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♦ Meeting the Challenge -- Making Every Day Count ♦

(**Editor's Note**: Peter Collins, a WRAMC Us TOO member, participated in the 2007 LiveStrong Century Challenge biking event sponsored by the Lance Armstrong Foundation. His experience was described in a September 2007 issue of *STRIPE*, a WRAMC community newspaper. It has been modified and expanded here.)

Pete and Karen Collins are avid bicyclists who participate regularly together in long distance bicycling events. But their mutual enthusiasm for the sport was dampened suddenly when Pete was diagnosed with prostate cancer in February 2007 at the age of 48. He initially had sought medical attention for what he thought was a gastrointestinal problem. Prostate cancer was never a concern and Pete had never had a PSA test. An examination revealed an enlarged prostate and a PSA test was in order. It produced a PSA of 22 ng/ml; sixty days later, his PSA had climbed to 34 ng/ml! The combination of his relatively young age and a high PSA dictated an aggressive approach to the disease—a radical prostatectomy with adjuvant radiotherapy if needed. The combination of surgery and radiation is a common approach in the treatment of men in Pete's situation. He had the surgery at WRAMC on May 8, 2007, one month before he turned 49.

Karen, Pete's wife, had been looking forward to participating in the 2007 Philadelphia LiveStrong Century Challenge, one of several annual events sponsored by the Lance Armstrong Foundation to inspire and empower persons affected by cancer. It was scheduled for August 26. On July 8, Pete's PSA was still at 1.9 ng/ml and the process to start radiotherapy got underway. Pete had never planned to ride the Century course (a 100 mile loop in the Philadelphia area), but Karen held out hope. The LiveStrong event was less than four months after his prostatectomy, and Pete wasn't even allowed on a bicycle for seven weeks after the surgery. He also assumed his radiation therapy would be in progress at the time of the event.

Getting the medical "OK" to participate in LiveStrong caught the Collins off guard. Neither thought the radiation schedule would permit the ride or that he would be medically allowed to ride so far so soon after surgery. Pete always planned meticulously and trained methodically for participation in a major bicycling event such as LiveStrong, so now he was behind the power curve in his preparation. His longest ride of the summer had been 35 miles. Karen was no better off because they usually rode and trained together. Even though they quickly stepped up the training pace to 60-mile distances, they were still concerned about their readiness for LiveStrong.

Then came the equipment calamities! The day before the event and four hours before departing for Philadelphia, Pete decided to do "a nice, easy stretch ride." Some ride! His front derailleur (a mechanism to move the chain from one sprocket to another) fell apart three miles from home. A local bike shop found a replacement derailleur and did a quick fix, but the adjustment was still off. Earlier, Pete noticed that Karen's bike had a case of the "wobblies!" He did his best but he doubted his repairs would sustain her for 70 miles. Looking back later, the Collins departed for LiveStrong with the deck stacked against them—lingering concern for his recuperation, limited training time, and fragile equipment. **(Continued on page 6)**

♦ INSIDE THIS ISSUE ♦

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♦ FROM THE EDITOR'S DESK ♦

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♦ NOVEMBER SPEAKER'S REMARKS ♦

Dr. Steven Wilson, Radiation Oncologist, WRAMC Radiation Oncology Service, was our speaker for Wednesday, November 7, 2007. His topic was "Radiation Therapy for Prostate Cancer: How New Technology Benefits Prostate Cancer Patients." A summary of Dr. Wilson's remarks is presented on page 7.

♦ MEETING SCHEDULE FOR FEBRUARY 2008 ♦

We have discontinued our February quarterly evening meetings with speaker. The early onset of darkness and the uncertainty of wintry weather conditions affected attendance to the extent that it was not feasible to continue the meeting. Nevertheless, we still offer 27 other meetings per year.

Our two regular informal discussion meetings for February will be held on **Wednesday, February 13, 2008**. The day session meets from 1:30–3:00 pm and the evening session meets from 6:30–8:00 pm; both sessions meet in the conference room of the Center for Prostate Disease Research (fifth floor-Ward 56) in the main hospital building.

Speak Up, Dear; I'm Hard of Hearing, Too! The US Food and Drug Administration warns that sudden loss of hearing has been reported in patients taking erectile dysfunction drugs. In some cases, the sudden loss or decrease in hearing was accompanied by symptoms such as tinnitus, vertigo, and dizziness. The warning was based on 29 cases that apparently occurred after men took sildenafil (*Viagra*), tadalafil (*Cialis*), and vardenafil (*Levitra*). Other cases had been reported during clinical trials. Hearing loss was temporary in about 33% of patients; for the remainder, hearing loss was either ongoing at the time of report or the final outcome not described. In almost all cases, the condition was one-sided. Because follow-up information was often limited, it remains unclear whether these events were caused by medication use, underlying medical conditions, or a combination of these or other factors. No information is currently available to determine whether hearing loss is related to dosage. The safety labeling information has been revised to warn of this potential risk. Men who experience hearing loss while taking these PDE-5 inhibitors for the treatment of erectile dysfunction should immediately discontinue therapy and seek prompt medical attention. (Source: Medscape Medical News, October 19, 2007)

Combined ADT and EBRT. The addition of 4 months of androgen deprivation therapy (ADT) to external beam radiotherapy (EBRT) seems to have a dramatic impact on clinically meaningful endpoints in men with locally advanced prostate cancer without significantly increasing the risk for fatal cardiac events. According to Roach, et al., University of California, San Francisco, the study was the first major trial to test the hypothesis that short-term neoadjuvant ADT combined with EBRT would improve treatment outcomes compared with EBRT alone. The study enrolled 456 patients between 1987 and 1991 whose median age was 70 years. Inclusion criteria were bulky (5x5 cm) tumors, stage T2-4, with or without pelvic lymph node involvement. The patients were randomized to receive EBRT alone or with combined ADT three times daily for two months before and during EBRT. The main outcome measures were overall survival, disease-specific mortality, distant metastases, disease-free survival, and biochemical failure.

The researchers concluded that "the addition of four months of ADT to EBRT appears to have a dramatic impact on clinically meaningful end points in men with locally advanced disease with no statistically significant impact on the risk of fatal cardiac event. They also felt that patients with high-risk, locally advanced disease who decline or who, for medical reasons, are not considered candidates for long-term ADT should be offered short-term neoadjuvant and concurrent ADT in combination with EBRT. (Source: *J Clin Oncol* 2008; 26:1-7. January 2, 2008, via *Healthday News)*

New Nomogram Available. A nomogram developed by US and Canadian researchers appears useful for predicting low-volume and low-grade prostate cancer in men with a single positive biopsy core, which may help in selecting patients for active surveillance. Babaian, et al., M.D. Anderson Cancer Center, Houston, studied data on 258 men who underwent radical prostatectomy without neoadjuvant therapy and in whom prostate cancer had been detected in only one core of an extended biopsy scheme. Low-volume, low-grade cancer was defined as organ-confined disease with a tumor volume less than 0.5 cc and the absence of Gleason grade 4 or 5 cancer. Patient age, PSA density (PSA level divided by prostate volume), and tumor length in the biopsy core were the variables used in the nomogram to determine the probability of low-volume, low-grade cancer. The team established that 138 patients (51.6%) had low-volume, low-grade cancer, and the nomogram predicted this outcome with "good" discrimination and "good" predicted probability. The researchers concluded that the model may offer an effective tool with which to select men who are suitable candidates for active surveillance protocols. (Source: *Cancer* 2007; 110:2441-2447, via Reuters Health, December 26, 2007)

More on ADT, This Time with Prostatectomy. In men who undergo radical prostatectomy for localized prostate cancer, the use of androgen deprivation therapy (ADT) appears to increase the risk of death from cardiovascular causes, according to new research. Tsai, et al., Harvard Radiation Oncology Program, note that previous studies have shown ADT to be associated with an increased risk of diabetes and cardiovascular disease. They investigated whether these changes induced by ADT might contribute to death from cardiovascular disease. The researcher assessed the risks of ADT use among 3,262 patients treated with radical prostatectomy and 1,630 treated with radiotherapy, brachytherapy, or cryotherapy. The median follow-up period was 3.8 years.

Overall, 1,015 patients used ADT for a median duration of 4.1 months. The report indicates that both ADT use and increasing age were associated with increased risks of death from cardiovascular causes among men treated with surgery. For patients 65 years of age and older who underwent prostatectomy, the 5-year cumulative rates of cardiovascular death with and without ADT use were 5.5% and 2.0%, respectively. ADT use also raised cardiovascular mortality in older men treated with other modalities, but the association did not reach statistical significance. The researchers concluded that treatment with ADT can be beneficial in patients with unfavorable prostate cancer; however, clinicians should carefully weigh the potential risks and benefits of ADT, and consider a cardiovascular evaluation for their patients prior to initiating ADT. They also cite the need for additional studies to confirm the association between ADT and cardiovascular disease and mortality. (Source: *J Natl Cancer Inst* 2007; 99:1516-1524, via Reuters Health) October 9, 2007)

Radiation After Prostatectomy. A recent study finds that immediate post-prostatectomy radiotherapy appears to benefit only those prostate cancer patients with positive surgical margins. Although two large trials convincingly demonstrated a very favorable effect of adjuvant radiotherapy after prostatectomy for advanced prostate cancer, this new study demonstrates that the beneficial effects seem to be mainly seen in the subset of about 35% of the patients with positive surgical margin. Van der Kwast, et al., Mount Sinai Hospital and University Health Network, Toronto, Canada, studied 1,005 patients with stage pT3 prostate cancer who were assigned after prostatectomy to a wait-and-see arm or to an adjuvant radiotherapy arm. They found that immediate postoperative radiotherapy would prevent biochemical relapse by year 5 in 291 of every 1000 patients with positive margins, compared with 88 of 1000 patients with negative margins. They emphasized that given the potential impact of positive surgical margins for the treatment decision, pathologists who are specialized in urogenital pathology should read these slides or confirm the surgical margin status. (Source: *J Clin Oncol* 2007; 25:4178-4186, via Reuters Health, October 8, 2007)

Prostate Biopsy Site and Cancer Detection. The number of core needle biopsies appears to be less important in detecting prostate cancer than the location of the biopsy, according to a recent study. Haas, et al., State University of New York Medical University, Syracuse, found that biopsies taken from the lateral peripheral zone and mid peripheral zone of the prostate to be the most useful in prostate cancer detection. The research team performed 18-core needle biopsies at autopsy from 164 men with no history of prostate cancer. Six-core biopsies were taken from the mid peripheral zone, the lateral peripheral zone and the central zone. Thirty percent of the prostates contained cancer cells and 43% were considered clinically significant. The most effective results were achieved by combining the mid peripheral zone and lateral peripheral zone. This resulted in a sensitivity of 80% for clinically significant cancer and 33% for clinically insignificant cancer. The researchers concluded that a twelve-biopsy schema is optimal to detect most clinically significant prostate cancers, and that the biopsies should be directed at the mid and lateral peripheral zones of the prostate. (Source: *J Natl Cancer Inst* 2007; 99:1484-1489, via Reuters Health, October 5, 2007)

U.S. Cancer Death Rates Dropping. Death rates from cancer have been dropping by an average of 2.1 percent a year recently in the United States, a near doubling of decreases that began in 1993. The rate of decline deepened recently, averaging 2.1 percent a year from 2002 to 2004, the latest dates for which statistics are available. For men, the average decline during that period was 2.6 percent, and for women 1.8 percent. Every 1 percent drop amounts to 5,000 people who aren't dying from cancer. Much of the progress resulted from mundane improvements in prevention, early detection and treatment of some of the leading causes of cancer death— lung, colorectal, breast and prostate tumors. Years of pleading by health officials are finally beginning to pay off in smoking cessation, increased use of mammograms and colonoscopies, and other screening tests for colorectal and prostate cancer.

Now the bad news: American Indians and Alaska Natives are not benefiting the same as the rest of the population. They have higher rates of preventable cancers and late-stage tumors that would have had a better prognosis had they been detected sooner. Researchers attribute the problems to poverty, lower education levels, lack of insurance and access to medical care. (Source: The New York Times, October 15, 2007)

Prostate Cancer: Surgery as an Option. There are several treatment options for early prostate cancer: surgical removal of the prostate, external beam radiation therapy, implantation of radioactive seeds (brachytherapy), freezing the tumor (cryotherapy), hormone therapy, and watchful waiting. Each treatment has a different set of benefits and a different set of risks. A Swiss study says that men who choose surgery for early prostate cancer are more likely to be alive 10 years later than men who opt for other treatments. Bouchardy, et al., Geneva University, analyzed data on all 844 prostate cancer patients diagnosed with early prostate cancer from 1989 through 1998 in Geneva, Switzerland. They found that in the short-term, up to five years, there was little difference in survival among men based on the kind of treatment they received. However, the survival rates after 10 years were 83 percent for surgery, 75 percent for radiation, 72 percent for watchful waiting, 41 percent for hormone therapy and 71 percent for other treatment. The researchers also said that surgery patients with recurrent disease also have more options than radiation patients with recurrent disease.

The study results are not as decisive as they may seem to the casual reader. The researchers note that surgery is not the best choice for every patient. They found that elderly patients and those with very early-stage tumors did just as well after radiation therapy as surgery patients. Therefore, radiation therapy remains an option for patients with short life expectancy, with contraindication to surgery, or who refuse surgery. They also note that survival isn't the only factor to consider when weighing prostate cancer treatment options. Quality of life after treatment is an important factor. An observer warns that only a clinical trial, in which matched patients are randomly assigned to different treatments, can prove whether one treatment offers better long-term survival than another. (Source: *Archives of Internal Medicine*, October 8, 2007, via WebMD Medical News, October 8, 2007)

Stress Levels and Watchful Waiting. In men with localized prostate cancer, active surveillance (watchful waiting) of their condition does not appear to increase levels of psychological stress any more than undergoing immediate radical treatment does, according to a recent study. Whitaker, et al., University College London, UK, found that men on active surveillance were no more likely to have anxiety and depression than those who were receiving, or had received, immediate treatment. The finding supports active surveillance as an approach for managing localized prostate cancer; some had considered active surveillance to be a source of prolonged stress to the patient.

To determine if active surveillance increases psychological stress, the researchers evaluated 329 men with localized disease. One hundred were on active surveillance, 81 were currently receiving radiotherapy plus neoadjuvant hormone therapy, and 148 had previously received radical prostatectomy. Overall, 16% met criteria for anxiety and 6% met criteria for depression. Analysis showed that higher anxiety scores were significantly associated with being younger and with a longer interval since diagnosis. Depression was also significantly associated with a longer interval since diagnosis. However, anxiety and depression were not significantly associated with management by active surveillance. The study showed that other measures of coping and quality of life might also be important. However, they conclude that close monitoring was not associated with greater psychological distress than more immediate treatment for prostate cancer. (Source: *BJU Inter* 2007; 100:540-543, via Reuters Health, September 28, 2007)

The current issue of the WRAMC Us TOO Newsletter and back issues are available on line at web site of the Center for Prostate Disease Research. Just log on and go to www.cpdr.org/patient/newsletter.html.

(Meeting the Challenge--Making Every Day Count – continued from page 1)

The tide started to turn upon their arrival in Philadelphia. A vendor tent manned by Bike Line had mechanics that got both bikes in peak condition within minutes. Then there was the opportunity to mingle with the other bikers, a process that participants value, especially when they share a common cause—cancer awareness. The next morning, Lance Armstrong and other dignitaries said all the right

things, and at 7:30 am, the ride was on. Pete showed his colors throughout the race; he had painted three awareness ribbons on his arms—a blue one for prostate cancer; a grey ribbon for Karen's dad who died of brain cancer; and a maroon one for his dad who had died from myeloma. He also affixed an 18 x 24 inch American flag to his bike. The ribbons and the flag evoked much favorable comment from the event staff and other riders, and the State Police manning the intersections were very impressed by the flag.

Concerned about certain aftereffects of his surgery, Pete made it a point to stop at every rest stop to use the "facilities" even though it would increase his overall time. It also gave opportunity to rest, snack, and replenish fluids. The hills started to get tough at about Mile 42 and the "killer hill" was at Mile 52. The combination of heat, distance, and hills caused many riders to drop out by Mile 80, and this was where Pete's limited preparation began to take its toll.

Marathon runners and distance bikers often say that at a certain point in a grueling event emotional changes often occur that make the difference in completing the race. Mile 80 was it for Pete. Something took over. Perhaps it was the three ribbons he displayed, the flag he flew, and the Army jersey he wore; maybe it was certain fond memories of past special friendships, or the appreciation of the new friendships associated with his prostate cancer experience. No matter the reason--Pete, nearly in tears at the rest stop, soon was back on his bike determined to finish no matter what.

After a near miss with a wayward motorist near the finish line, Pete entered the chute designated for cancer survivors (he considers himself a "survivor in training") where he was rewarded with a yellow rose and an enthusiastic hug from Karen who had completed her 70-mile route earlier.

Only 110 days after major surgery, Pete Collins, age 49, battled for 100 miles over a course with "killer hills" for a yellow rose and a hug. Why did he really do this? Here is the answer in his own words:

"I could have stayed home and watched a movie or TV show or visited a museum that day. But then that day wouldn't have counted. Funny thing about cancer, you never know what news or event the next day will bring. It makes it worrisome to put things off. So every day now has to count.

"My ride that day will be remembered by a lot of people: the State Police who saw that flag go flying by for 100 miles; everyone who saw the Army cycling jersey proudly worn; all the cancer survivors who now know the only limit to what you can do is you. Some day, I hope to get a picture of that flag flying and send it to the Wounded Warriors at Walter Reed, so they know that someone will never forget about them.

"And I will remember that day as another day I threw out excuses and just pushed hard on the envelope. And somehow, my life is better now because I did."

(**Editor's Note**: Pete Collins served 12 years in the Army and is now a Department of the Army Civilian; Karen Collins was an Army nurse, now retired. Following a PSA spike in September 2007, Pete began hormone blockade therapy and radiation therapy on October 15, 2007. His radiation therapy ended on December 5, 2007. Thirty days later his PSA had dropped to 0.02 ng/ml. There is some indication that he has distance site metastasis. He will continue hormone blockade therapy for at least 15 more months depending on circumstances.)

"WHAT IS IMRT AND WHAT CAN IT DO FOR YOU?"

Dr. Steven S. Wilson
Staff Radiation Oncologist, Walter Reed Army Medical Center

(A summary of a presentation to the WRAMC Us TOO Chapter on November 7, 2007)

INTRODUCTION

I am pleased to be with you tonight. We are going to talk about radiation therapy for prostate cancer, and what new technology can offer, not only here at Walter Reed Army Medical Center, but at many other medical centers across the country. The simplified title of my presentation is “What is IMRT and What Can It Do for You?” If you are going to choose radiation therapy for prostate cancer, you need to be aware of the recent innovations.

Intensity modulated radiation therapy (IMRT) might also be more descriptively termed “dynamic adaptive radiotherapy” to make it understandable, but no matter the terminology, it implies movement of multi-leaf collimator leaves during treatment to optimize the treatment. IMRT minimizes hot spots and cold spots, evens out the dose to the target, e.g., the prostate gland, and minimizes the dose to adjacent normal tissues by relying on computer optimization. Thus, IMRT results in a sharper cut-off between the organs we wish to avoid treating and the target organs such as the prostate. Certain organs adjacent to the targeted area are sensitive to radiation and can be easily damaged; other organs are less sensitive. For example, arteries are not very sensitive; the nerves are not terribly sensitive. Even the rectum, which is right next to the prostate, is resistant to a degree, compared to the small bowel. Nevertheless, it can be damaged with a high enough dose. The name of the game is to deliver a high dose to the prostate to kill the tumor while

reducing risk to adjacent tissue. So we have to find ways to distinguish the rectum and other organs like the bladder from the targeted prostate. There are ways to improve accuracy. We do it, for example, with improved accuracy in outlining the borders of the prostate on a scan and locating the normal organs; using IMRT to perform the treatment is another way to improve the results. If you're going to choose radiation for prostate cancer treatment, IMRT is the way to go, and that is why I am here tonight.

As I have already noted, better target definition results in improved tumor control and decreased "toxicity", or side effects. External beam radiation therapy has greatly improved over time to make the following gains: better precision; accuracy in “painting” the target and determining the appropriate dosage; image fusion or "marrying" between the MRI, PET, and diagnostic CT scan; intensity-modulated radiation therapy (IMRT); image-guided radiation therapy (IGRT) that uses imaging techniques to check the patient’s position daily at the time of treatment; smaller “leaf” size; multiple beam angles to spread out the dose; and fractionation or spreading out the treatment over time to protect normal organs without sparing the tumor from damage. So these are ways we use to “tease” the tumor away from the normal organs so we can deliver a high dose to the diseased prostate while minimizing damage to adjacent structures. In short, if we can define where the target is, hold it still or track it as it moves, deliver the dose, and reduce risk to the normal organs, we are getting the job done.

THE TEAM APPROACH

At the outset, let me describe the team approach commonly employed in a radiation oncology clinic. A patient would have an initial consultation and obtain a treatment recommendation from a doctor—a radiation oncologist. If radiation is an appropriate therapy, and the patient selects it, he would meet a nurse, a patient educator, who would help him understand the radiation process, explain the potential side effects and how to deal with them. A simulation team acquires data for treatment planning: for example, the radiation oncologist will be outlining targets and normal structures on the CT scan

obtained at the time of simulation for treatment (scanning with the body in treatment position); dosimetrists will be calculating the dosages much as a pharmacist follows a doctor's prescription for medications, but using radiation doses instead of medication doses; the physicist (staff with advanced training in the measurement of X-rays) will be checking the calculated doses for accuracy and doing constant checks on the accuracy of the treatment machine's calibration; and when the patient arrives a week or two later for treatment, the therapists will be placing the patient in the proper position to receive the radiation. There are also tiny tattoos placed at the time of the simulation scan that indicate the center of the radiation field on the patient's skin.

So there is a lot that goes on after this first simulation appointment that patients are not usually even aware of - the case moves from one team to the next, sequentially, from doctor to dosimetrist to doctor to physicist and then to therapists on the appointed day of treatment. The entire simulation procedure is first visit after the initial consultation; it takes a couple of hours to put the patient into a reproducible treatment position, insert a urinary catheter into the bladder, take a CT scan in the treatment position and place three tattoos on the skin in the middle of the treatment area at the end of the simulation process. Finally, after the patient is off the scanning table, the patient gets his appointment dates after he indicates the time of day he prefers to receive his daily treatment. The next step is to return on the appointment date to start the radiation therapy a week or two later.

So this was a general description of the treatment planning process, starting with the simulation for which the patient is present. For the other steps in the treatment planning and verification process after the date of the simulation scan, the patient is patiently waiting at home until the date that treatment is scheduled to begin. Typically treatment then lasts for approximately eight weeks, five days a week, once it actually begins.

(**Editor's note:** Dr. Wilson then displayed and explained a series of slides demonstrating the improvements over time in determining the precise position of the prostate gland by means of computer-generated imaging techniques; intensity-modulated radiation therapy (IMRT); and image-guided radiation therapy (IGRT). These are the basis for state-of-the art radiation therapy. He presented slides describing the earlier method using the so-called lead block technique for treating prostate, lung, and brain cancers and contrasted it with the newest techniques. He emphasized the need for the radiation to be directed from varying angles in order to spread the dose within the target area.

(**Editor's note:** These slides have been placed in a PowerPoint presentation and are available at: http://www.wramc.com/prostate.ppt. They can be downloaded by either PowerPoint or the free PowerPoint viewer available online at http://www.microsoft.com/Downloads. Also, the text of this talk in PDF format is at http://www.wramc.com/prostate.pdf)

INTENSITY-MODULATED RADIATION THERAPY (IMRT)

Let me get more detailed about intensity-modulated radiation therapy (IMRT). It's fairly new; we began using it at WRAMC in 2003. As noted earlier, it allows us to deliver a higher dose to the prostate without damaging the other organs. The higher dose to the prostate cancer, the higher the chance of cure; the lower the dose, the more likely the chance of some local residual tumor. It's as simple as that. In the past, we used to rely on lead blocks to make the radiation field match the shape of the tumor in order

to focus the beam. This resulted in certain hot spots and cold spots within the target area. Instead of cutting large custom blocks from lead, we switched to multiple leaf collimators--picture them as little piano keys. Instead of large lead rectangles, we now have many tiny lead rectangles that we can move to obtain the perfect shape we seek that fits the tumor shape from any given angle from which we're aiming. These leaves have sensors and feedback mechanisms to help the computer verify that they are in the intended shape. This development made IMRT possible.

(**Editor's note:** Dr. Wilson then demonstrated the IMRT process by a series of slides. He first showed the older lead block technique, noting its inflexibility, i.e., the blocks cannot be moved during treatment, nor can their shape be changed. He then demonstrated the flexibility provided by the multi-leaf collimators--the piano keys. They move, and have sensors and feedback mechanisms to fit a particular tumor shape. Dr. Wilson showed slides of an actual treatment to illustrate the dosage delivery using both the conventional lead block technique and IMRT and the superior control provided by IMRT. He noted that radiation oncologists are finding that IMRT is providing the control they had hoped for with brachytherapy.)

IMRT AND QUALITY ASSURANCE

Now for some quality assurance data. First, we have found that the higher doses permitted by IMRT result in a higher chance of cure. Next, we learned that overall side effects from these higher doses are about the same as pre-IMRT when lower doses were used, with a correspondingly lower chance of cure. In short, IMRT improves cure rate without increased side effects.

IMAGE GUIDED RADIATION THERAPY (IGRT)

Obviously, the position of the patient during radiation therapy is absolutely crucial to the precise delivery of the radiation, and organ movement during therapy is a major concern. We needed an imaging technology to complement IMRT. Image guided radiation therapy (IGRT) is meeting that need. It uses imaging methods such as X-rays, CT scans, and ultrasound to check the patient's position daily during treatment. We used to take an X-ray once a week, relying on skin lines to show the bones to check alignment. Then we would make adjustment as deemed necessary. To compensate for these adjustments, we had to make our targets bigger with all that implies for increased side effects. To capitalize on IMRT, we wanted image guidance on a daily basis, not a weekly basis. And we did not want to rely on the bones for adjustments; we wanted to see the prostate, bladder and the rectum to make sure they are in the right position relative to each other. We bought an ultrasound machine specially designed for radiation therapy to do the daily check. We now have started using these special gold marker seeds called fiducials. These marker seeds are placed in the prostate gland to show us where the prostate is. Now at last we can see the prostate! On a daily basis, we can compare our treatment planning CT scan with the X-ray provided by our new ultrasound equipment.

Our newest treatment machine was installed during 2007. It has the ability to use a CT scan daily to check the prostate position. It theoretically is even more precise than using the gold marker seeds to mark the position of the prostate. We will implement this process once we have upgraded software that allows us to compare old to new CTs. So technology marches on.

In any case, this new image-guided capability (IGRT) is used daily and therefore

is more accurate than simply trusting skin marks and bony anatomy to make adjustments. It allows us to shrink the size of the radiation field to target the tumor more precisely and lessen the exposure of normal tissue. Thus, IGRT is the next innovation after IMRT and enhances IMRT.

BRACHYTHERAPY - INTERNAL VS EXTERNAL RADIATION

Now I want to offer some comments about brachytherapy. IMRT is a form of external beam radiation therapy, or EBRT. Brachytherapy is not delivered from the outside but is internal radiation, coming from the prostate gland itself after seeds are inserted into it using needles inserted though the skin through ultrasound guidance. It gained in popularity because some radiation oncologists were dissatisfied with the external beam techniques in use 15-20 years ago. They sought a way to "wrap" the dose around the prostate without leakage outside of the prostate. That's called being conformal, i.e., conforming to the shape of the target. So seed implants are very conformal. The idea was perhaps they could get higher doses, and thus better cure rates without more toxicity, by having a steeper fall-off as the dose comes from the inside to outside the gland. And it's true that at least some parts of the gland get higher doses using seed therapy, although there is a problem with evenness of the dose using this technique and some parts of the gland do not get much higher equivalent doses than with current IMRT techniques. In any case, compared to EBRT, one down side of seed implants is that they tend to produce more intense urinary side effects, at least in the short term, such as urinary burning and frequent nocturnal urinary urges, causing loss of sleep for two or three months. There is also more potential for urinary obstruction after the procedure, potentially requiring insertion of an indwelling catheter for weeks to months, particularly if patients are not chosen carefully to avoid those without already severe urinary blockage symptoms. The other side effects are similar to those associated with EBRT. This slide that illustrates the brachytherapy procedure. The seeds are placed using ultrasound and a preplanned template. We typically place about 120 seeds using about 30 different needles, about four to six seeds per needle. This CAT scan shows the location of the seeds within this patient's prostate. The idea is to spare the urinary tract and the rectum in order to reduce the risk of urinary and rectal side effects. But it's a balancing act because the first objective is to destroy the cancer. As with any medical procedure, seed implantation has its advantages and disadvantages compared to EBRT. I'll mention these comparisons later in my presentation. We are seeing less patient interest in brachytherapy despite some claims for higher potency rates. The jury is still out on that matter. Although we still offer the procedure here at WRAMC, IMRT is giving the kind of results that many hoped brachytherapy would provide.

SELECTING A THERAPY AND MYTHOLOGY

The biggest challenge to the newly diagnosed man is his selection of the appropriate therapy. So I thought you would appreciate a brief discussion of the various options and some of the mythology surrounding the process. Not very long ago, 2002 or so, controversial articles appeared regularly in the popular press claiming that watchful waiting had "cure rate" similar to active intervention, so why treat? A study of Connecticut Tumor Registry data on watchful waiting led some to say that certain low-risk men did very well after 15 years—only 23% died of prostate cancer. Could active intervention improve on that? For many years, we really didn't know. This was the so-called "competing risks" issue. The

older the patient, the more likely the existence of co-morbidities affecting him. Some pundits (including yours truly) said no randomized trial of watchful waiting versus active intervention would ever be done. We were wrong! The New England Journal of Medicine subsequently published a Swedish study comparing watchful waiting and active intervention. It showed that eight years after diagnosis, untreated low-risk prostate cancer patients had more metastasis to the bones, but an equal number were surviving their cancers; by year ten the researchers began to see a difference in longevity as well. Now we know that active intervention can make a difference. Treatment decisions made at diagnosis by low-risk men (Gleason 6 or lower) will come home to roost about eight to ten years later. One final comment about therapy selection. If the clinical data suggest that a cure is possible and you intend to do something about it, the best time to do it is yesterday, so to speak, because excessive delay may let the cat out of the bag and the patient may become incurable due to spread of cancer distantly to become metastatic disease. Thus, for those who plan any treatment ever I advise them to get treatment now. For these men I am not a fan of watchful waiting. For those who choose watchful waiting due to age or other competing risks of death, I feel that is appropriate as long as they know they are not trying to be cured, simply trying to outwait the cancer.

Cure Rate. Cure rate comparisons among the primary therapies always generate interest. It is difficult to compare radiation and surgery as far as the cure rates are concerned because they are both moving targets. It takes 10 or 15 years, if not longer, to get reliable statistics on prostate cancer. So we often found ourselves comparing 20-year-old radiation outcomes with 20-year-old surgical outcomes and by that time the technology has moved far ahead of the old technology, both for surgery and radiation.

Therefore, insofar as we can ascertain, EBRT, brachytherapy, and surgery are all equally effective in curing low-risk patients (Gleason 6, PSA 5). For higher risk patients (Gleason 7 or above and a PSA of a least 7.5), we find that adding hormones before and during radiation improves the apparent cure rate, particularly if we treat the lymph nodes and the pelvis. (The issue of treating the lymph nodes has become a hot controversy in late 2007 and people are no longer as sure as they once were.) Higher-risk patients selecting surgery have a fairly high likelihood of needing radiation afterwards because not all of the tumor is removed. (i.e., surgical margins end up being positive for tumor.)

Side Effects. Side effects fall in two categories: temporary side effects and permanent side effects. Comparing EBRT with brachytherapy, brachytherapy has more intense temporary side effects, such as urinary discomfort and soreness in the perineum area; otherwise the side effect profile of EBRT and brachytherapy are similar both in the short term and permanently. The problem with comparing the side effects of brachytherapy is that it is very operator-dependent - in the hands of some implanters rectal side effects may be lower than with EBRT, but those with little experience may produce side effects much worse than that of EBRT, including IMRT. It is easier to standardize results of IMRT because there is not such a steep learning curve to the technique.

When comparing either form of radiation with surgery, the most prominent permanent side effect of radiation is a very small percentage (1-2%) of patients developing permanent rectal dysfunction with urgency of defecation; whereas surgery tends to have more permanent urinary impact. And both

surgery and radiation cause problems with sexual function in about half the patients who start out with good function. Finally, radiation as the primary therapy makes subsequent salvage surgery very difficult if it made sense to resort to it. (The logic behind it is against ever doing that for salvage, particularly with today's higher doses achievable using IMRT. At WRAMC we go to a dose of 7800 cGy when feasible and the chance of local failure without concomitant distant failure should be in the single digits.) Again compared to EBRT, brachytherapy has more exclusionary criteria such as high grade tumors and patient prostate gland size. Earlier hopes for improved cure rates for seed implants have not materialized, and claims of better post-therapy potency remain unsubstantiated by unbiased data.

DEALING WITH MISCONCEPTIONS

Finally, let me present you with some misconceptions I have dealt with over the years in counseling and treating men with prostate cancer.

"I want the least invasive form of therapy possible so I want brachytherapy." This man was influenced by comments in the popular media that said seed implants were less invasive than surgery. Well, that's right, but they are more invasive than EBRT.

"I prefer seed implants because they have fewer side effects than external beam." Wrong again. Seed implants are likely to cause more urinary problems. External beam is the gentlest way to go in terms of temporary side effects. The seed implant is about intermediate.

"I want the best chance of retaining sexual function, so I prefer seed implants." Several studies made this claim for seed implants, but their conclusions are far from certain. Younger men tend to select seed implants; therefore they are likely to have better outcomes as far as sexual potency is concerned. This age factor applies to all the primary therapies. Surgery, EBRT, and seeds are likely equal in maintaining potency.

"I have a friend that swears by Therapy A, B, or C." Patients should avoid this anecdotal evidence. Instead, why not attend an Us TOO support group meeting for a frank discussion with other men who have had various treatments and benefit from their experiences?

"I want the cancer out of there so I know that I am cured. The surgeon will be able to say he got it all out." This is a frequent comment. For sure, the surgical patient will get the news (good or bad) faster with surgery. He will get the pathology results to tell him more prognostic information, and the PSA falls faster after the gland is removed than after radiation, which takes a few months to totally kill the cancer. However, if the cancer has escaped the capsule, "taking it out" won't do any better than killing it with radiation, as most patients with positive margins will require radiation after any surgery to finish the job of eradicating tumor in the area of the prostate. "Taking it out" doesn't imply a cure; the tumor may have metastasized (spread distantly) before surgery and these are the patients - those with micrometastases - who will likely not be cured whether they elect surgery or radiation as an initial option. Surgery or radiation—in either case you must take care of the local problem before it becomes a systemic problem. Whether getting it out or destroying it with radiation, the options are very similar in outcome. When the clinical evidence indicates a good chance of cure, I always recommend a careful review of potential side effects for that particular patient.

"Radiation has no back-up if it fails; failed surgery can be followed by radiation." I hear this very often. The surgeon has to cut fairly tight around the prostate gland to excise it with some risk that cancer cells may remain. It's true that residual cancer cells after surgery can be treated by follow-up radiation. On the other hand, when EBRT is the primary therapy, the radiation oncologist can and does add, as a matter of routine, a more generous safety margin than the surgeon can afford to do. So in that sense, EBRT doesn't need a "back up" plan; it is its own safety net, so to speak. Furthermore, if a patient's PSA rises after radiation, the site of failure would almost always be at a distant site and not the local site. Then hormones would be the next step for what is at that point most likely to be metastatic disease. Besides the fact that it's not needed nor helpful, for reasons described above, there is also considerable reluctance to employ salvage surgery after failed radiation because of morbidities associated with that procedure.

QUESTIONS AND ANSWERS

Question: You have frequently mentioned "the tumor," but more likely there are several tumors present. Is the treatment for that the same in that case?

Answer: Good question, and I should clarify that. The target, whether for surgery or for radiation, is really the entire prostate and part of the seminal vesicles. I have read that that the typical prostate cancer patient has 4.3 tumors. We would never just treat where the biopsy was positive. We always treat the entire prostate.

Question: I recently had the IMRT and it worked very well for me. I had a PSA of 4.9 and four months after therapy it had dropped to 2.3. My next follow-up PSA will be in two months. I've had zero side effects--nothing in terms of incontinence, ED, or bowel issues. I guess I'm very fortunate. My question is since I've experienced no side effects in the short term, what can I expect in the long term?

Answer: If you are going to get a permanent side effect, it usually starts around the sixth month after therapy is complete. If you haven't experienced side effects by six months, you have reason to be optimistic for the long term. You still might have softer stools with certain foods or occasional diarrhea from things you eat and you'll learn what foods to avoid over time.

Question: Let's take a man who has recurrence after radical prostatectomy. Are there any new developments in radiation therapy about targeting local sites?

Answer: Salvage target definition is interesting. In the past, we thought a CT scan before surgery might give us better target definition in the event that salvage radiotherapy became necessary. But it didn't work out because the anatomy is so changed. We know where the prostate bed was, and we have reliable techniques for standard radiation fields for that area. If a PSA rises after surgery we generally favor doing salvage radiation unless it is clear that the disease has metastasized. The best scenario is one that holds promise of a cure because the recurring cancer is within the prostate bed and nowhere else. And the only way to determine this is to give radiation and see if the PSA goes down as a result. The Prostascint scan is sometimes helpful in that situation, such as when the margins were negative but we're contemplating giving radiation for a rising PSA, but it hasn't been the wonder test we had hoped for.

Question: How long does it take for the PSA to come down after IMRT?

Answer: I usually put it between 12 and 18 months after therapy until the PSA reaches its nadir, its lowest point, but it starts dropping almost immediately and usually goes down by half every 3-4 months until it starts to bottom out to the nadir. Some brachytherapy studies cite something like three or four years for the final nadir. But in my opinion, you get most of the drop in the PSA 12 to18 months after treatment whether it is IMRT or brachytherapy. You just want it never to rise again, no matter what number it gets to.

Question: In our support group we have a man who has had both brachytherapy and external beam radiation. What about that?

Answer: We've done it here at WRAMC a few times in certain situations. Let me be blunt and say that external beam is a way to make up for ineffective implants. Brachytherapy takes a lot of skill and you don't always get it perfect. When the two therapies are combined, the radiation reaches further outside the prostate, which is needed for tumors that tend to extend outside the capsule. So, it can be used for a patient who really wants the seed implant, but he's Gleason 7 or 8 and there is concern that the disease has escaped the prostate. That's probably the best reason you would combine them if you are willing to deal with the increased side effects without any known improvement in the chance of cure. Some men have heard so many good things about seed implants from the media or from friends, or occasionally from their doctors, that they want the seed therapy even though they're a high risk patient, and that's one way of reaching a compromise.

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♦ WRAMC US TOO COUNSELORS ♦ (As of February1, 2008)

(These persons are willing to share their experiences with you. Feel free to call them.)

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