WRAMC Us TOO, Inc.

A PROSTATE CANCER SUPPORT GROUP
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NEWSLETTER

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♦ LOOKING AHEAD ♦

Our May 2011 issue advised readers of the merger of the Walter Reed Army Medical Center and the National Naval Medical Center, Bethesda, scheduled to occur this September. The merger was directed by the Base Realignment and Closure Commission in September 2005. The board of directors of WRAMC Us TOO Prostate Cancer Support Group met on May 4, 2011, to consider courses of action to accommodate the potential impact that the merger would have on our activities. Subject to any unanticipated developments arising from the merger, we decided to retain our traditional schedule of informal monthly meetings, as well as the quarterly meetings with invited speakers.

WRAMC Us TOO Prostate Cancer Support Group has been sponsored by WRAMC for eleven years and we expect that the sponsorship will continue under the emerging organization. The support group receives considerable support and encouragement from the WRAMC staff, but its all-volunteer leadership is responsible for obtaining the funding for its activities. Our major expense is the production and distribution of the quarterly newsletter. The newsletter began as an eight-page publication distributed to about ninety readers who had received prostate cancer therapy at WRAMC. It is now produced in 2,100 copies and distributed nationwide on request and without charge to any interested persons at an annual cost of approximately $13,300.

Given the expense and effort now required to produce and distribute the newsletter, our board of directors decided to cease the conventional printing and mailing processes in favor of a "virtual newsletter" available on line at the web site of the WRAMC Center for Prostate Disease Research. This will result in a practically "no cost" and less labor-intensive publication. Accordingly, this is the last issue produced and distributed by conventional means. We realize that some readers may not have access to the Internet, but this action will sustain our ability to continue publication of the newsletter.

We are working with the CPDR staff to develop a notification system to alert readers when each newsletter is available on-line. If you want to be included in this notification system, send an email to Jane Hudak at jane.hudak@amedd.army.mil. Please do so no later than August 15, 2011. If you now receive Jane Hudak's "CPDR e-News," you will be automatically included in the notification process. If you do not have email access, consider arranging with a friend or family member to accept it for you. In that case, arrange to send that person's email address as noted above. The first on-line quarterly newsletter will be our November issue.

♦ *INSIDE THIS ISSUE* ♦

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♦ FROM THE EDITOR'S DESK ♦

This newsletter marks the end of an era. After eleven years this is the last issue of the WRAMC Prostate Cancer Newsletter distributed in hard copy via the US Postal Service. Starting in November 2011, the newsletter will go "electronic," by being posted quarterly to the web site of the WRAMC Center for Prostate Disease Research. We realize that some readers may not have access to the Internet, but the realities of production and mailing expenses and reliance on an all-volunteer effort necessitate movement to what is, relatively speaking, a no-cost operation. And the imminent merger of the Walter Reed Army Medical Center and the National Naval Medical Center, Bethesda, is a timely event to make the change.

♦ MAY SPEAKER'S REMARKS ♦

Our May program featured Dr. Stephen Brassell, Associate Director, Center for Prostate Disease Research, WRAMC. His topic was "To Treat or Not to Treat? That is the Question." A summary of Dr. Brassell's presentation begins on page 6.

♦ MEETING SCHEDULE FOR AUGUST 3, 2011 ♦

We know that improved nutrition reduces risk of heart disease, diabetes and obesity, and improves overall quality of life. Additionally, a healthy diet helps to increase energy levels, facilitate recovery and enhance the immune system. But what about the relationship between nutrition and prostate cancer? Differences in diet and lifestyle may account for the variability of prostate cancer rates in different countries. Good nutrition also may reduce the incidence of prostate cancer and help reduce the risk of prostate cancer progression. There are many studies currently being conducted to understand how diet and prostate cancer are related.

You can learn more about this important subject by joining us at 7:00 pm, Wednesday, August 3, 2011, at Joel Auditorium, WRAMC, when Dr. Stacey L. Koff, Department of Urology, Fort Belvoir Hospital, presents "Nutrition and Prostate Cancer: Can Diet and Lifestyle Improve Your Cancer Outcomes?" Your family members and friends are always welcome. Come join us.

Discussing the sexual consequences of therapy during urology consultations with couples affected by prostate cancer. Men with prostate cancer are likely to experience a range of treatment-related side-effects including deterioration in sexual functioning as a consequence of surgery, radiotherapy and hormone treatment. Despite the clear links between treatments and changes in sexual functioning, sexual concerns are infrequently discussed in clinic settings. Data indicate the need to use clinical consultations appropriately to support both patient and partner in sexual recovery and rehabilitation, going beyond discussions of assistive technologies to offer psychosexual couple support.

To explore the ways in which prostate cancer treatment-induced sexual changes are presented for discussion, researchers at the University of Stirling, Stirling, UK, observed 60 consultations between clinicians, patients and partners in prostate cancer urology clinics. Sexual functioning was discussed infrequently in the clinic sessions. Despite the presence of partners in nearly half of consultations, involvement of the partner tended to be minimal. Overall, discussions of wider psychosexual concerns were marginalized in consultations, and there were limited opportunities for couples to discuss the specific impact of prostate cancer and its treatments on sexual functioning. Given the potential burden of symptoms and side-effects, there is a need to include discussions of sexual recovery and rehabilitation in consultations, and to provide opportunities to discuss the sexual consequences of treatment with men and their partners. (Source: BJU Int. Jun 1, 2011)

When is active surveillance the appropriate treatment for prostate cancer? The incidence of prostate cancer has increased dramatically worldwide during the past few decades in part because of increased testing for prostate specific antigen (PSA). The aggressive use of this screening tool has resulted in the identification of many localized prostate cancers, many of which are relatively low volume, low grade tumors. Older autopsy studies have documented that incidental prostate cancer is quite common especially in older men. The finasteride chemoprevention trial confirmed these findings. Many prostate cancers are not destined to progress to clinically significant tumors. Several case series have documented the natural history of clinically detected prostate cancer. The progression of disease identified by PSA testing is less certain. These studies uniformly show that many men with low grade tumors can survive for over two decades in the absence of treatment. Furthermore, randomized clinical trials have shown only a modest ten year survival advantage for those men undergoing either surgery or radiation.

As a consequence, men with low risk of disease progression may wish to consider active surveillance as a treatment option. To date, several case series have documented that men following an active surveillance protocol that includes regular PSA testing and periodic re-biopsy have an excellent outcome. The majority of these men have not demonstrated evidence of progression during the first decade of follow-up and among those that have, the majority have undergone either surgery or radiation without compromise of their long-term outcome. Unfortunately, until better biomarkers become available, the outcome of any individual patient defies accurate prediction.

Men with newly diagnosed prostate cancer must weigh the risk of disease progression against the potential efficacy and safety of treatment when making a decision whether to consider active surveillance as an appropriate treatment. (Source: *University of Connecticut Health Center, Farmington, CT;* Acta Oncol. 2011 Jun;50 Suppl 1:120-6)

Curative radiation therapy in prostate cancer. Radiotherapy has experienced an extremely rapid development in recent years. Important improvements such as the introduction of multileaf collimators and computed tomography (CT)-based treatment planning software have enabled three dimensional conformal external beam radiation therapy (3DCRT). The development of treatment

planning systems and technology for brachytherapy has been very rapid as well. Development of accelerators with integrated on-board imaging equipment and technology, for example, image-guided radiation therapy (IGRT), has further improved the precision with reduced margins to adjacent normal tissues. This has, in turn, led to the possibility to administer even higher doses to the prostate than previously. Although radiotherapy and radical prostatectomy have been used for the last decades as curative treatment modalities, there still are no randomized trials published comparing these two options. Outcome data show that the two treatment modalities are highly comparable when used for low- and intermediate-risk prostate cancer. (Source: *Depart of Oncology/Pathology, Karolinska University Hospital and Institutet, Stockholm, Sweden.* Acta Oncol. June 2011; 50 Suppl 1:98-103)

Testosterone and prostate cancer: What are the risks for middle-aged men? With increased recognition of the benefits of testosterone therapy for middle-aged men, there has been a concomitant re-examination of the historical fear that raising testosterone levels will result in more prostate cancer (PCa). Recent studies have failed to show increased risk of PCa in men with higher serum testosterone, and supraphysiologic testosterone fails to increase prostate volume or prostate-specific antigen in healthy men. This apparent paradox is explained by the Saturation Model, which posits a finite capacity of androgen to stimulate PCa growth. Some modern studies indicate no increased risk of PCa among men with serum testosterone in the therapeutic range. (Source: Urol Clin North Am. 2011 May;38(2):119-24; via *Uro Today*, June 17, 2011)

Recovery of erectile function after robotic prostatectomy. Several reported advantages of the robotic-assisted laparoscopic approach to the treatment of clinically localized prostate cancer include superior results for erectile function as one of the critical outcomes of radical prostate surgery. Researchers at the Department of Urology, University of Florida, provided a critical assessment of the evidence that exists for erectile function outcomes based on a systematic literature review. They found that the low methodological and reporting quality of existing studies did not appear well-suited to guide clinical practice. A new framework of prospective investigation using validated patient self-assessment instruments would seem critical to the future advancement of this field. (Source: Urol Clin North Am. 2011 May;38(2):95-103.; via Urology Today, June 17, 2011)

Effect of long-acting testosterone injections for treatment of hypogonadism after brachytherapy for prostate cancer. Despite historical concerns regarding testosterone replacement therapy (TRT) in any men with a history of prostate cancer, there is increasing awareness that it is safe in selected patients. There has been greater acceptance for TRT in men following radical prostatectomy than radiation therapy (RT), including brachytherapy (BT), since PSA monitoring is easier after surgery. In a paper presented at the AUA 2011 conference, Morgentaler, et al., reported their experience using long-lasting testosterone (T) undecanoate in symptomatic hypogonadal (low testosterone) men following BT for prostate cancer. A total of 116 patients were followed monthly with serum PSA and total T levels for the first three months, then every 3 months for the rest of the first year, every 6 months during the second year, and annually thereafter.

Mean PSA at diagnosis was 6.6 ng/ml, with Gleason score ranging from 2+3 to 4+4. Following BT, baseline mean PSA was 0.65 ng/ml and baseline mean T was 343 ng/dl. At a median follow-up of 9 months, all patients had clinical improvement in hypogonadism symptoms while PSA showed no significant variation (0.55 ng/ml). Many urologists are relatively hesitant to give TRT to patients with a history of prostate cancer treated with BT, especially with a relatively long-lasting T formulation. Morgantaler and colleagues, however, did both for this cohort and did not have any patients with PSA progression at 9 months.

Although the indications for safe use of TRT in patients with a history of prostate cancer are expanding, it is important to communicate the theoretical risks with patients. The use of

a validated predictive nomogram for PSA recurrence, based on a patient's individual cancer characteristics, can be as useful tool for helping patients and physicians make informed decisions together regarding TRT in this context. (Source: *Uro Today*. June 13, 2011)

A large cohort study of long-term acetaminophen use and prostate cancer incidence. Use of aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), particularly long-term use, has been associated with modestly reduced risk of prostate cancer in previous epidemiologic studies. Acetaminophen, a commonly used pain-reliever, is not traditionally considered an NSAID but can have anti-inflammatory effects. Few studies have examined the association between long-term acetaminophen use and prostate cancer incidence.

Researchers examined the association between acetaminophen use and prostate cancer incidence among 78,485 men in the Cancer Prevention Study II Nutrition Cohort. All models were adjusted for age, race, education, body mass index, diabetes, NSAID use, and history of prostate-specific antigen (PSA) testing.

During follow-up from 1992 through 2007, 8,092 incident prostate cancer cases were identified. Current regular use of acetaminophen (≥30 pills per month) for ≥5 years was associated with lower risk of overall prostate cancer. Current regular use of less than 5 years duration was not associated with prostate cancer risk. These results suggest that long-term regular acetaminophen use may be associated with lower prostate cancer risk. If the association between acetaminophen use and lower risk of prostate cancer is confirmed, it could provide clues about biological mechanisms that are important in prostate carcinogenesis. (Source: Epidemiology Research Program, American Cancer Society, Atlanta, GA; via *Uro Today*, June 7, 2011)

Trends in PSA, age and prostate cancer detection among black and white men from 1990-2006 at a tertiary care center. Prostate cancer is the most frequently diagnosed malignancy in men in the United States, with even higher prevalence and death rates among black men. A recent study sought to compare trends in prostate-specific antigen (PSA), age, and prostate-cancer detection among black and white men in one region during a 16-year period.

This retrospective study of patient archives between 1990 through 2006. Data collection produced 5570 patients, of whom 911 were black, whose records were analyzed statistically.

During this 16-year period, mean age at the time of initial diagnostic prostate biopsy did not change in either group, despite what we had believed about the effects of patient education and screening campaigns. However, prostate-cancer detection rates did decrease during the time period studied. Over time, the authors also observed significant decreases in the sensitivity and specificity of PSA as a screening tool. In fact, analysis of more recent cases demonstrated a positive predictive value comparable to a coin toss. While Gleason scores remained relatively stable over time, reporting of prostate intraepithelial neoplasia (PIN) and inflammation increased.

Using lower PSA thresholds, promoting younger screening age, and increasing efforts to educate the public have not seemed to influence age at time of diagnostic testing, which may reflect other factors such as usefulness of screening, physician referral patterns, patient compliance, and other sociodemographic issues. The usefulness of PSA as a screening tool appears to be diminishing. (Source: *Cancer* May 17, 2010, via *Euro Today,* July 17, 2011*)*

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♦ TO TREAT OR NOT TO TREAT? THAT IS THE QUESTION ♦

by

DR. STEPHEN BRASSELL, MD

Associate Director of the Center for Prostate Disease Research, WRAMC

(A summary of a presentation to the WRAMC Prostate Cancer Support Group on May 4, 2011)

INTRODUCTION

Thanks so much for that gracious introduction and for having me here this evening. Our goal tonight is to review some of the recent literature, especially regarding some of the controversies affecting prostate cancer. In the process I trust it will help you make more informed treatment decisions

THE PSA

In order to understand the state of the art in prostate cancer therapy we must be aware of history, and what is prostate cancer history without knowing about PSA? PSA is actually an enzyme called serine protease that acts to liquefy the semen to enhance sperm motility. It also works to dissolve the cervical mucus cap, thereby allowing the sperm to enter the uterus to facilitate fertilization. It was discovered in the 1970's but it really wasn't used for prostate cancer screening until much later. PSA is found not only in prostate tissue, but in other tissues and fluids of the body and that is important when we consider specificity of PSA testing. It was approved by the FDA in the mid-1980's for prostate cancer screening and for the evaluation of people after treatment with prostate cancer. But a lingering issue is that the PSA test is highly sensitive, but with low specificity, i.e., the PSA test will detect all those in the tested population who have a problem, but at the same time, it produces a lot of false positives. So clinicians have tried to improve the specificity of PSA by looking at PSA derivatives such as free PSA and complexed PSA. These are not easy concepts to explain. Suffice to say that PSA derivatives are not ready for prime time, but I wanted to mention them because you will be hearing and reading about them in the future.

BACK TO BASICS

Let's review some basic facts. We know that prostate cancer is very common. As you can see on this graph, it ranks as the leading cause of cancer in men. In fact, its prevalence matches that of lung and colon cancer combined. Despite its prevalence, prostate cancer is not the leading cause of cancer death in men. Lung cancer is. Prostate cancer ranks second, tied with colon and rectal cancer as the most common causes of cancer death in men. Why is this the case?

Well, something has been going on over the years. During the period 1975-1977, the five-year survival rate for a man with diagnosed prostate cancer was about 69 percent. By the mid-1980's the five-year survival rate had increased to 76 percent, and during 1996-2004, the rate further improved to 99 percent. Nowadays, it is exceedingly rare for someone to be diagnosed with prostate cancer and die from it within five years of therapy. In addition to the five-year survival rate, over the past decade we have seen a stage migration of prostate cancer to clinical stage T1C as opposed to the earlier clinical stages of T2 or T3 prostate cancer. Furthermore, more men are presenting with localized disease that is nonmetastatic. For example, the incidences of metastatic disease at the time of diagnosis has decreased from 17 percent to 4 percent, a fourfold decrease since we have been tracking it, and the incidence of finding disease outside of the capsule has decreased by almost fifty percent.

MAKING PROGRESS

What has been going on here? These improved outcomes could be due to the natural biological progression of the disease. Or they could be due to the increased screening for the disease, improvements in technology and technique, or the better overall health of our patients. A study done 2005 in Sweden sought to address the matter. It was published in the New England Journal of Medicine in 2005. It looked at 700 patients who were randomized after diagnosis to either surgery or watchful waiting. It found that the patients who underwent surgery had a much lower risk of death due to prostate cancer than those that underwent watchful waiting. They also found that the surgery patients had a much lower death rate due to other causes than those who underwent watchful waiting. We surgeons felt pretty good about ourselves because we were making a clinical impact. Furthermore, the study showed that the risk of having distant metastatic disease over eight years was almost tenfold less and local progression also was markedly less. So this was encouraging. The Europeans emphasized that this

was a treatment study. The patients had already been diagnosed with prostate cancer and the searchers were looking at treatment options, and surgery seemed to be a good treatment.

SCREENING

But how about screening? Should we really be screening patients for prostate cancer and is our screening helping overall outcomes? These questions led to the design of the European Randomized Study of Screening for Prostate Cancer or ERSPC trial. The trial enrolled almost 200,000 patients in the age group between 50 years old and their mid 70's in seven European countries. The study was flawed in several respects, many of them associated with the varying procedures within the participating nations. Nevertheless, it was a good effort. It found that those patients in the screened arm of the trial had a higher incidence of cancer being diagnosed; they had a lower incidence of higher-stage cancer; a lower incidence of aggressive Gleason scores; as well as a 41 percent reduction in positive bone scans by the end of the trial. In short, it appears that patients were being diagnosed earlier with more treatable disease or organ-confined disease. The actual end point of the study was prostate cancer-specific deaths. It found that at seven years the patients in the control arm had more deaths from prostate cancer than the patients in the screening group, and the risk of dying from prostate cancer was decreased about 20 percent by undergoing screening.

Regarding death from any cause, the study also found there wasn't any change. So prostate cancer-specific death was affected by PSA screening, but death from any cause was not. This outcome translates into some interesting data. To prevent one prostate cancer death, over 1,000 patients were screened in order to treat 48 patients. Some experts question whether this is a proper use of healthcare dollars and is it worth the risk in order to prevent one prostate cancer-specific death. On the other hand, this screening effort is equivalent to mammography screening for breast cancer and fecal occult blood testing for colon cancer. Overall, the ERSPC is considered to be positive evidence that PSA screening does help reduce prostate cancer-specific deaths. There is always more to the story and one study does not a rule make.

Here in the United States the Prostate, Lung, Colorectal, Ovarian Cancer Screening Trial (PLCO) was a similar study. It looked at PSA screening and the digital rectal exam to see the effect on prostate cancer-specific death. There were some substantial differences between the ERSPC and the PLCO. For example, patient enrolment was substantially less; there was a difference in the employed PSA cut-off value; the follow-up periods differed; and the prevalence of screening here in the United States complicated the comparative findings. The PLCO found that overall there were few prostate cancer-specific deaths--only 174 out of the 70,000 enrolled men. Unfortunately, the researchers relied on death certificates to judge the cause of death. Death certificates often rely on generic terms that can mask the precise cause of death. Yet despite these warts, the trial found that PSA screening for prostate cancer increased the incidence of detection. It also revealed that the higher stages of prostate cancer were found more in the control group than in the screened group, and that PSA screening led to less high-grade disease. The medical community felt good about that, but when it looked closely at the number of prostate cancer-specific deaths in the screening arm compared to the control arm, there was no difference between the two-- the screening and non-screened patients had similar rates of prostate cancer-specific deaths. Similarly, when it look at deaths from any cause, it found that there was no difference between the two groups. Again, the question arose as to whether PSA screening is the best use of healthcare dollars. And, of course, there are the attendant risks of screening-related complications such as dizziness, bruising and hematoma, as well as the potential treatment-related complications of surgery, radiation, and hormonal therapy. At any rate, the PLCO will have additional follow-up at 13 years to ascertain whether there will be different results.

CHALLENGES TO PRACTICES

The two studies cited above present certain challenges to current medical practices. There is the difficulty in designing and implementing an ideal trial; there is the conflicting data in the research literature; physicians' attitudes have shifted from medical paternalism where the physician tells the patient what to do to peer to peer counseling where physicians counsel patients about risks and benefits, then let the patients decide; legal implications may arise (for instance, when a physician recommends against PSA screening and the patient actually has prostate cancer); and time constraints to office visits may limit the physician's ability to adequately address the issues with the patient. Even the recommendations of authoritative organizations contribute to the confusion about PSA screening. *The US Preventative Task Force* states that there is insufficient evidence in men under 75 to assess the benefits or the risks of PSA screening; and certainly for patients over 75 they should not be screened. In contrast, *the American Urological Association and the Na-*

tional Comprehensive Cancer Network recommend PSA testing and digital rectal exams starting at age 40. The *American Cancer Society* took the middle ground, recommending that physicians have risk-benefit discussions with patients starting at age 50, and even 45 for higher-risk men, such as men with a family history of prostate cancer and for African Americans. Currently, only about half the men over 55 in the US are being screened. Perhaps the ongoing PROTECT study in the UK will provide more definitive PSA screening guidelines.

PREVENTIVE MEASURES

Now let's talk about efforts to prevent prostate cancer. WRAMC participated in the so-called SELECT trial and no doubt some of you were involved in it. It evaluated the roles of selenium and vitamin E in preventing prostate cancer. The trial enrolled more than 35,000 men who were about 50 years old or older and who had a negative DRE and a PSA of less than 4.0. We found that those patients in the vitamin E group actually an had an increased risk of prostate cancer. Those patients in the selenium group and those in the combined vitamin E/selenium group essentially were found to be about equivalent to no treatment. So this was a negative study. Selenium and vitamin E do not prevent prostate cancer despite the claims of some that they promote "prostate health." In fact, excessive reliance on selenium may result in a higher risk of type II diabetes.

A more positive study was the more recent REDUCE Trial that looked at dutasteride (Proscar) in reducing the risk of prostate cancer. The trial enrolled over 8,000 men whose PSAs ranged between 2.5 and 10. They all had negative biopsies prior to getting into the study and they were either placed on dutasteride or a placebo for four years. They underwent biopsies at 24 and 48 months. There was a 23 percent risk reduction for prostate cancer in the dutasteride arm that was seen as early as 24 months. This was a very exciting news. We finally had something to help prevent prostate cancer! There was no increase in high grade cancer and dutasteride improved the diagnostic potential of PSA. It also decreased a lot of the voiding symptoms that men have as they age. On the other hand, there were some minimal side effects to these drugs, such as erectile dysfunction, decreased ejaculate, and gynecomastia (breast enlargement).

NOVEL TREATMENTS

Here at the Center for Prostate Disease Research, we view prostate disease and prostate cancer as a continuum starting at benign prostatic hyperplasia (BPH) and progressing all the way to hormone-refractory metastatic disease. We seek to engage in clinical trials that can lead to treating patients at any stage of this process. One of the trials that we are very excited about is Genprobe, a urine test that may provide more specificity and prognostic value than the PSA. Earlier tonight, I mentioned that while the PSA was very sensitive, it was not as specific as we would like. Well, we found that this urine test can increase the specificity of PSA testing by testing for molecular markers in the urine. It works like this: a patient would come in, have a digital rectal exam and a prostate massage, then patient would provide a urine sample for analysis. Genprobe can not only improve the detection of prostate cancer, but it can also be used to predict adverse pathologic features in the prostate cancers such as tumor volume and extracapsular extension. There is still work to be done, but we are optimistic that the Genprobe process will be available in the next year or so.

THE ROBOTIC PROSTATECTOMY

Many of you are familiar with the robotic prostatectomy. We have been doing it here at WRAMC for several years. The procedure has been widely reported in the popular press, and some medical centers actually market the procedure. Practice makes perfect and we have reached the point where the robotic prostatectomy offers equivalent, perhaps even better outcomes than the traditional open prostatectomy. (Dr. Brassell then showed several slides depicting the robotic equipment) One of the downsides of the robot is that the surgeon does not get the tactile feedback experienced in the traditional procedure, but it does offer improved visualization. With expertise, the surgeon has certain visual cues to compensate for the lack of tactile feedback. The robotic procedure is a 3D optical system, and this is an advantage over traditional laparoscopy which is just 2D and it has less magnification.

PROTON BEAM THERAPY

This radiation therapy is based on a biological principal called the Bragg Peak. Protons are a bit heavier, and when they enter the body and hit the targeted tissue, they immediately get absorbed by that targeted tissue and their energy drops off, theoretically limiting the radiation scatter to the rectum and adjacent tissue. This permits an increased radiation dosage to kill the cancer while lessening potential side effects. This would also potentially decrease secondary malignancy to other tissue. One of the limits of proton beam is that you cannot apply

focal therapy, so conventional radiation or IMRT can also play a role as one of the treatment modalities. Prostate cancer is usually multifocal, but in 10 percent of patients it can be unifocal, i.e., just on one side of the prostate. Conventional IMRT may allow us to actually apply the radiation dose to the side of the prostate that is affected while applying a much more limited radiation dose to the other side, thereby limiting side effects. Proton beam therapy's theoretical advantage must be balanced with the cost of machine. One of these machines costs about $100-150 million. The per patient cost is more than double that of conventional IMRT-about $25,000 per patient for IMRT and $58,000 per patient for proton therapy. Furthermore, the research to date does not indicate any proven efficacy for proton therapy compared to IMRT. Also, proton beam therapy is only available at relatively few sites in the US, so it is not always conveniently available. In this day and age of concern about rising healthcare costs, the cited cost differential is hard to overlook without a better demonstrated efficacy of proton bean therapy. Nevertheless, proton beam therapy is an exciting technology and holds promise for the future, but it remains an experimental mode.

HIGH INTENSITY FOCUSED ULTRASOUND

High Intensity Ultrasound (HIFU) is a truly non-invasive procedure to treat prostate cancer. As yet, HIFU remains a non-FDA approved treatment, but it is in clinical trial here at Walter Reed and elsewhere. It works like this: The patient lies on an operating table and a probe is placed in the rectum. It is similar to the probe that is used during a prostate biopsy. The ultrasound waves are passed from the probe to the prostate to apply energy to destroy tissue. The ultrasound wave propagates through tissue causing increased and reduced pressure cycles, the technical name for that is compression and rarification. And when it does so, it can apply a focal point of extreme heat, 80-100 Celsius, at a specified location in the prostate. Thermal delivery occurs very quickly, occurring within one second and the spread of this energy is minimal, only 2 millimeters. There are no incisions, the only thing that needs to be done postoperatively is to keep a Foley catheter in the urethra and then a suprapubic tube in the bladder to assist in urine drainage. The HIFU procedure can be done under regional anesthesia, such as a spinal or epidural, and the procedure is repeatable. This is really exciting technology. (Dr. Brassell then showed a series of slides illustrating the HIFU procedure).

Unfortunately, HIFU is not for everyone. The ultrasound beam can be affected by intervening tissue, i.e., any bone or calcification encountered during the procedure will block or even reflect the ultrasound wave. Air encountered may attenuate or interfere with the imaging. And, of course, there is also the possibility for such documented complications as urinary urgency; erectile dysfunction in at least 20 percent of patients; urinary stricture rate in 20 percent of patients (slightly high as compared to our other contemporary treatments); and very slight potential for urinary retention and rectal fistula.

Again, HIFU is not yet FDA-approved within the United States. It is approved for use by nations in Europe, Latin America, the Caribbean, Canada and the Far East. The on-going clinical trial in the United States is considering HIFU as both a primary therapy and a salvage therapy. We at WRAMC have been offering it in both the primary and salvage treatment modes under the FDA trial, but of late we offer it almost exclusively as a salvage therapy because of FDA clinical trial considerations. WRAMC is the highest patient accrual center in the United States, enrolling over 50 percent of the patients in the clinical trial. As for our outcomes as a salvage therapy, we are seeing impressive drops in PSA at the outset, but at about eighteen months of follow-up, we are seeing slight rises in PSA in some patients. We are trying to sort this out, so HIFU may not be quite ready for prime time.

One final comment on HIFU. If HIFU becomes a leading prostate cancer therapy, its use may limit the amount of tissue available for translational research for vaccine therapy and genetic correlates, thereby limiting potential advances in prostate cancer management. Furthermore, HIFU does not permit definitive pathologic staging because the prostate is never removed, so our ability to advise patients about adjuvant therapies may be affected. Finally, HIFU may make the pelvis inoperable for other diseases, such as bladder cancer and rectal cancer.

FUTURE TECHNOLOGY

Tissue change monitoring (TCM) is associated with HIFU. During the HIFU procedure, TCM gives the physician enhanced feedback via a color-coded display showing the change in tissue at the point of HIFU delivery. We are hopeful that TCM will refine the HIFU technique and improve our HIFU outcomes.

THE BOTTOM LINE

Let's look at our five-year biochemical recurrence-free survival for the several therapies for prostate cancer: radical prostatectomy, external beam radiation, brachytherapy, HIFU, and cryotherapy. For our

low risk patients, surgery seems to provide the best overall results with radiation (including brachytherapy) being almost equivalent. HIFU not quite there yet as a primary therapy. For intermediate risk patients, we see a slightly different picture. Our results with surgery are somewhat lower, as is the case with radiation. Our results with HIFU have stayed about the same.

CLOSING

Finally, I want to talk about dendreon (Provenge). This is one of the most exciting developments in prostate cancer management in the recent years. Dendreon is immunotherapy for patients with metastatic disease who are not responding to hormones. It did extend the median survival of such patients by four months. And remember, these patients had very advanced disease, so four additional months of survival is significant. Dendreon is the first vaccine to prolong survival for any type of cancer. We were part of that trial here at Walter Reed. In fact, we have the longest surviving patient in the trial. I want to thank everyone for participating in the trial. It really has led to advances in the treatment of hormone refractory metastatic prostate cancer. So we will end here on that positive note and open up the floor to any questions.

QUESTION: What is the PSA level that indicates recurrence?

ANSWER: Some years ago urologists started experimenting with something called supersensitive or ultrasensitive PSA which carried out the reported PSA to three decimal points, i.e., you could actually have a PSA of .001. We soon found that due to the issues with PSA specificity that this was much too sensitive. Patients were testing positive at that decimal point who did not have prostate cancer or recurrence At some centers such as Walter Reed that are involved in research, PSA is taken to the hundredth level (.01). But that is only for experimentation to see if we can detect clinically significant rises in PSA before the PSA reaches our recurrence threshold value which is typically 0.2 after surgery. As a practical matter we consider less than 0.2 to be undetectable.

PSA is also produced by other tissues in the body, such as the male adrenal glands. So after surgery, there may be some PSA "background noise," especially with the supersensitive PSA tests. Patients must be cautioned not to seek adjuvant treatments such as radiation after surgery when they learn of these oscillations. If a patient's PSA reaches 0.2 after surgery, urologists likely will wait until it reaches 0.3 or 0.4 before they recommend adjuvant therapy to make sure that the rise is not due to the "background noise" I mentioned above. Patients who had radiation as a primary therapy still have prostate tissue in place. In their case, the practice is to observe three consecutive rises in PSA before considering that there has been recurrence.

QUESTION: I am reading that in some cases only part of the prostate is being treated after prostate cancer has been diagnosed.

ANSWER: At present the approved treatments for prostate cancer are those that treat the whole gland. When we do surgery, we take out the whole prostate. When we do radiation, whether it be external beam, brachytherapy or proton beam, we treat the whole prostate. When we do HIFU, we treat the whole prostate. Realizing that some men may have unifocal disease, there is some experimentation that may make it possible to treat the part of the prostate with the largest volume of cancer in an effort to mitigate side effects, but right now every standard of care treatment deals with the entire gland.

QUESTION: How do you differentiate between distant metastasis and local recurrence?

ANSWER: It is not easy. In the case of radical prostatectomy, we consider the time factor after the surgery. If recurrence is detected within 18 months, then it is probably due to metastatic disease, perhaps in the lymph nodes or bone. If it is detected after 18 months, then it is probably a local recurrence. We also take PSA doubling time into account, and we may order bone scans and CT scans to help further define the situation. So we rely on clinical parameters as well as radiological processes. Even with all of that, no one can be 100 percent sure of whether it is distant or local recurrence. We use the tools at hand to help us with our certitude.

♦ WRAMC US TOO COUNSELORS ♦ (As of July 31, 2011)

(THESE PERSONS ARE WILLING TO SHARE THEIR EXPERIENCES WITH YOU. FEEL FREE TO CALL THEM.)

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Robert Gerard	Carlisle, PA	(717) 243-3331	
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INCONTINENCE

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♦ MEETING ANNOUNCEMENT ♦

WEDNESDAY, AUGUST 3, 2011
7 PM

JOEL AUDITORIUM (SECOND FLOOR)
MAIN HOSPITAL BUILDING, WRAMC

♦ SPEAKER ♦

Stacey L. Koff, MD

Department of Urology, Fort Belvoir Hospital

♦ TOPIC ♦

"Nutrition and Prostate Cancer: Can Diet and Lifestyle Improve Your Cancer Outcomes?