A Short Course in Prostate Cancer

by

Thomas J. Leih, Ph.D.

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I would like to thank the men and women of the Us TOO Inspire Community who regularly share their wisdom and knowledge with people who are desperate for helpful information. The influence of this community can be felt throughout this small book.

Above all, I want to thank my wife for supporting and encouraging me during my prostate cancer journey. She made a heavy load much lighter.

About the Author

Thomas James Leih is the son of a Dutch immigrant. He grew up in Los Angeles, is a product of public education, and is now happily retired in Austin, Texas. Thomas earned a Ph.D. in pure mathematics from the University of California, Santa Barbara, in 1972, and spent his working life as a mathematician in academics and the defense industry. He has been married to his wife Marlene for forty-eight years, and they have three adult children and five grandchildren.

Thomas was diagnosed with prostate cancer in 2007, after which he elected to have robotic surgery. He began writing about his experience as part of his healing process, but soon realized he had more to say than just his story. He was concerned about the business end of prostate cancer and what he perceived as an unhealthy profit driven bias in some cases. He was also concerned that many practitioners were reluctant to embrace new approaches to diagnosis and treatment. These concerns led him to the conclusion that men must become their own advocate if they are to maximize their chance of beating this terrible disease: this requires an informed patient.

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Prologue

The purpose of this little book is to provide men facing prostate cancer with a lot of up-to-date information in a compact format. You will accumulate a lot of knowledge in an hour or two of reading. I believe it is essential for men to be involved in making healthcare decisions that affect them personally, and this is particularly important if you are dealing with prostate cancer or the possibility of having the disease. So get informed and start participating in the process.

For more information read my book, "PROSTATE CANCER Asking the Right Questions." This book is broader in scope and contains a check list that can help you through the process of dealing with this disease. There are no easy answers when it comes to prostate cancer, but being informed and asking good questions can definitely increase your chance of having a good outcome.

Chapter 1: You Must be in the Loop

Those who have been diagnosed with prostate cancer know that dealing with it is a process, not an event. This process involves determining what to do about the whole thing, from testing and diagnosis through treatment and follow-up. The key phrase is "what to do about it." This is where you need to be involved.

During my journey with prostate cancer, I learned that the medical community was selling and I was buying. Normally, we don't see ourselves as consumers when it comes to healthcare, but with prostate cancer this is just a fact. The prostate cancer market place exists because, in a lot of cases, there are multiple forms of acceptable treatment. So it is essential that the man with prostate cancer or an elevated PSA be aware of the following:

(1) Prostate cancer is **not just a disease**; it is also big business and you are the consumer.

(2) There is **no single preferred treatment** endorsed by the medical community.

(3) Many doctors are unaware of or simply

choose not to consider **alternative diagnostic and treatment options**.

(4) Many doctors are **biased toward their form of treatment**.

All of this leads to the conclusion that you must be part of the solution process. Of course you listen to the experts, you listen to people who have "been there done that," and you **do your own research.**

Chapter 2: PSA

Prostate Specific Antigen (PSA) is found in your blood. When your PSA is high or is rising over time you may have prostate cancer. The following is a partial list of things that can raise your PSA.

Things that can Raise Your PSA

(1) *Sexual relations*. How about that! If you have sex 48 to 72 hours before your blood test, it can elevate your PSA. I know of a case where a man's PSA went from a previous 3.7 to 4.49. He is an MD and suspected that sexual relations may have caused the elevation. A repeat of his test after he abstained from sex for longer than 72 hours resulted in a 3.99 reading.

(2) *Constipation*. You may think I'm kidding, but I'm not. When your rectum is full of stool it can press on your prostate and cause your PSA to rise. I know a man who experienced this phenomenon

(3) *Rough treatment of your prostate*. If your doctor digs in there a little too far or too roughly during the digital examination (i.e., the doctor feels your prostate with his finger), you can experience a rise in your PSA. Even riding a bicycle can be rough on your gland and can cause an increase in PSA.

(4) *An enlarged gland*. Your prostate can increase in size as you age: Technically, this condition is called Benign Prostatic Hyperplasia (BPH). If this happens, it is usually accompanied by an elevation of your PSA. BPH is not prostate cancer.

(5) *An infection*. This is why your doctor may give you some antibiotics if your PSA has jumped. Clearing up an infection (i.e., prostatitis) will bring your PSA back down to your normal level.

(6) *Prostate cancer*. This is the one that scares everyone. Prostate cancer usually raises your PSA—but remember, interpreting the significance of an increase is more complicated than just looking at a simple threshold.

So an elevated PSA does not mean that you have prostate cancer, but it does mean you **might** have the disease.

PSA Screening: Past and Present

PSA screening used to be simple. In my case, I would get tested once a year during my regular physical. I was told that if my number was under 4.0, I was OK. What this really meant is that the number of men with prostate cancer and a PSA less than 4.0 is small. I was never told what "small" meant, but I've read that the number of men with prostate cancer who have a normal digital rectal exam and a PSA less than 4 is 15%. I'm not sure 15 out of 100 is "small."

In addition to comparing your PSA number to a threshold, many doctors take into consideration PSA rate of increase or so called *PSA Velocity*. An increasing PSA is suspicious. There are formulas on the Internet that assess risk as a function of PSA doubling time. One such test can be found on the Memorial Sloan Kettering Cancer Center website.

Interpreting your PSA is difficult. In the past, total PSA (i.e., your number), free PSA, PSA density, and PSA Velocity were used as aids in trying to determine your risk. Also, there are a number of additional tests (e.g., PCA3) that also aid in interpreting your risk. However, in my opinion, the advent of 3T Multi-parametric MRI [see Chapter 3: Imaging] has simplified the risk assessment process. This is just my opinion, but a man with an elevated or significantly rising PSA that does not respond to antibiotics should **get a "picture."**

Chapter 3: Imaging

Introducing *imaging* at this point probably sounds strange to some, but the best way to begin dealing with prostate cancer is to try to find out what you are dealing with: like where is it located, how much is there, what are the chances that you have

prostate cancer? 3T Multi-parametric MRI can provide answers to these questions.

3T Multi-parametric and 7T MRI

The term *imaging* simply means pictures. In the past getting a picture of your prostate cancer was almost impossible. Then 3T Multi-parametric MRI came on the scene and things began to change. For over twenty-five years, CT scans, ultrasound, or Magnetic Resonance Imaging (1.5 T MRI) were too inaccurate to detect prostate cancer, and urologists were forced to rely on random biopsy—a method that misses high-grade cancer 15% of the time. Then 3T Multi-parametric MRI showed up. According to Dr. Mark Scholz, 3T Multi-parametric MRI (3T MP MRI) processing "detects high-grade disease accurately and, thankfully, overlooks low grade disease, thus sparing the shock of an unnecessary cancer diagnosis and, in many cases, unwarranted treatment. Any suspicious lesions that are detected can be further investigated with a targeted biopsy [see Chapter 4]; a more accurate way to find high-grade disease that requires far fewer biopsy cores. Men with a clear scan can usually forgo biopsy altogether." If you have a consistently elevated PSA, then the first thing you should do is get a 3T Multi-parametric MRI from a **highly qualified provider**. Expertise in the use of this technology varies.

The use of 3T MRI is now fairly common in clinical medicine, but men need to be aware that 7T MRI exists. For example, at the Center for Magnetic Resonance Research at the University of Minnesota, researchers have used 7T MRI to image the prostate on a small group of patients. This is important because 7T MRI gives a clearer picture (about twice as clear as 3T MRI). So be in the loop and keep up with the rapid advances in MRI technology. You want the best that is available to you.

MRI Parameters: Four Different Pictures

You've probably asked yourself, "What are the parameters in 3T Multi-parametric MRI?" I'm not qualified to explain this. It involves parameters like: TR, TE, Flip Angle, Inversion Time and so on. However, all of this boils down to the following common imaging techniques that are used to take pictures of your prostate:

- *T2 weighted images* give excellent anatomic detail and thus show the location of a suspicious area.
- *Diffusion-weighted imaging (DWI)* gives functional information about the movement of water molecules, which is different in healthy tissue than in tumors.
- *Dynamic contrast-enhancement (DCE)* can point to a tumor by revealing abnormal blood flow from the network of abnormal blood vessels that feed the tumor (angiogenesis)
- *MRI spectroscopy (MRIS or MRS)* is used to show concentrations of biochemicals called metabolites, since the presence of certain metabolites characterizes prostate cancer.

Getting good pictures using all of these different techniques requires skilled technicians. You also need skilled doctors to score these pictures using the Prostate Imaging Reporting and Data System (PI-RADS) for prostate cancer detection. PI-RADS is based on an earlier system for breast imaging.

Scoring Your MRI via PI-RADS

A scoring system for 3T Multi-parametric MRI has been developed to assess the chances that you have prostate cancer based on your pictures. Remember, I'm not an MD so what I'm going to say is not coming from an expert. Discuss this with your doctor.

PI-RADS is a subjective system that begins by assigning a score of 1 to 5 to each parametric image:

- PI-RADS 1: very low (clinically significant cancer is highly unlikely to be present)
- PI-RADS 2: low (clinically significant cancer is unlikely to be present)
- PI-RADS 3: intermediate (the presence of clinically significant cancer is equivocal)
- PI-RADS 4: high (clinically significant cancer is likely to be present)
- PI-RADS 5: very high (clinically significant cancer is highly likely to be present)

These scores are then used to classify your situation by summing scores for the various parametric pictures. As you can see in the table below, Class I or II suggests that you probably don't have cancer. Class III is a "Who knows?" and Class IV or V is something to be concerned about.

PI-RADS Classification System

Class	Meaning	Total of T2, DWI, DCE	Total of T2, DWI, DCE, MRIS
I	Most probably benign	3, 4	4, 5
II	Probably benign	5, 6	6-8
III	Indeterm-inate	7-9	9-12
IV	Probably malignant	10-12	13-16
V	Most probably malignant	13-15	17-20

The term *benign* is "good" and *malignant* is "problematic." This system is useful in guiding decisions about whether or not to proceed with biopsy. Some doctors don't use MRIS hence the two "Total" columns.

Color Doppler Ultrasound (CDUS)

Recall that *Dynamic contrast-enhancement (DCE) 3T MRI* pictures can point to a tumor by revealing abnormal blood flow from the network of abnormal blood vessels that feed the tumor. This procedure requires the use of IV gadolinium contrast—a contrasting agent introduced intravenously shortly before the pictures are taken. Some patients cannot tolerate IV gadolinium contrast due to impaired kidney function, an allergic reaction, or other conditions. For these patients, Color Doppler Ultrasound (CDUS) provides an alternative procedure.

CDUS is a non-invasive way to evaluate for prostate tumors with their abnormal blood vessels, without the use of an IV contrast agent. This process involves exploiting Doppler Shift. The Doppler Effect can be described as the effect produced by a moving source of waves in which there is an apparent upward shift in frequency for observers towards whom the source is approaching and an apparent downward shift in frequency for observers from whom the source is receding. Perhaps as a child you stood by a train track and noticed the shift in frequency as the train passed by. CDUS exploits the Doppler Effect associated with blood flow to color enhance ultrasound images, thus highlighting increased blood flow (hypervascularity) of suspected tumors.

You are probably wondering which technique is better? I have seen studies suggesting that DCE 3T MRI is better. One study concluded that "...the MRI was significantly more sensitive than CDUS in the peripheral (outer) zones of the prostate, where 70% of cancers begin. While the CDUS proved marginally better than MRI regarding the innermost gland zones." There are doctors in the United States who prefer to use DCE 3T MRI, and there are doctors in the United States who employ CDUS and get very good diagnostic results. I received an email from an Us TOO group leader suggesting that I include CDUS in the booklet because many members of his support group have benefited from this technology. I'm of the opinion that it is best to leave no stone unturned when it comes to prostate cancer. If it is possible to get a CDUS picture, then, "Why not?"

Positron Emission Tomography (PET) Scans

It is also important to be aware that other forms of advanced imaging are available. These forms of imaging are usually thought to apply when prostate cancer returns or has metastasized (i.e., spread). These techniques inject a tracer that lights up the prostate cancer cells under a PET scan.

The C-11 Acetate PET Scan

Obviously, I am not an expert on PET scans, but it sounds like new tracers are achieving results in detecting recurrent prostate cancer that go way beyond the results realized by conventional means. It is important to realize that conventional bone scans, CT scans, and some tracer/PET scans aren't very good at finding prostate cancer in many cases. Things are changing fast, but as far as I know, C-11 Acetate PET Scan/CT is one of the best. This is a Positron Emission Tomography (PET) scan that uses a special chemical tracer called C-11 Acetate Injection. The University of Kansas says: "At the University of Kansas Medical Center, we believe C-11 Acetate PET may be the new standard in localizing recurrent prostate cancer." Another excellent source of information regarding C-11 Acetate PET is Dr. Fabio Almeida, Medical Director of the Arizona Molecular Imaging Center. Dr. Almeida is one of the most experienced providers of C-11 Acetate PET in the United States.

I'm not an MD, but if you have a consistent elevated or increasing PSA and 3T Multi-parametric MRI shows nothing, then taking a look at C-11 Acetate PET seems reasonable to me. The down side is it may be difficult to obtain, and it will probably cost you some money.

Other PET Scans

There are other PET scans to consider. The C-11 Choline PET Scan uses the chemical tracer C-11 Choline Injection and is provided by Mayo Clinic. People at UCLA say that 68Ga-PSMA PET/CT shows great promise. Getting into a clinical trial for any of the above scans can save you money.

Some will be critical and say that these PET scans are just for recurrent prostate cancer. However, I have included them because they provide a very good picture, whether the cancer is recurrent or not. I believe that men should at least be aware that these "alternative pictures" exist. Finding the cancer when it is early stage and localized is the key to beating the disease. This also affords the prostate cancer victim more treatment options. This is more likely to occur if you get can good "pictures" early.

Chapter 4: Biopsy

Prostate cancer is really a disease with two stories. Many men with prostate cancer have low-risk, "lethargic" tumors that are unlikely to grow or cause harm for many years, if ever. Other men have high-risk tumors that can quickly become lethal if they are not detected and treated as early as possible. Because the combination of PSA testing and TRUS biopsy provides incomplete assessment of the prostate gland, many men with low-risk, indolent disease elect to receive radical treatment that could be more harmful than beneficial. Numerous men unnecessarily suffer from treatment complications like impotence and incontinence. This is the great prostate cancer dilemma: Is your cancer of the indolent or aggressive variety?

If you have a continuously elevated or rising PSA, your urologist will, almost surely, eventually recommend biopsy. Biopsy consists of taking core tissue samples out of your prostate using a "needle gun." This is the gold standard in diagnosing prostate cancer. Chapter 3: Imaging suggests that this be undertaken **after you get the pictures**. The reason for this is obvious: Knowing where to stick the needle helps a lot in finding prostate cancer and hence characterizing your risk. This is not to say that your doctor should not take random samples too. But, the old method of just taking TRUS guided random samples has its obvious limitations. Think about it: the doctor samples less than one percent of your prostate with this method. Moreover, for various reasons your doctor will not sample certain regions of the prostate, and these regions can contain cancer. A picture may show a cancer that would never be detected under random biopsy.

Today, there are different types of prostate biopsy available. Prostate biopsy has its risks (e.g., you can get a serious infection that puts you in the hospital) so you want the one that is best for you, and you don't want to repeat it if you don't have to. It is incumbent on every man to research this area before taking the plunge.

The word *targeted biopsy* is bandied around a lot nowadays. In the "old days," a biopsy was guided by ultrasound. A high frequency transducer, about

the size of a finger, with a "needle gun" apparatus attached, is pushed into your rectum and against your prostate, producing a picture of your prostate that is displayed on a monitor. This picture is not sharp enough to resolve prostate cancer, but it is clear enough to guide the doctor in taking core samples from various prostate lobes. A targeted biopsy goes further and exploits MRI pictures. If your MRI shows regions of possible cancer, then your doctor uses this information to better direct the taking of tissue samples with the "gun."

Types of Biopsy

There are essentially two types of biopsies currently in use: Ultra-sound guided biopsies and Targeted MRI biopsies. Moreover, there are two distinct techniques.

Ultra-sound Guided Biopsies

TRUS-guided biopsy TRUS stands for TransRectal UltraSound, meaning that the biopsy needle gun and ultra-sound wand (i.e., transducer) are inserted in the rectum and the needles are guided through the rectal wall into the prostate by observing the ultrasound image. Ultra-sound reveals the size and shape of the prostate, and each needle is observable so a doctor can "see" which area of the prostate is being sampled. Since ultra-sound is "blind" to differences in tissue (i.e., it can't distinguish normal prostate tissue from cancerous tissue), it does not show a doctor exactly where to target the needle—hence the term random sample. This is why most TRUS biopsies entail 10-14 needles, with half that number going to each side of the gland. The doctor does try to take samples from areas where cancer is more likely to occur. This is called a *systematic blind random biopsy*. ADVANTAGE: It can be done in the doctor's office using local anesthetic for numbing. DISADVANTAGES: It tends to miss cancers in the anterior region of the gland, leading to repeat biopsies. The small risk of infection from rectal bacteria increases with the number of needles used.

Transperineal or 3D-mapping biopsy The perineum is the outer skin area between the scrotum and anus, so "transperineal" means the needles are directed into the prostate through this skin area instead of through the rectum. However, an ultra-sound wand is inserted rectally to provide image guidance, but cannot show tissue differences. Rather than using a biopsy gun, the doctor positions a rigid plastic grid against the perineum, and directs needles through grid holes marked by coordinates. In this way, a doctor can sample tissue systematically every 5mm throughout the gland, watching the needle insertion on the ultrasound monitor. ADVANTAGE: Transperineal biopsies are very thorough, taking anywhere from 40-60 samples. There is no risk of infection from rectal bacteria. DISADVANTAGES: It must be done in an outpatient surgical setting due to general anesthesia. It is the most expensive type of biopsy, both because of the need for anesthesia and also the number of samples a lab must analyze. Ultra-sound does not show tissue differences and therefore cannot direct the doctor to suspicious areas of the prostate.

Targeted MRI Biopsies

Cognitive MRI/TRUS Guided Biopsy An MRI of the prostate is obtained prior to the biopsy, and any suspicious areas will be the doctor's reference for placing needles using ultra-sound guidance. In other words, this is a TRUS Guided Biopsy with the advantage of having an MRI picture that shows suspicious areas of the prostate. Whether the doctor doing the biopsy is a radiologist or a urologist, s/he must be experienced at reading prostate MRIs. As the word "cognitive" suggests, the doctor mentally calculates where to place the ultrasound-guided needles based on the MRI images. Thus, it is considered more targeted than random. ADVANTAGES: By utilizing MRI scans, the biopsy may require fewer needles since the MRI images act as a guide. When done by someone experienced in reading MRI, it has better accuracy rates than conventional TRUS biopsy (as high as 80+%). It can be done in a doctor's office. DISADVANTAGE: The images are not real time so a certain amount of educated guessing goes into the procedure.

Cognitive MRI Fusion TRUS Biopsy The image guidance is provided by co-registering or "fusing" (crudely think overlaying) an earlier MRI prostate scan with real-time transrectal ultrasound images. This requires special software that recognizes and matches, point by point, the shape of the prostate

and projects a 3-dimensional synthetic prostate image onto a monitor. Because a very good MRI result reveals the suspicious lesion(s), the computer can highlight that "region of interest" within the fusion image. The software "plans" the number and trajectory of the biopsy needles, and the doctor can confirm placement with the real-time ultrasound. ADVANTAGE: By incorporating MRI, the monitor reveals the area with abnormal tissue, allowing the doctor to target that area. DISADVANTAGES: Co-registering the images has room for error due to the MRI having been done at a different time with the patient in a different position, so targeting may be somewhat off; patient breathing and movement can affect the real-time ultrasound and distort the co-registration.

In-bore Real-time MRI/MRI Guided Targeted Biopsy Direct MRI-guided biopsy is performed "in-bore," that is within the MRI tube, by a radiologist, who fuses a prior MRI identifying a probable cancer lesion with the MRI scan currently being generated, to confirm biopsy needle localization. This can be performed transrectal or transperineal—the former being more common. After each biopsy sample, the patient is rescanned to confirm localization. Typically, only a few targeted cores are taken; systematic sampling is not performed. A paper describing a large experience with real-time in-bore biopsy has been published by the Barentsz group at Radboud University in Nijmegen, the Netherlands. The Sperling Prostate Center website states, "This ... type of biopsy ... is performed transrectally under real time MRI guidance. This ensures that we can target the minimum number of needles directly into the suspicious area(s); if necessary, we can also selectively sample other areas of the gland, again with a minimum number of needles." In-bore real-time biopsy is an active area of research that is incorporating the application of robotics and sophisticated software. ADVANTAGE: The advantages of this method are the limited number of cores taken, the exact localization of the biopsy, and the reduced detection of insignificant tumors. DISADVANTAGE: The disadvantages of this method include the time and expense required, including the in-bore time and the two MRI sessions necessary to obtain the biopsy specimens. Further, as only suspicious lesions are sampled, tissues with a "normal" appearance on MRI are not obtained, which is problematic, as any false-negative aspects of prostate MRI are not yet known.

Conclusion

You can decide which biopsy best meets your needs, but the above suggests that the incorporation of MRI in the process is a must.

Chapter 5: Pathology

If you have gotten this far in the process, you've had a biopsy and the tissue samples have been sent to a pathologist. Be aware that it is not the case that all pathologists are created equal. **Always** have your tissue samples sent to a center of excellence for a second opinion. I had mine sent to MD Anderson in Houston, Texas. A friend of mine did not do this, and it turned out his post-op pathology indicated that his cancer was not as aggressive as the original pathology report implied. He wishes he had this information before selecting a form of treatment.

A pathologist slices and stains the tissue samples taken in your biopsy and examines them under a microscope. S/he is looking for the presence of cancer. However, it is not the simple case that it's cancer or not cancer. Sometimes *Prostatic Intraepithelial Neoplasia (PIN)* is found, which is thought to be a precancerous condition. If you are unlucky, cancer will be found, but it comes in different grades and scores.

Gleason Grades

The professionals use the term "differentiation" when they talk about Gleason grades, which vary from 1 to 5. Good differentiation means the tissue looks a lot like normal prostate tissue. Grade 1 has reasonably good differentiation, and grade 5 has very poor differentiation. I think the idea is that tissue which looks very similar to normal prostate tissue probably behaves a lot like normal tissue, so it poses less of a threat. The more the cancer varies from "normal," the more threatening and invasive it becomes. Therefore, the higher the grade the more problematic things become.

Gleason Score

The patient is given a Gleason score, which is derived from his Gleason grades. After preparation a pathologist microscopically examines the tissue samples and determines the Primary Grade (the Gleason grade that is given to the majority of the tumor, i.e., the portion of the tumor greater than or equal to 50% of the whole) and the Secondary Grade (the Gleason grade given to the minority of the tumor, i.e., 5% to less than 50% of the whole**). The sum of the Primary and Secondary Gleason Grades is the Gleason score**. Thus, the Gleason score doesn't tell the complete story. If you are told your Gleason score is 7, are you a 3+4 or a 4+3? It definitely makes a difference. If you are a 6 are you a 3+3 (i.e., only grade 3 present), a 2+4, 4+2, 1+5, or 5+1 (I assume some of these combinations are more likely than others).

Interpreting your Gleason Score

Some doctors say that a Gleason 6 should be ignored. Personally, I think this is irresponsible. This is where you need a good doctor. A Gleason score of 6 that includes a grade of 4 should not be ignored. Frankly, I don't think any score of 6 or higher should be ignored. Your doctor needs to look at the score, the two grades, the volume of cancer present, the location or locations of the cancer (e.g., is it extra capsular—moving out of the gland; has it invaded the seminal vesicles; is it multi-focal, i.e., in more than one location), and so on to assess your condition and give you a prognosis. Your doctor will explain staging and will *stage* your cancer. S/he can go to various data bases and give you an estimate of your expected life. I asked my doctor the following question: Without treatment, what is the chance I will die from prostate cancer? He asked how long I thought I would live and then went to his computer. The answer to my question was 25 out of a 100 men with my situation will die from their cancer. Coming up with answers like this is difficult, and if your case is complex, then definitely **get a second opinion from a recognized expert.**

Additional Risk Assessment Options

As mentioned before, many men with prostate cancer have low-risk, "lethargic" tumors that are unlikely to grow or cause harm for many years, if ever. Other men have high-risk tumors that can quickly become lethal if they are not detected and treated as early as possible. This is the elephant in the room: Which type of cancer do you have? There are new tests that claim to give additional insight into assessing the aggressiveness of your cancer.

Oncotype Dx Once a prostate biopsy has been done, the tissue samples can be used for this further analysis. Based on the activity of certain prostate cancer genes, Oncotype Dx assigns a Genomic Prostate Score. The score indicates the probability that, if left untreated, the cancer would progress and eventually spread. For patients considering Active Surveillance, as well as those who will be treated, this helps both patient and doctor make an informed choice.

ProstaVysion This analysis also uses biopsy tissue to examine a sequence of certain genes. By determining the genetic aggression profile, it can help predict the risk of future growth and spread. In particular, patients considering Active Surveillance can be guided by the results of this profile.

Prolaris Unlike gene sequencing, Prolaris calculates how fast the cancer cells are dividing as a measure of aggressiveness. Patients whose biopsy indicated low risk disease can benefit from this additional information. This analysis is also often used after radical prostatectomy, when the actual tumor and additional body tissue can be tested to predict the likelihood of cancer recurrence elsewhere in the body. For prostatectomy patients, it can help determine if additional treatment (e.g. radiation or hormone) is indicated after surgery.

Negative Biopsy: What to Do

My first biopsy was negative—not even the presence of PIN. I thought I was home free, but unfortunately that was not the case. What do you do if you have a negative biopsy, but continue to have an elevated PSA? Personally, I think it goes without saying that you adopt an Active Surveillance "like" regimen [see Chapter 6)]. But can you do more? The answer is, "Yes."

ConfirmMDx Genomic analysis of prostate cancer works at the DNA level to help distinguish

patients who have a true-negative biopsy from those who may have occult (hidden) or extremely early stage cancer. This works by identifying something called the Field Effect—an epigenetic field or "halo" associated with the cancerization process at the DNA level in cells adjacent to cancer foci. This epigenetic halo around a cancer lesion can be present despite having a normal appearance under the microscope or even at times on an MRI image. Since these changes appear only at the molecular level, they cannot be seen by the standard microscopic evaluation or even the most advanced Multi-parametric MRI study. This analysis is valuable if your biopsy missed a cancer that is too small to detect or observe but hit the larger halo area surrounding the cancer. This can give you a "heads up" regarding areas to watch in the future.

The above tests can be expensive and insurance companies may refuse to pay for them. However, I have included this information because I believe a man has the right to know all that is available to him.

Chapter 6: Treatment

Prostate cancer is either localized to the prostate or prostate area, or it has spread to other parts of the body. Advanced prostate cancer can be found in many different areas (e.g., the lymph system, bones, lungs, brain), and this is why getting local control is so important.

At a high level, the man who has been diagnosed with localized prostate cancer has three treatment choices: Active Surveillance, Focal Therapy, and Radical Treatment.

Active Surveillance

Active Surveillance (AS) is a strategy to manage early stage, "low risk" prostate cancer. AS actively follows patients in order to delay the possibility of treatment-related complications. AS involves regular PSA testing (including Total PSA, Free PSA, PSA Velocity), regular digital rectal exams, and periodic 3T Multi-parametric MRIs. Be advised that this is *not* a fatalistic strategy. It is a strategy that accepts the risk of delaying treatment until the situation becomes more compelling. It is basically a tradeoff between risk and quality of life.

Focal Therapy

Focal therapy is an emerging treatment modality for clinically localized prostate cancer. It was introduced with the aim of reducing the damage to the prostate gland and surrounding areas that is associated with standard whole-gland therapy, such as radical prostatectomy (i.e., surgery) and external beam radiation therapy, without jeopardizing cancer control. What I am saying is focal therapy is associated with a lower risk of bad side effects such as incontinence (i.e., you can't control your urine) and impotence (i.e., you can't get an erection). Dr. Gary Onik (aka Dr. Hope) was the first to advocate this form of therapy. Dr. Onik suggests that focal cryoablation is appropriate for all localized grades of the disease. Not everyone agrees with this statement.

Focal therapy exists because of the advent of 3T Multi-parametric MRI. In short, if you can see it you may be able to treat it locally and not destroy the entire gland. Focal therapy is sometimes called the *male lumpectomy*—making the association with lumpectomy in breast cancer. There is a difference of opinion as to when focal therapy is appropriate, and you will have to make the final decision. Thus talk to more than one doctor. The following lists the benefits of focal therapy asserted by its supporters:

(1) Focal therapy effectively destroys the tumor within the prostate while preserving normal tissue and function.

(2) Side effects from the treatment (including changes in urinary and sexual function) are very often temporary and usually less severe than those associated with aggressive treatments.

(3) Focal therapy causes minimal injury to the prostate and does not eliminate the possibility of further treatment with radical prostatectomy, radiation therapy, or additional focal treatment to another part of the gland.

(4) Focal therapy usually can be performed on an outpatient basis or with a single overnight hospital stay.

Focal therapy may not be right for you. Some

men "just want it out of there" while others are more focused on "quality of life." Moreover, the presentation of your disease may rule out focal therapy completely. Regardless, focal therapy should be part of your evaluation process when deciding what to do about your cancer.

Focal Therapy Methods

Focal Cryoablation With focal cryoablation, the practitioner uses a needle-thin probe to deliver a solution that surrounds the cancerous tumor and kills it by freezing it to a very low temperature. Because focal cryoablation targets just a small area within the prostate, it tends to cause fewer side effects.

Focal Laser Ablation Laser ablation generates intense heat that completely encompasses the targeted cancerous area. Under real-time MRI guidance, a special optical fiber is guided precisely into place at the core of the tumor. When activated, the laser emitted at the tip of the fiber destroys the tumor within minutes while special tracking called thermometry confirms the proper temperature. Afterward, multi-parametric MRI scans reveal that the destruction is complete, and the laser fiber is removed.

High-Intensity Focused Ultrasound Ablation High-intensity focused ultrasound (HIFU) uses the energy of sound waves, directed to the tumor with the help of MRI scans, to superheat and eliminate small tumors. Some men find HIFU an attractive focal therapy approach because it is relatively noninvasive (i.e., no needles etc.). The effectiveness of this treatment is monitored in real time, using MRI to measure the temperature within the prostate during therapy.

NanoKnife® Ablation Irreversible electroporation is a technique that uses a device called the NanoKnife to pass an electrical current through the cancerous tumor. The electricity creates very tiny openings (called pores) in the tumor's cells, leading to the death of the cells. An ultrasound or a CT scan is used to focus the current precisely on the tumor, sparing blood vessels and other tissues.

Vascular Targeted Photodynamic Therapy Tumor ablation using vascular targeted photodynamic therapy is accomplished by giving you a drug through an IV that destroys cancerous tumor cells and the blood vessels that support them. The drug travels to the inside of the tumor and is activated when exposed to light of a very specific color, which is delivered through specially designed fibers placed within the prostate. Currently, the drug used in this therapy is approved for use only outside the United States. However, eligible patients can receive it through a clinical trial.

Focal therapy is relatively new, and, as far as I know, large long term efficacy studies do not exist. Some treatments are only available through clinical trials. Dr. Gary Onik has conducted a small study that has led him to conclude: "The long-term results of focal therapy using cryoablation appear to be equivalent or better to other more traditional therapies in all grades of disease." This is an amazing statement. If you select focal therapy you should be carefully monitored. In addition to PSA testing and digital rectal examination, further MRI and ultrasound studies to assess the effectiveness of your treatment are a very good idea.

Radical Therapy

Radical therapy for localized prostate cancer involves destroying the entire gland and possibly some surrounding tissue. The idea is to try to leave nothing to chance by removing or destroying all cancer and potential cancer cells. These treatments present the greatest risks with respect to side effects. They are also the oldest and most studied.

Radical Therapy Methods

There are four radical therapy methods that I am aware of: surgery, radiation, cryotherapy, and HIFU. Surgery and radiation have sub categories.

Surgery

Surgery refers to physically removing your prostate (i.e., cutting the thing out). During this procedure the surgeon attempts to preserve the nerves (i.e., neurovascular bundles) that are located on the surface of the prostate. which are necessary to get an erection. The surgeon essentially attempts to peal them off while preserving the blood supply.

I use the word "necessary" because the neurovascular bundles are not sufficient. There is

a *deep nerve* that is required to complete the process of getting rigid. The neurovascular bundles on the surface of the prostate get you enlarged while the deep nerve gets you hard: you need both types of nerves. The deep nerve is usually thought to be located outside of the field of surgery and therefore not a problem, but research has shown this is not always the case. This may partially explain why some men, who have had their "nerves" spared, are impotent. This deep nerve issue will be further addressed under the topic, *robotic surgery*.

The great leap forward in prostate cancer surgery came when Dr. Patrick C. Walsh developed the first nerve sparing technique. Now there are two recognized nerve sparing procedures

Conventional Nerve Sparing As far as I understand things, this is the surgical technique pioneered by Dr. Walsh. Walsh and Donker discovered, contrary to popular belief at the time, that "the nerves" do not run through the prostate but are located in two vascular bundles on the surface of the prostate. With this correct understanding of the anatomy of the prostate, he developed a surgical technique to save these bundles, which has become known as *Conventional Nerve Sparing*.

Veil of Aphrodite Nerve Sparing is a competitor to Walsh's conventional technique. The Veil of Aphrodite is a superficial membrane on the anterolateral (i.e., front and away from the middle) surface of the prostate. Dr. Mani Menon feels this is important because he has identified nerves on the surface of the prostate in this area. Conventional nerve sparing leaves *prostatic fascia* (i.e., tissue) on the surface of the prostate. In contrast, this competing technique does not leave a shred of tissue over the prostate. When done correctly, *Veil of Aphrodite Nerve Sparing* removes the neurovascular bundle, leaving it held in a veil of tissue—the so-called "Veil of Aphrodite." Proponents of the Veil of Aphrodite technique make exorbitant claims regarding reduced radical prostatectomy impotence. I'm not taking sides in this debate; I'm just trying to make you aware of two competing nerve sparing techniques so you can do your own research and make an informed choice.

The above discussion of nerve sparing is an over simplification. The UCLA website states: "In fact, it has been shown that prostate nerve-sparing surgery is performed with tremendous variation." I hope that the above information will at least help you start a meaningful discussion with your doctor on this important topic.

Some may say, "Sometimes it may be that one can know too much." I don't agree with this. Every prostate treatment procedure has positives and negatives that men need to be aware of so they can make an informed decision. With surgery you need to be aware that you will probably lose one of your sphincter muscles. A man has muscles (i.e., valves) above and below the prostate that control the flow of urine, and the upper muscle is usual lost. This means that the remaining muscle has to do all of the heavy lifting. This is why it is important to go to a physical therapist specializing in incontinence before and after surgery. You go to a physical therapist to get the lower muscle as strong a possible before the surgery and after to rehab the muscle since it has been weakened by the surgery. I will speak more about this in Chapter 7: Impotence, Incontinence, and Cancer.

Assessing the Risks

The greatest risks associated with surgery are impotence and incontinence. Of course there are others: not waking up from the anesthesia, infection, nicking your bowel, etc., but these are quite small. However, the chance of being impotent or incontinent or both are not what I would call small.

I suggest you choose a surgeon with a lot of experience (e.g., a robotic surgeon should have performed a thousand or more procedures) and one who keeps good records. By this I mean successes and failures. When I asked my surgeon about my chance of being incontinent he went to his spread sheet, calculated the number based on his personal outcomes, and said, "Just under 5 percent or 5 out of 100 men." For some surgeons this number is closer to 10 percent or higher.

In addition to ascertaining your chances of being incontinent and/or impotent, ask the surgeon about the chance of having a *positive margin* based on his data. In other words, what is

the chance that the post-op biopsy will show cancer at the edge of the removed gland. If this happens you are probably in for some radiation treatment to clean things up.

Finally, ask about the chance that your cancer will return. Estimates of this depend on a lot of different factors including the aggressiveness of the disease to start with, but I have seen numbers as high as 30 percent in 3 years and 40 percent in 5 years. These numbers are very loose so please don't take them to the bank, but hopefully, the surgeon you are interviewing can provide you with numbers that are a lot better than these—mine did. After my post-op biopsy results and zero PSA, I was told my chances of return were 2 out of 100.

Getting answers to the above questions assumes the surgeon keeps very accurate records of his or her outcomes. If the surgeon you are talking to does not keep accurate records, then maybe you should talk to one that does.

Finally, in general, surgery and radiation are not commutative. If you have radical radiation treatment, then it is unlikely that you can follow it with surgery. I say "unlikely" because there are a few surgeons who will accept the challenge.

`Surgical Methods`

I am familiar with four surgical methods regarding radical prostatectomy.

Retropubic Prostatectomy. In laymen's terms this is the "traditional" or "open" surgery. You'll have an eight- to ten-inch cut in your abdomen and a significant recovery time. Bleeding can be an issue and blood transfusion is more likely than with robotic surgery. I was told that the surgery itself takes about three to six hours (of course this is totally dependent on your situation and your surgeon), during which you are in a head-down position. Surgeons that perform this surgery say it is the best because they can feel the tissue with their hands. They say feeling the tissue makes it less likely that they will cut into the gland and thus possibly leave some cancer cells.

Perineal Prostatectomy. This type of surgery is less common. The surgeon reaches the prostate through an incision between your scrotum and anus. It is my understanding that this method does not allow the surgeon to check the lymph nodes for cancer, and it is also more difficult to spare the nerves that control erections. If you examine the anatomy of the prostate you can see why this is the case.

Traditional Laparoscopic Surgery. First of all, this type of surgery avoids the big cut in your abdomen. It is done by inserting slender tubes through very small incisions (i.e., roughly half-inch cuts) in your lower abdomen. The tube with the camera requires a slightly larger cut. The surgeon sees through the eye of the camera while he directly controls the surgical instruments with his hands—there is no robot involved. The benefits of laparoscopic surgery are: no big incision, your hospital stay is usually shorter, your recovery is faster, and there is less blood loss and pain. However, the surgeon obviously cannot feel the tissue with his hands, and the instruments' movements within the body have only four degrees of freedom. I think most physicians think robot-assisted laparoscopic surgery is a much better choice.

Robotic-Assisted Laparoscopic Surgery (i.e., Robotic Surgery). This is laparoscopic surgery with the surgeon controlling a robot that assists with the laparoscopic instruments. It kind of looks like the surgeon is playing a 3D video game, and the robot looks like something out of a 1950s science fiction movie. This is the latest development in laparoscopic surgery. In theory, the surgeon could be in a different part of the building or even in a different town and still conduct your surgery, while a surgical crew stood by you to assist. I think most people would agree that robotic-assisted laparoscopic surgery offers advantages over the traditional laparoscopic approach. One such advantage is that the new surgical instruments act more like the human wrist and have seven degrees of freedom instead of four. This is important when the surgeon needs to "reach" behind the prostate. Another benefit is a strong camera zoom feature that supports close inspection of tissue. However, obviously the surgeon still cannot feel the tissue with his hands. (I've heard some robotic surgeons say that they have developed a pseudo feel, but I am skeptical regarding this claim.) I assume the benefit of minimal blood loss is the same as traditional

laparoscopic surgery.

Nerve Mapping

I don't know if this applies to other forms of prostate surgery, but it is possible to map the deep nerve during robotic surgery and maybe some others that I don't know about. If any of the vascular bundles or deep nerves are bruised, stretched, burned or cut, they will be damaged and erectile response will suffer. With robotic surgery, nerve mapping/ real-time monitoring is available, but it is **not always used**. This technology is necessary to find (i.e., map) the critical deep nerve and alert the surgeon when he is getting too close. The distances we are talking about can be as small as one or two millimeters. It only takes about five minutes to set up the system (i.e., the ProPep Nerve Monitoring System), thus having a minimal impact on the length of the surgery. For decades, nerve mapping/ monitoring have been standard procedure in spine and neurosurgery, where potential nerve damage is a significant risk. I don't know how much nerve mapping decreases your chances of being incontinent or impotent, but if it helps 1 out of 100 or 1 out of 500 for that matter, and you happen to be the one then it is a big damn deal.

Radiation Therapy

Radiation therapy, also called *Radioytherapy*, uses radiation, such as x-rays, gamma rays, electron beams or protons, to kill cancer cells or damage them so they cannot grow or multiply. *External Radiation (i.e., radiation delivered outside the body)* includes the following modalities: 3D conformal radiation therapy, intensity-modulated radiation therapy, proton beam therapy, and stereotactic body radiation therapy. *Internal Radiation (i.e., radiation delivered inside the body)* includes: high-dose-rate prostate brachytherapy, and low-dose-rate prostate brachytherapy. Some times external and internal radiation are combined and then given a fancy name to make it sound as if it is something new.

Assessing the Risks

The main risks associated with radiation therapy are: incontinence, impotence, and damage to healthy tissue; particularly healthy tissue in organs like the bowel, bladder and urethra. I think most people agree that the risk of being incontinent is lower with radiation than with surgery. Some argue the same is true of being impotent. I suggest you do your own research on this, keeping in mind that most practitioners want to sell you their form of treatment. The risk of damaging the bowel, bladder, or urethra is greater with radiation than with surgery. With surgery, bad side effects show up without delay. For example, most men are incontinent immediately after surgery and then proceed to get better. With radiation therapy, bad side effects may not show up immediately, but can show up months after treatment. Finally, there is the risk of introducing secondary cancers. Radiation has to go through healthy tissue before reaching the cancer it is trying to destroy, and damaged healthy tissue can eventfully become cancerous. I don't know if we are talking years or decades, but it seems to me that a conversation regarding this risk is appropriate.

Of course, in all of this the practitioner's experience and skill need to be factored in, and that is why you want a radiologist who keeps very accurate records. As with surgery, you want the radiologist to tell you your chances of experiencing these bad side effects based on his or her personal data. Of course you also want to know the chance of being "cured."

External Radiation Therapy

External radiation is delivered outside the body with machines that are manufactured by different companies. I am not qualified to comment on who is the "best" manufacturer. However, if you go to a center of excellence for your treatment you are probably going to get state of the art technology. This isn't always true at the community level.

3d Conformal Radiation Therapy (3D-CRT) Before 3D-CRT, something called *electron beam radiation therapy (EBRT)* was used. Today, I think it would be hard to find someone in the United States using this technology to radiate your prostate. As far as I know, *3D conformal radiation therapy* will be the oldest technology you encounter in your research. I include it because it is still in use and in some cases may be preferable. 3D-CRT is a modified form of EBRT and is designed to be more accurate and deliver higher radiation doses. After the patient is immobilized

by being placed in a mold, the radiation oncologist uses a CT scan to take 30 to 40 pictures of the pelvic region from 3 centimeters below the prostate gland to 3 centimeters above the upper tips of the seminal vesicles. Using these images, a computer reconstructs a 3-dimensional model of the patient's pelvic region. 3D-CRT delivers a larger number of beams than EBRT with each day of treatment. The conformal beams are shaped to the targeted area so the dose is higher. An automated computer controls a multileaf collimator (MLC) which automatically conforms the beam to the specific shape, no matter how irregular the treated area appears. The amount of radiation delivered to the targeted areas is manually determined in advance by the radiation oncologist.

Image Guided-Intensity Modulated Radiation Therapy (IG-IMRT) The prevailing wisdom is that IMRT is a step up from 3D-CRT. This is because it has the potential to do less damage to healthy tissue. *Helical-tomotherapy* is a form of IMRT that delivers radiation inside a large "donut." For this treatment, you lie on a table that slowly slides through the donut as the machine spirals around you. It delivers many small beams of radiation at the tumor from different angles around the body. This may allow for more precisely focused radiation.

Note that IMRT can be delivered without real-time image guidance, which you probably don't want to do. When you have your prostate radiated, you want the radiation to go where it is supposed to go. Missing by a couple of millimeters can burn a vital organ like your colon. Body molds and tattoos do not guarantee that you end up in exactly the same position each day of treatment. Moreover, just breathing can alter the position of your prostate.

At this point I am quickly getting way out of my league, but Image Guided Radiation Therapy (IGRT) is so important I feel compelled to say something. When undergoing external radiation therapy, it is important that the position of the patient be repeated for each treatment. Historically, the patient has been aligned using body molds and tattoo marks placed below the skin. The exact way proper alignment is accomplished day-after-day is complicated and is beyond my knowledge, but it depends in part on images gathered during treatment and subsequently analyzed off-line. It is important to be aware that there is also an on-line capability that makes adjustments to patient and beam position **during the treatment process**, based on continuously updated information throughout the procedure

Off-line analysis reduces systemic errors, and on-line analysis reduces systemic and random errors. When you get into your mold, you are not going to be perfectly lined up every time, and during the procedure the prostate gland can move due to breathing or passing gas for example. Now on-line analysis/adjustment capability includes the placing of gold fiduciary markers in the prostate to provide a surrogate position for the gland. With these markers, very small real-time position corrections can be made. I think you can see that you want state-of-the-art IGRT if you choose external beam radiation therapy. It's worth having an in-depth discussion with your radiation oncologist on this topic. Tumors are moving targets, and image-guided radiation therapy uses dynamic tumor tracking to pinpoint the exact size, location, and coordinates of a tumor just prior to and during treatment. Ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), position emission tomography (PET), and x-ray imaging may be used to obtain a detailed imaging of pelvic contents. The increased precision of IGRT allows for higher doses of radiation to be focused and delivered directly to tumors and cancer cells.

As suggested above, IMRT is a specialized form of 3D-CRT that allows radiation to be more exactly shaped to fit the tumor. The statement, "more exactly shaped to fit the tumor," catches my eye.

IMRT takes the patient's tumor extension into account by using stronger doses of radiation on more affected parts and weaker doses of radiation for the less affected parts. The goal of intensity modulated beam therapy is to deliver higher levels of irradiation to the cancerous tissue while avoiding the healthy tissue. The result is more effective prostate cancer treatment and increased avoidance of severe radiation therapy side effects. With IMRT, every beam is broken down into tiny

"beamlets", and each beamlet can be given a different dose. This results in beams with different intensities across their surfaces. Multiple beams are used for each treatment. Although the beams are all different in shape and intensity profiles, once they all converge on the prostate you are left with a high dose of radiation covering the prostate gland, and a lower dose hitting normal tissues. The result of all of this is potentially less damage to healthy tissue. I've read that IMRT reduces the chance of experiencing rectal bleeding from ten to two percent.

Radiation damage can be near-term (e.g., rectal bleeding after treatment) or delayed. With any form of radiation therapy there is the potential to introduce latent (i.e., secondary) cancers that show up years after treatment. If IMRT is potentially less likely to damage healthy tissue and introduce latent cancers, and is at least as good as 3D-CRT in treating the cancer, then it gets one of my votes. Of course, you need to research this on your own to see if this is true. Just remember you want to consider IG-IMRT, not just IMRT.

Intensity-Modulated Proton Beam Therapy (IMPBT)
Due to technological advances in the past few decades, it is important to frame any comparison between proton beam therapy (PBT) and photon therapy in the context of contemporary techniques. Currently, PBT can be delivered by two methods.

The older method uses a three-dimensional (3-D) conformal technique where passively scattered proton beams of differing energies are combined to form a spread out Bragg peak (SOBP, i.e., the total radiation dosage of the protons) that fully encompasses the target. The most common beam arrangement uses two opposed lateral beams, and customized apertures and compensators are fabricated to shape the field and alter the dose–depth profile to better conform the SOBP to the actual tumor.

The second newer method utilizes proton pencil-beam scanning, which allows more conformal and complex "IMRT-like" distribution. This is known as intensity-modulated proton beam therapy (IMPBT) and has a greater ability to conform the radiation dose to irregularly shaped targets.

Perhaps a little more information regarding the pencil beam scanning (PBS) that IMPBT employs is in order. PBS "paints" small groups of protons back and forth through a tumor. The protons fill the depth and contour of the tumor, allowing greater control of radiation doses, shorter treatment times and reduced side effects, compared with most other proton therapy systems. This next generation of PBT sounds important to me when it comes to treating prostate cancer—be sure to check it out.

Proton Beam Therapy (PBT) for prostate cancer is surrounded by debate. This is because it costs more than other treatments and some insurance companies are refusing to pay. There are many supporters and critics of PBT. If you want to connect with PBT enthusiasts explore the Brotherhood of Balloon, but remember you may only be hearing about the successes of the treatment. I think it is fair to say at this point it is not clear that IMPBT gets rid of cancer better than IG-IMRT, but in theory it has certain advantages. You see, X-rays enter the body releasing a lot of energy, pass through the tumor, and then continue on through any fluids or soft tissue. So X-rays pass through good tissue before and after the tumor is hit. With IMRT, the smaller beamlets zap the tumor where they overlap. Since the beamlets are smaller they are less likely to damage tissue where they don't overlap, but the X-rays produced still proceed through the body. On the other hand, protons are positively charged particles with tremendous energy and tremendous mass. Moreover, they are easier to control because they slow down after entering body tissue, and they can be set to release most of their energy at a specific point in the body. "Proton beams don't emit energy in a constant stream. They typically release it in increasing amounts as they start to slow down, because the slower they move the more atoms they have time to hit. And when they stop moving, they release most of their energy in one giant burst of radiation. After that burst, there's very little energy left, and they just stop. There's no 'exit dose' of radiation like there is in X-ray therapy." It seems to me that no "exit dose" after hitting the desired spot translates into potentially less damage to healthy tissue unless they miscalculate. Of course, that is a big "unless." If they miss the target by just a little bit

and the "burst of radiation" occurs in healthy tissue like your colon, then there can be problems. To be fair, missing the target can occur with IMRT too, but one radiation oncologist told me that the consequences were not as great. Of course, he had just purchased a new IMRT machine which I'm sure influenced his opinion.

Stereotactic Body Radiation Therapy (SBRT) It is hard to get a handle on what SBRT is exactly. Is it really something that is different from conventional IMRT? When you read about SBRT the benefits of lower cost and shorter treatment time are emphasized, but this doesn't tell you what it is. I read one study that stated the average cost of prostate cancer SBRT treatment is around $13,000 and IMRT around $21,000. If time and money are your priorities, then SBRT may be the way to go. By the way, PBT is the most expensive form of radiation therapy. With one treatment per day, SBRT takes about five days compared to around eight or nine weeks or more for IMRT. It makes sense that if you use the machine more the treatment will cost more. But again, "What is SBRT?"

As far as I can tell, the distinction is found in the term *hypofractionation*. *Gray (Gy)* is the unit used to measure the total amount of radiation a patient is exposed to. Your radiologist wants to expose your cancer to a certain number of Grays in order to kill it. However, delivering this amount of radiation all at once would wreck you. Therefore, the total radiation dose is divided into several *fractions*. The more fractions the smaller the amount of radiation that is delivered per fraction per day. H*ypofractionation* refers to dividing the total amount of radiation desired into fewer fractions, which obviously means each fraction contains a higher dose of radiation. This is what SBRT incorporates—fewer fractions. SBRT takes fewer days of treatment because it exposes you to grater amounts of radiation per day. Some people use the term *Alpha:Beta* ratio to argue that this is a more effective way to treat and destroy prostate cancer. I don't know, and it is incumbent that you check all of this out yourself.

There is always a trade-off between killing the cancer and unwanted side effects. As a rule of thumb, higher doses of radiation bring higher risks. Is it better to have more fractions with lower doses spread over more time or just go for it and try to nail the stuff in five days? I can't answer this question. I've seen studies that show SBRT beats IMRT in five year survival rates, and I've seen studies that assert SBRT does more damage to healthy tissue than IMRT, which can really affect your quality of life. I'm sure you can find studies that say the two treatments are about the same. What I fear is that insurance companies will gravitate to SBRT simply because of cost savings. In this the patient loses.

If you want a concrete example of an SBRT system to investigate, take a hard look at the Cyberknife. This system has a robotic arm with articulating joints that can be positioned at different angles. It also includes **continual image guidance** software that allows the delivery of high radiation doses with good accuracy, while automatically correcting for tumor movement. Since radiation beams adjust in real-time to the patient's breathing cycle, there is the potential for less damage to surrounding healthy tissue. In other words, the Cyberknife incorporates a form of Image Guidance.

`Internal Radiation Therapy`

Internal radiation therapy, also called *Brachytherapy,* is commonly known as the "seeds" approach. There are two types of "seed" therapy: *Low Dose Rate (LDR)* and *High Dose Rate (HDR).* With LDR, usually 40 to 100 "seeds" are inserted into various spots in your prostate. Each "seed" has a small amount of radioactive material that emits radiation within a localized area. The "seeds" are left in your prostate after their radioactive material has expired. In very rare situations, the seeds can become dislodged from the prostate and cause problems. In the HDR case, a radioactive source is inserted in pre-positioned catheters and then removed in five to fifteen minutes.

Brachytherapy is a form of radiation therapy that does not pass radiation through the body, which is good. The radiation is localized to the prostate, but it can affect nearby tissue. I don't know if this type of therapy poses more risk or less risk than others, but I do know there are risks. I say this because sometimes the "seeds" are presented as being almost risk free. As with all forms of prostate cancer treatment,

Brachytherapy with or without external irradiation can be associated with severe complications.

Other Forms of Treatment

In addition to being a candidate for focal therapy*, High-Intensity Focused Ultrasound (HIFU)* can be used as an aggressive form of treatment. Recall this treatment uses a machine to project focused high-frequency sound waves. These waves raise the temperature of the target tissue to around 190 degrees in a few seconds. Basically, this treatment "cooks" your prostate or tumor locally without using radiation; thus, it claims to avoid many of radiation's side effects. You don't have to worry about damaging healthy tissue on the way in or out. Moreover, it is a minimally invasive one day procedure. To me, this procedure sounds attractive because of reduced risks, and it is easer on you—particularly if you are older.

HIFU has been used outside of the United States for over fifteen years, and the total number of men treated exceeds 50,000. The question is, "How well does it perform?" One study stated, "Success rate was represented as follows: 94.2% in the low risk group, 83.4% in the intermediate risk group and 0% in the high risk group." So it would seem that this is something to consider if you are "low risk." Be advised that there are HIFU providers in Europe that charge substantially less (i.e., about one-half) than United States providers. If you are paying your own way, then this is a consideration.

Cryotherapy has already been mentioned as a reasonable possibility for focal therapy. In the past it has also been used for radical treatment, but as far as I know, bad side effects rule it out.

Metastasized and Recurrent Cancer

What do you do if your cancer is not local to the prostate (i.e., it has spread to other parts of the body) or has returned after treatment? If you chose radical radiation therapy, then it is unlikely that you can have surgery as a *salvage treatment*. However, either radiation, cryotherapy, or HIFU are possibilities depending on your situation. If you are in this position, then definitely review Chapter 3 on imaging. Do your best to get pictures that show what is going on.

Standard forms of imaging may not help you find your cancer. For example, it takes the presence of billions of cancer cells for it to show up on a standard bone scan. A friend of mine found himself in this position three years after radiation treatment. He paid the freight and got a C-11 Acetate PET Scan that revealed a small tumor on his spine and a small tumor near his radiated prostate. These spots were treated with the Cyberknife and IG-IMRT, respectively, and with a hormone therapy shot. It has been quite a while, and as far as I know he is doing fine. All of this was possible because he was able to get a picture that showed the locations of his recurrent cancer.

Which Practitioner?

If your cancer has spread, you should be under the care of a *medical oncologist specializing in prostate cancer*. Do some serious research to find a good one. Treating advanced prostate cancer is where art and science meet—different doctors believe in different approaches to this problem. Your urologist or radiologist is not qualified to treat you; obviously, I have nothing to add beyond this point.

Regardless of the treatment type, there is no substitute for experience. The more procedures a practitioner performs, the more accomplished the practitioner becomes. I mentioned above that a robotic surgeon should have performed at least 1000 prostate surgeries. Actually, I was told by one of the best robotic surgeons in the country that the number is 500 , but I doubled the number because the pool of experienced robotic surgeons has grown considerably in the last ten years. To reiterate, there is no substitute for experience, regardless of the form of treatment.

An equally important requirement is good performance numbers. I can't emphasize enough the fact that you want a practitioner who keeps accurate records. If this is not the case, then how can you quantify the quality of care that you will receive? Without the practitioner's own data, how can you quantify the risks associated with his or her treatment? Statistics quoted in papers and books are fine. They give you a general idea about your chances of having a successful outcome with a particular form of treatment, but in the end, if possible, you want to know the

statistics associated with the person performing the procedure on you! It is just a fact that some people are better at their trade than others.

Chapter 7: Impotence, Incontinence, and Cancer

When I was diagnosed with prostate cancer I remember thinking, "If I get this stuff I might do nothing about it." I was terrified of being impotent from treatment. My next worry was incontinence. If you think about it, being significantly incontinent is as life changing as being impotent: maybe more. Getting rid of the cancer was a distant third in my priorities. After all, I knew guys who had been treated and were fine. Then I learned more about this vicious disease, and I changed my priorities. Getting rid of the cancer became number one. After my surgery appeared to be successful, the importance of being potent and continent took center stage. I learned there are things you can do to increase the odds.

Penile Rehabilitation

Tragically, this is a topic that you don't hear much about. Most men know that impotence is a very realistic possibility after prostate cancer treatment. This is probably more likely with surgery than any other form of treatment except radical cryotherapy. What men usually don't know is that the chance of damage to the penis, called "atrophy," increases the longer a man goes without a post-treatment erection. What occurs is scarring of the erectile tissue, which can yield permanent damage. Dr. John Mulhall states, "The incidence of erectile tissue damage, as measured by the presence of venous leak is very uncommon before the fourth month after surgery. However, at eight months after surgery it occurs in about 30% of men and at one year in 50% of men." This is why it is absolutely essential that everything possible be done to ensure that erections occur before the fourth month after surgery and probably after any other form of treatment. Simply waiting for the nerves to heal and then addressing this issue is not good. You can employ strategies such as taking ED medications like Viagra or Levitra two weeks before treatment, taking them after the catheter is removed, getting penile injections, using intra-urethral suppositories, and so on. For a no holds barred discussion of this topic read *Saving Your Sex Life: A Guide for Men with Prostate Cancer* by Dr. John Mulhall. [Dr. Mulhall is Director of the Sexual and Reproductive Medicine Urology Service located at Memorial Sloan-Kettering Cancer Center.]

Incontinence and the Golden Year

As I mentioned before, a man has two sphincter muscles that control urine flow: one above the prostate and one below. After surgery only the lower muscle remains. This remaining muscle is usually weak and possibly traumatized by the surgery, which results in incontinence. As with any injury, it is important to begin a period of rehabilitation as soon as possible to repair the damage that has occurred. Unfortunately, many times this "rehabilitation" merely consists of being told to do a large number of *kegels* every day. This approach can actually weaken the muscle because of muscle fatigue. Overworking a muscle does not build it up—it tears it down. Moreover, there is a right way and a wrong way to do kegels, and you need someone to explain how it's done correctly.

Fortunately there are physical therapists who specialize in treating incontinence; however, most of them emphasize treating women because pregnancy and subsequent incontinence go hand-in-hand. It sounds strange, but postpartum women and men who have had prostate surgery have something in common—they both have only one sphincter muscle to control their urine. Therefore, techniques used by physical therapists to treat female incontinence readily adapt to treating male incontinence for prostate surgery patients. Personally, I was given many different exercises to address leaking problems associated with position: laying horizontal, sitting up, standing, bending over, etc. I was even given exercises to train me to pass gas and not urinate. I actually got to the point where I could squeeze the front and the back of the muscle independently. I also happily watched the strength of my muscle go from a post surgery value of 10 to 35 as measured by the therapist. I don't know what these units mean; all I know is I watched

myself regain reasonable control. It has been ten years, and I'm still in pretty good shape.

It is important to go to a physical therapist before and after treatment. The stronger the muscle is before treatment, the faster you will regain control after treatment. This goes for any form of treatment—not just surgery. As far as surgery goes, I was told I had a year to get control. After that improvement usually drops off substantially. Don't waste this "golden year." Go to a physical therapist who specializes in treating incontinence.

Epilogue

I hope I have provided you with some useful up-to-date patient-oriented information. Now you know there is no silver bullet for prostate cancer treatment, but there are some good options. However, you will have to make decisions that no one should have to make, and I hope this little book will assist you in your journey. I can't help but feel a kinship with you. You've joined the Brethren, we who must face this disease. You are my brother, and I truly wish you the best.

Sincerely,

Tom