, that it may take years before it ever even begins to cause problems. As an extreme example, an 85 year old man with prostate cancer may have other significant medical issues and only expect to live a few years related to those other problems. His prostate cancer may not ever get to a life threatening stage in his expected lifetime. Treatments for a cancer that would otherwise never threaten him could be more dangerous than the cancer itself. As such, some patients elect to merely observe the cancer behavior untreated. In these cases of watchful waiting, a PSA monitoring plan is developed. If symptoms arise or if the PSA gets too high (suggesting imminent problems), then androgen deprivation therapy is begun. Otherwise, no treatments may ever be needed.

Most cases of prostate cancer are well controlled with one or more of the above treatment options. However, sometimes the initial cancer treatments fail and the cancer recurs or metastasizes (spreads). The mainstay of treatment once cancer has spread is androgen deprivation therapy or chemotherapy. **Androgen Deprivation Therapy** (ADT) is a non-curative management option that seeks to control growth or spread of the prostate cancer by manipulating the patient's testosterone levels. Testosterone, the male sex hormone, is considered to be a "fuel" for prostate cancer. In most cases, if you take away this fuel, then the prostate cancer growth slows down dramatically. In many cases, the cancer goes into a dormant state as evidenced by the PSA going to undetectable levels. Eventually, the cancer cells will develop growth potential in the absence of testosterone, but this may take years, even decades. This ability to control the prostate cancer growth may allow patients to live out their normal life expectancy without cancer ever threatening them. The basis of hormone deprivation therapy is to force the body to stop making testosterone. This is done with medications (Eligard, Lupron, etc.) or with surgical removal of the testicles. Androgen deprivation therapy brings on a male version of menopause, because there is no circulating testosterone. Usually the symptoms are mild, but may include hot flashes, moodiness, tiredness, loss of libido and irritability. Long-term consequences may include osteoporosis and muscle wasting. The general consensus among physicians regarding hormone deprivation therapy for prostate cancer is that the cancer control outweighs the treatment risks. Because progressive osteoporosis increases the risk of dangerous bone fractures, long-term ADT therapy is usually accompanied by a bone health preserving medication like Denosumab (Prolia or Xgeva).

Patients may continue on ADT for many years. Over time, the prostate cancer cells that were suppressed may begin to grow

CRYOTHERAPY



independent of the hormone blockade. At this stage, the disease is called **Castrate Resistant Prostate Cancer**. Further testing as to the extent of the cancer is needed so that appropriate next steps can be planned. If there is no evidence of metastatic cancer, then a variety of oral medications that further block testosterone can be added (Xtandi, Erleada, Nubeqa). Studies have shown these medications can increase survival with only mild side effects. If metastases are identified, several additional advanced prostate cancer options are available. **Provenge** is an immunotherapy consisting of the patient's own blood, which is sent off to a lab where the white blood cells are energized to target prostate cancer cells, and then put back in the patient in a series of transfusions. **Androgen Receptor Inhibitors** (like Zytiga) are another option to slow advanced prostate cancer activity by blocking hormone activity. Finally, like many other cancers, metastatic prostate cancer can be treated with various types of **Chemotherapy** (Taxotere). This is usually reserved for cases where no other medicine combinations are having any effect. Several new drug classes that target genetic defects in cancer cells are being developed, including PARP inhibitors and Check Point Inhibitors, that offer future promise as well.

Complications

All treatments for prostate cancer can have side effects or complications. With any type of surgery, there can be bleeding or infection. Traditionally, radical surgery had the highest risk of bleeding, with blood transfusions being commonly required during surgery. Today's refined surgical techniques and robotic applications have made the major concern of blood loss much less worrisome. Radiation therapy, either external beam or seed therapy, can cause radiation injury to the bladder or rectum which sometimes can bleed. Cryotherapy, while not surgically removing the prostate gland, will cause destruction of the gland which can cause temporary bleeding.

Any manipulation of the urinary tract can cause infection. Usually, antibiotics are prescribed following prostate treatment, and the risk of major infection is low with all of these options.

Because the prostate gland is situated very near the rectum, injury to the rectum is possible. Whether it be surgery, radiation, cryotherapy or HIFU, if the rectum is injured an abnormal connection to the urinary tract (called a fistula) can develop. If this develops, further surgery to correct the fistula will be required. Sometimes a colostomy (making the bowels empty onto the skin) is required to treat a fistula or other rectal complications. Less than 3% of people undergoing prostate cancer treatment will have a rectal injury or develop a fistula.

Erectile Dysfunction and Incontinence are usually the major concern for patients faced with treating prostate cancer. All treatment options can effect sexual function and urinary control. For patients already having problems in these areas prior to treatment, the problem almost certainly will worsen. Return to preoperative status and function is the hope. Best results are achieved in younger patients with early cancer in general good health.

All cases involving general anesthesia have certain risks associated with being put to sleep for surgery. Most patients with significant pre-existing medical conditions will need to get evaluated by the internist or cardiologist prior to surgery. Such evaluations can identify situations where the risk may outweigh the benefit of surgery. Even in ideal cases, however, problems can arise. While rare, we have to accept the chance that heart conditions or lung conditions may complicate the course of surgery and recovery. It is possible to have a heart attack, a stroke, a seizure, or another problem that might necessitate being on the ventilator ("breathing machine") or in the Intensive Care Unit. Most of these situations, while complicated, are managed to recovery, but even death is a possibility. Assessing the health of every patient prior to treatment allows for the safest considerations.

There are only a few known risk factors for prostate cancer.

Age: Prostate cancer is more common with advancing age.

Race: It is more common in African American men than in other races. Asian American men have the lowest rates of prostate cancer.

Family History: A man's risk for prostate cancer increases if he has had a family member with prostate cancer (i.e. a father or a brother). Other genetic syndromes also show higher risk, particularly if the family has clusters of breast, ovarian, colon or prostate cancer)

Diet: Less conclusive studies have suggested that a high fat diet may also increase risk.

Germantown Office and Surgery Center
1325 Wolf Park Drive, Suite 102
Germantown, TN 38138
901-252-3400

Cordova Office
8066 Walnut Run, Suite 100
Cordova, TN 38018
901-252-3400

Southaven Office
125 Guthrie Drive
Southaven, MS 38671
662-349-1964

phone: 901.252.3400
fax:901.763.4305

Please visit our website at
www.conradpearson.com