WRNMMC Us TOO, Inc.
A PROSTATE CANCER SUPPORT GROUP
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WALTER REED NATIONAL MILITARY MEDICAL CENTER
NEWSLETTER

VOLUME 25	NUMBER 4	NOVEMBER 2016

♦ The Testosterone Conundrum: The Putative Relationship between Testosterone Levels and Prostate Cancer ♦

The controversy surrounding the relationship between testosterone and prostate cancer has existed for decades. The literature surrounding this topic is confusing and at times contradictory. There is no level-one quality evidence that confirms or refutes the relationship between either high or low serum testosterone levels and the subsequent development of prostate cancer. This commentary summarizes the issues involved and provides an interpretation as to the causes of the confusion and provides a framework for ongoing discussion and investigation.

A Medline and PubMed search was conducted using search terms: testosterone levels and prostate cancer to identify pertinent literature. There is no consistent evidence that a single testosterone level is predictive of prostate cancer risk.

The development of prostate cancer is a complex biologic process potentially involving genetics, dietary, life style and hormonal factors. Serum testosterone levels do not accurately reflect the internal prostatic milieu. Finally, if testosterone levels are to be considered in the etiology of prostate cancer they should be measured and interpreted on a chronic basis with multiple measurements over a period of years. (Source: Urologic Oncology. July 13, 2016 [Epub ahead of print])

♦ An Invitation ♦

The Fairfax-Falls Church Prostate Cancer Education and Support Group at the Inova Life with Cancer Center invites the Walter Reed Prostate Cancer Support Group to attend a special presentation by Dr. Charles "Snuffy" Myers on Monday, November 7, 2016 at 7:30 pm. Dr. Myers, a medical oncologist, is popular as a speaker on prostate cancer because of his ability to explain the science and medicine in understandable terms. **(See page 10 for more details)**

♦ *INSIDE THIS ISSUE* ♦

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♦ FROM THE EDITOR ♦

Dr. Charles "Snuffy" Myers speaks often in the Northern Virginia area where he has an avid following. No doubt, some of you are familiar with his presentations.

♦ SPEAKER'S REMARKS - AUGUST 4, 2016 ♦

Our speaker for Thursday, August 4, 2016, was Dr. William Lloyd Glover, Jr., a urologist in private practice. His topic was "**A Urologist is Diagnosed with Prostate Cancer. Now What?"** Dr. Glover discussed his own diagnosis with prostate cancer as well as providing a comparative analysis of high intensity focused ultrasound (HIFU) with the primary therapies such as the radical prostatectomy and radiation.

♦ MEETING SCHEDULE FOR NOVEMBER 3, 2016 ♦

Our speaker for Thursday, November 3, 2016, is Dr. Camille McCann Williams, a radiation oncologist at WRNMMC. Her topic is "**Radiation Therapy Treatment Options for Prostate Cancer: Understanding the Basics.** Please join us at 7:00 PM in the America Building (Bldg 19), 2nd floor, Room 2525. Remember, your family and friends are also welcome.

(The presentation also may be viewed via video teleconference at the Fort Belvoir Community Hospital. Go to the Oaks Pavilion, 1st floor, Room 332, to participate.)

SEE THE BACK PAGE OF THIS NEWSLETTER FOR IMPORTANT INFORMATION ABOUT THIS MEETING.

♦ PROSTATE-SPECIFIC ISSUES ♦

Appropriateness Criteria for Active Surveillance of Prostate Cancer. Adoption of active surveillance (AS) is widely variable across urological communities. This suggests a need for more consistency in the counseling of patients. To address this need, this study used the RAND/UCLA Appropriateness Method to develop appropriateness criteria and counseling statements for AS.

Panelists were recruited from Michigan urology practices. Combinations of parameters thought to influence decision-making were used to create and score 160 theoretical clinical scenarios for appropriateness of AS. Recent rates of AS among real patients across the state were assessed.

Low volume Gleason 6 was deemed "highly appropriate" for AS, whereas high volume Gleason 6 and low volume Gleason 3+4 were deemed "appropriate" to "uncertain." No scenario was deemed "inappropriate" or "highly inappropriate." Prostate specific antigen density, race, and life expectancy (LE) impacted scores for intermediate and high volume Gleason 6 and low volume Gleason 3+4. The greatest degree of score dispersion (disagreement) occurred in scenarios with long LE, high volume Gleason 6, and low volume Gleason 3+4. Recent rates of AS utilization among real patients ranged from 0% to 100% at the provider level for low or intermediate biopsy volume Gleason 6 demonstrating a clear opportunity for quality improvement.

By virtue of this work, urologists have the opportunity to present specific recommendations from the panel to their individual patients. Community-wide efforts aimed at raising rates of AS and reducing practice- and physician-level variation in the choice of AS versus treatment are warranted. (Source: The Journal of Urology. 2016 Jul 12 [Epub ahead of print])

Is "Active Surveillance" an Acceptable Alternative?: A Qualitative Study of Couples' Decision Making about Early-Stage, Localized Prostate Cancer.

The objective of the study was to describe decision-making by men and their partners regarding active surveillance (AS) or treatment for early-stage, localized prostate cancer. Fifteen couples were recruited from a cancer center multispecialty clinic, which gave full information about all options, including AS. Data were collected via individual, semi-structured telephone interviews.

Most patients were white, non-Hispanic, had private insurance, had completed at least some college, and were aged 49-72 years. Ten chose AS. All partners were female, and couples reported strong marital satisfaction and cohesion. All couples described similar sequences of a highly emotional initial reaction and desire to be rid of the cancer, information seeking, and decision making.

The choice of AS was built on a nuanced evaluation of the man's condition in which the couple differentiated prostate cancer from other cancers and early stage from later stages, wanted to avoid/delay side effects, and trusted the AS protocol to identify negative changes in time for successful treatment. Treated couples continued to want immediate treatment to remove the cancer.

The study concluded that having a partner's support for AS may help a man feel more comfortable with choosing and adhering to AS. Using decision aids that address both a man's and his partner's concerns regarding AS may increase its acceptability. The research shows that some patients want to and do involve their partners in the decision-making process. Ethical issues are related to the tension between desire for partner involvement and the importance of the patient as autonomous decision-maker. The extended period of decision making, particularly for AS, is also an ethical issue that requires additional support for patients and couples in the making of fully informed choices that includes AS. (Source: Narrative Inquiry in Bioethics. 2016 [Epub] via UroToday, July 19, 2016)

1 in 12 Chance of Second Cancer in Many Survivors. In the United States, more than 8% of adults diagnosed with the most common cancers develop a second malignancy (of any type, including rare cancers), according to an analysis of US data from the last two decades.

The top-diagnosed second malignancy was lung cancer (18% of all second primaries), followed by colorectal cancer (12%), prostate cancer (9%), and bladder cancer (8%). Second cancers were often lethal: More than half of patients (55%) died of their second cancer, while 13% died of their first cancer.

Oncologists, other specialists and primary care providers should be on the lookout not just for recurrence of an initial cancer but for second cancers, lead author Nicholas Donin, MD, a urologist at the David Geffen School of Medicine, University of California, Los Angeles, told *Medscape Medical News*.

Donin, et al, Geffen School of Medicine, University of California, identified more than 2.1 million adults diagnosed with a primary malignancy from the 10 most common cancer sites (prostate, breast, lung, colon, rectum, bladder, uterus, and kidney, along with sites affected by melanoma and non-Hodgkin lymphoma) in 1992–2008 from Surveillance, Epidemiology, and End Results data. From that group, 170,865 (8.1%) developed a second primary malignancy; mean follow-up was greater than 6 years in all primary cancer types (except for primary lung cancer, which was 4.18 years).

Patients with bladder cancer had the highest cumulative incidence, with 19% having a second cancer at 10 years and 34% at 20 years. Most commonly, that second malignancy was lung cancer (25% of the time) Bladder cancers are often associated with a significant smoking history. Urologists should think about referring these patients for lung cancer screening," according to the researchers.

It is understandable that patients with bladder cancer had the highest rate of a second primary cancer, they also observed. Most bladder cancers are of low grade and stage and not lethal. The 5-year relative survival from bladder cancer is 80%, and the disease is highly prevalent (in 2012, there were 577,403 bladder cancer survivors in the United States).

Primary treatments have gotten so much better, so there more survivors living for longer periods of time. So screening for other cancers should not be ignored.

The researchers also found that second cancers are often lethal. In the group of patients with 2 primary cancers, a lung cancer diagnosis was most deadly, accounting for 12% of all deaths in this group, which amounted to more overall deaths than the combined total from melanoma,

bladder cancer, thyroid cancer, kidney cancer, or endometrial cancer that were second primaries. The prominence of lung cancer both as a second cancer and as a cause of death was arresting. So smoking cessation becomes especially important in cancer survivors.

The study authors say that cancer survivors may be "especially susceptible" to developing second primary malignancies because of a variety of unique factors, including genetic syndromes, common etiologic exposures (especially smoking), and the late effects of chemotherapy and radiotherapy.

One observer argued that second malignancies from cancer treatment are "more an issue with survivors of childhood cancers." This study did not include patients with cancer under age 18 years. He argued that "there is a tiny risk of second cancer from radiation treatment."

The study authors acknowledged that there was a chance that some second cancers were actually metastases of initial cancers. However, this was unlikely, said the authors, because they excluded cases in which the second primary malignancy was diagnosed within 1 year of the first malignancy. Also, many common secondary malignancies (e.g., prostate, breast, colorectal, and bladder cancer and non-Hodgkin's lymphoma) are in unlikely sites for metastases. (Source: *Cancer*: published online July 5, 2016, via Medscape Medical News, July 21, 2016)

Survival Outcomes in Gleason 9-10 PCa Similar with Radiation, Surgery. Radiation therapy and radical prostatectomy (RP) offer men with Gleason score 9–10 prostate cancer (PCa) equivalent cancer-specific and overall survival, according to a new study. Findings also suggest that extremely dose-escalated radiation therapy plus androgen deprivation therapy (ADT) might be the optimal upfront treatment for these patients, researchers concluded in a paper published online ahead of print in *European Urology*.

The investigators noted that their study is the largest comparative study of outcomes exclusively for patients with Gleason score 9–10 PCa. The study, led by Kishan, et. al., the University of California Los Angeles, included 487 patients with biopsy Gleason 9–10 disease. Of these, 230 underwent external beam radiation therapy (EBRT), 87 were treated with EBRT and brachytherapy (BT), and 170 underwent RP. Most radiation therapy patients received androgen deprivation therapy and dose-escalated radiation therapy.

The median follow-up was 4.6 years. Local salvage and systemic salvage were performed more frequently among RP patients (49% vs. 30.1%) when compared with EBRT patients (0.9% and 19.7%) or EBRT plus BT patients (1.2% and 16.1%), the group reported.

The 5- and 10-year rates of cancer-specific and overall survival were similar across the 3 cohorts after adjusting for age, clinical stage, biopsy Gleason score, initial PSA level, year of treatment, and use of salvage therapies, according to the investigators The 5-year and 10-year distant metastasis-free survival rates were significantly higher with EBRT plus BT (94.6% and 89.8%) than with EBRT (78.7% and 66.7%) or RP (79.1% and 61.5%).

The researchers said their finding that EBRT + BT provides improved systemic control over both EBRT and RP in this setting is novel, and suggests that optimal local control (offered by extreme dose-escalation) and an upfront method of systemic control (offered by a frequent use of ADT in this cohort) may represent the best up-front treatment strategy for these patients who are at high risk of harboring micrometastatic disease at presentation.

The equivalence of cancer-specific and overall survival following EBRT-based treatments and RP in the current study differs from most prior comparative studies, the investigators pointed out. “Importantly, the majority of EBRT patients in prior studies received neither long-course ADT nor high-dose RT,” they wrote. “In contrast, the majority of RT patients treated in our series were treated in accordance with contemporary standards.” (Source: Renal and Urology News, August 2, 2016)

Active Surveillance of Prostate Cancer Doesn't Dampen Quality of Life. Choosing no treatment and regular check-ups didn't seem to stress men with low-risk disease, a study has found. Men with low-risk prostate cancer report a good quality of life after choosing active surveillance as a treatment for their disease, a new study finds.

Active surveillance for prostate cancer means a man chooses not to have surgery, radiation or chemotherapy, but instead follows a regular schedule of tests and exams to make sure the cancer isn't growing rapidly, the U.S. National Cancer Institute says.

The new study included 89 American men with low-risk prostate cancer and 420 men without the disease. Over three years of follow-up, there were no significant differences between the two groups in health-related quality of life, according to the findings published in the *Journal of Urology*.

"To our knowledge, this is the first report of health-related quality-of-life outcomes of men on active surveillance for prostate cancer compared to men without prostate cancer in a prospective, multi-institutional study," lead investigator Dr. Christopher Porter said in a journal news release. "Our results suggest that for at least three years, men selecting active surveillance do not experience a substantial psychological burden or clinically significant problems due to untreated disease," he added.

Most men with prostate cancer have low-risk disease and must make the difficult decision between having their cancer monitored or receiving treatment. But treatments carry the risk of side effects, such as urinary, bowel and sexual dysfunction, the study authors noted. "The potential clinical impact of these results is significant and will allow clinicians to counsel patients effectively in regard to the potential health-related quality-of-life outcomes associated with active surveillance," Porter said. (Source: *Journal of Urology*, news release, July 25, 2016, via HealthDay)

Androgen Deprivation Therapy for Prostate Cancer May Increase Dementia Risk. Androgen deprivation therapy may be associated with an increased risk for developing dementia in patients with prostate cancer, according to a study published in *JAMA Oncology*.

Although growing evidence suggests a link between androgen deprivation therapy and cognitive dysfunction, including Alzheimer disease, whether androgen deprivation therapy may contribute to the risk of dementia more broadly is unclear. Therefore, researchers sought to examine the association of androgen deprivation therapy with the subsequent development of dementia in patients with prostate cancer.

For the study, investigators analyzed data from 9272 men with prostate cancer who received androgen deprivation therapy. After a median follow-up of 3.4 years, results showed that use of androgen deprivation therapy was associated with a significant 2-fold increase in the risk of

dementia. Researchers observed similar results when excluding patients with Alzheimer disease.

The investigators determined that the absolute risk of developing dementia among patients treated with androgen deprivation therapy was 7.9% at 5 years compared with 3.5% in those who did not receive androgen deprivation therapy.

The study further demonstrated that patients who received androgen deprivation therapy for at least 12 months had the greatest absolute increased risk of dementia, while patients 70 years or older had the lowest cumulative probability of remaining free of dementia. (Source: Oncology Nurse Advisor. October 14, 2016)

Urinary, Sexual Function Recovery Differs by Localized PCa Treatment. Urinary, bowel, sexual function, and quality of life among men with localized prostate cancer may vary depending on treatment with monitoring, surgery, or radiotherapy, according to a study published in *The New England Journal of Medicine*.

Through the Prostate Testing for Cancer and Treatment (ProtecT) Trial, researchers examined patient-reported outcomes of 1643 men who had completed questionnaires before diagnosis, at 6 and 12 months after randomization, and then annually after the first 12 months. At 5 years, the researchers assessed for cancer-related quality of life. Questionnaire completion upon follow-up was higher than 85% for most observed measures.

Prostatectomy had the greatest negative effect on sexual function and urinary continence, which remained worse among the 3 groups throughout the trial.

Radiotherapy had a negative effect on sexual function, which was greatest at 6 months, although it recovered soon after and remained stable. Little effect on urinary continence with radiotherapy was observed; bowel function was, however, worse at 6 months.

Among patients treated with active monitoring, sexual and urinary function gradually declined.

Quality of life among patients reflected the reported changes in function, with no significant differences observed among the groups in measures of anxiety, depression, or general health- or cancer-related quality of life. (Source: *New England Journal of Medicine*. September 20, 2016 [Epub ahead of print], via Renal and Urology News, September 20, 2016)

Early Prostate Cancer Diagnoses Continue to Fall in U.S.: Study Decline follows recommendation against routine screening, but experts not sure if trend is good or bad. Diagnoses of early prostate cancer continue to decline in the United States, following the U.S. Preventive Services Task Force recommendation against routine screening for the disease, researchers report.

The screening involves a blood test that identifies levels of PSA (prostate specific antigen), a protein produced by the prostate gland. That test can determine when cancer exists, but it often wrongly identifies nonexistent cancer. These "false positive" results can cause anxiety and lead to unnecessary follow-up tests. Because of this, the task force issued a draft recommendation against routine screening in 2011 and a final guideline in 2012.

Since then, diagnoses of early prostate cancer in American men aged 50 and older dropped by 19 percent between 2011 and 2012 and by another 6 percent the following year, said lead researcher Dr. Ahmedin Jemal.

But while many men may have been spared unnecessary anguish, less frequent screening may have a downside. Some experts worry more men will develop potentially fatal prostate cancer as a result. "Prostate cancer is a slow-growing tumor, so it takes time. We may see it over the next three to five years," Jemal said.

There is a balance in the task force recommendation, said Dr. Anthony D'Amico, chief of genitourinary radiation oncology at Brigham and Women's Hospital and the Dana Farber Cancer Institute, in Boston. "Some men who should not be treated are not being diagnosed, but that also means some men who should be treated are either losing the chance for cure or presenting later and needing to undergo more treatment and more side effects for a possible cure."

"The answer to this dilemma will come with personalized medicine based on risk-based screening -- screening men preferentially in good health and at high risk," D'Amico added.

The decrease in diagnoses of early-stage prostate cancer may be partly due to a misreading of the task force's recommendation, added Dr. Otis Brawley, the cancer society's chief medical officer. "I believe the task force guideline is being misunderstood," he said.

"The key word that is missed is 'routine' -- the task force does not recommend routine screening. This in my mind means they are not against all screening. Also, they do call for informed decision-making regarding potential risks and potential benefits," Brawley said.

Using the Surveillance, Epidemiology and End Results database, Jemal and colleagues looked at cases of prostate cancer diagnosed between 2005 and 2013 in men aged 50 and older. They found that from 2012 to 2013, early prostate cancer diagnosis rates per 100,000 men dropped from 356.5 to 335 in men aged 50 to 74. In men older than that, early cancer diagnoses fell from 379 to almost 354 per 100,000 men. Meanwhile, cases of advanced prostate cancer remained stable in both age groups.

The findings leave some room for interpretation. Other factors leading to the decline could include improved preventive measures and changes in the incidence of unknown risk factors, Jemal said. But D'Amico believes fewer screenings explain the statistics. The drop in the diagnosis of early prostate cancer "is consistent with the drop in PSA screening," he said.

The main issue is whether this is an early sign that more high-risk disease, more disease that has spread and more deaths from prostate cancer will happen, he added. "My opinion is that we are probably heading for more high-risk and metastatic [cancer that has spread] disease in the next year or two, followed by more deaths from prostate cancer if the decline in screening is maintained," D'Amico said. He added that the only hope for a boost in screening lies with the results of a British trial. If those findings, expected next year, show a benefit for PSA testing, perhaps testing rates will rebound, D'Amico said.

The American Cancer Society recommends that men "make an informed decision with their health care provider about whether to be screened for prostate cancer." The decision should

be made "after getting information about the uncertainties, risks and potential benefits of prostate cancer screening." The discussion about screening should take place at:

- Age 50 for men at average risk of prostate cancer who are expected to live at least 10 more years.
- Age 45 for men at high risk of developing prostate cancer. This includes blacks and men who have a first-degree relative (father, brother or son) diagnosed with prostate cancer at an early age (younger than 65).
- Age 40 for men at even higher risk (those with more than one first-degree relative who had prostate cancer at an early age).
- After these discussions, men who still want to be screened should get the PSA blood test. The digital rectal exam may also be used as a part of the screening, the cancer society says. (Source: *JAMA Oncology*, online via MedlinePlus, and Health Day News, August 18, 2016)

Urethral Atrophy of the Artificial Urinary Sphincter. A recent study investigated the concept of 'urethral atrophy', which is often cited as a cause of recurrent incontinence after initially successful implantation of an artificial urinary sphincter (AUS); its objective was to investigate the specific cause of the malfunction of the AUS in these patients and address them.

Between January 2006 and May 2013, 50 consecutive patients (mean age 54.3 years) with recurrent incontinence had their AUS explored for malfunction and replaced with a new device with components of exactly the same size, unless there was a particular reason to use something different. Average time to replacement of the device was 10.1 years. The mean follow-up after replacement of the device was 24.7 months. All patients without an obvious cause for their recurrent incontinence had preoperative urodynamic evaluation, including measurement of the Valsalva leak point pressure (VLPP) and the retrograde cuff occlusion pressure (RCOP).

After explantation of the AUS in patients without any apparent abnormality of the device at the time of replacement, the pressure generated by the explanted pressure-regulating balloon (PRB) was measured manometrically, when this was possible. In a select group of six consecutive patients of this type, the fibrous capsule surrounding the old cuff was incised then excised to expose and evaluate the underlying corpus spongiosum.

In 31 of the 50 patients (62%) undergoing exploration, a specific cause for the malfunction of their AUS was defined. In the other 19 patients (38%) no cause was found, either preoperatively or at the time of exploration, other than a low VLPP and RCOP. A typical 'waisted' or 'hour-glass' appearance of the underlying corpus spongiosum was demonstrable, to some degree, on explanting the cuff in all cases.

In the six patients in whom the restrictive sheath surrounding the cuff was excised, the urethral circumference immediately returned to normal after the compressive effect of the sheath was released. Manometry of the explanted PRBs, when this was possible, showed a loss of pressure in all instances. Replacement of the explanted AUS with a new device with the same size cuff and PRB in 14 of these 19 patients was successful in 12 (85.7%).

These results, and other theoretical considerations, suggest that recurrent incontinence, years after initially successful implantation of an AUS, is because of material failure of the PRB, probably attributable to its age and consequent loss of its ability to generate the pressure it was designed to produce, and that urethral atrophy does not occur. Simply replacing the old device with a new one with the same characteristics, unless there is a particular reason to do otherwise, is usually successful and avoids the complications of alternatives such as cuff downsizing, implanting a PRB with a higher pressure range, implantation of a second cuff or transcorporeal cuff placement, all of which have been advocated in these patients. Source: BJU International © 2015 BJU International via National Institutes of Health, August 12, 2016)

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DR. CHARLES "SNUFFY" SMITH PRESENTATION

The Fairfax-Falls Church Prostate Cancer Education and Support Group at the Inova Life with Cancer Center invites the members of the Walter Reed Prostate Cancer Support Group to attend a special presentation by Dr. Charles "Snuffy" Myers on Monday, November 7th at 7:30 pm at the new Inova Center for Personalized Health (ICPH) Conference Center (formerly the Exxon-Mobil Headquarters Campus) 3225 Gallows Road, Fairfax, VA 22037.

An innovator in prostate cancer oncology for more than 30 years, Dr. Myers is both a medical oncologist and prostate cancer survivor. Dr. Myers spent 20 years at the National Institutes of Health (NIH) before becoming Director of the Cancer Center of the University of Virginia. In 2002, Dr. Myers left the University of Virginia to establish the American Institute of Disease of the Prostate (AIDP), as well as the Foundation for Cancer Research and Education (FCRE) in Earlysville, VA.

As you drive into campus from either the North or South Entrance off Gallows Road

- Veer around corner (natural curve) and as you see property, note the surface parking lots on right or left of the Conference Center (T8).
- Park in either outdoor parking lot on both sides of the Conference Center.
- Enter TOWER 8 “T8”
- Go thru revolving doors of the Conference Center, keep to your right, and proceed up either by escalator or elevator to the second floor. Event host or signage will greet guests for the support group meeting that will be held in the Convention Center’s Ballroom on the second floor.

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"A Urologist is Diagnosed with Prostate Cancer - Now What?"

(Personal Experiences and Professional Perspectives on High Intensity Focused Ultrasound (HIFU) Prostate Cancer Ablation)

by

William L. Glover, Jr., MD, F.A.C.S. and Clinical Professor of Urology, George Washington University; and Director, Fairfax (VA) Urology Center

(A summary of the presentation to the WRNMMC Prostate Cancer Support Group on August 4, 2016)

INTRODUCTION

First of all, let me express my appreciation for your invitation to be with you this evening.

Therapeutic approaches to prostate cancer continue to advance. When new modalities are introduced – often in Europe, Canada, Japan, or other countries before approved for clinical use in the USA -- increasing experience enables refinements in technique, equipment and optimal application to the location and extent of patients' cancers and the patients' concerns of sequelae. Newer approaches, although less expensive, must prove their safety and efficacy compared to FDA-approved, accepted and usually insurance-reimbursed modalities. Examples of such established therapies with extensive cumulative clinical experiences include the radical prostatectomy and radiotherapy among others.

When impressed by cumulative reports of clinical outcomes of a new approach, wherever introduced, the urologist may go out-of-state – or even abroad -- to study the procedure so that, upon FDA approval for use in the USA, the new procedure's availability can be offered promptly to patients though suitably equipped and trained practices. My presentation tonight reviews clinical and technical features of the use of a relatively new and unfamiliar system: High Intensity Focused Ultrasound (HIFU). I want to review the two HIFU systems in commercial use in the US, providing both my analysis as a surgeon as well as my own personal experience as a patient. In fact, when diagnosed with prostate cancer myself not long ago, I chose a colleague whom I had trained in HIFU and other techniques to be my own urological surgeon for my HIFU therapy. I recognized at the time that there was no hope that Medicare, nor most other major medical insurance carriers, would cover the costs of this expanding option for prostate cancer patients. The FDA approved High Intensity Focused Ultrasound (HIFU) as a recognized therapy in October 2015.

TECHNOLOGY OF HIFU AND ITS CLINICAL APPLICATION

When prostate cancer is detected by any of several methods, the specific areas of involvement and any extension beyond the capsule must be assessed. With improved imaging techniques, including the increasing use of 3D Multi-parameter MRI Fusion and ultrasound, the urologist can better define the location of likely prostate cancer involvement as a target for diagnostic and therapeutic intervention for eventual discussion with the patient. HIFU is, as yet, relatively unfamiliar to most men.

Depending on the extent of prostate tissue to be ablated, the HIFU procedure takes about 2-4

hours. A rectal probe is placed inside the rectum behind the prostate. After positional adjustments, the probe's movements are controlled robotically via a operator's console. By extremely small movements across the prostate surface, the probe's first ultrasound function enables sonographical visualization of the deeper glandular tissue characteristics. The probe's second ultrasound function is for therapeutic purposes. Starting from a wider beam through the rectal wall covering the prostate, the HIFU is capable of focusing a beam down to about 3 mm diameter and 20 mm in length. By controlling the wattage (and hence energy and heat produced in the targeted area) and the timing (e.g., 2 seconds on), very precise areas can be targeted for heat-induced coagulation necrosis of suspicious tissue. Sequential robotic movements of the probe across the prostate surface during the procedure can enable either segmental or complete prostatic ablation.

Safety features are paramount. For example, the probe is constructed to cool the point of contact with the rectal wall so that the passage of the therapeutic beam through the rectal wall doesn't overheat the non-targeted intervening tissue. Although the procedure is considered painless, it is necessary to anesthetize the patient – either by spinal, epidural or general anesthesia. This prevents even slight voluntary or involuntary prostate position shifts during the procedure that could put normal tissue at risk of damage. The patient returns home with little or no bleeding unlike that so characteristic of surgical prostatectomy. Several days of urinary catheterization assures that the surrounding healing process (inflammatory response followed by fibrosis) minimizes urethral stricture/stenosis complications.

FDA-APPROVED HIFU SYSTEMS AND OUTCOMES

Two systems for HIFU have been approved to date for use in the USA: The *Sonablate 500* (manufactured in Charlotte, NC) and the *Ablatherm* (a French device). The two systems are conceptually similar but have practical distinctions, including transportability and accessibility.

Large, multicenter domestic and international studies suggest that experienced urologists using these HIFU ablation techniques can achieve outcomes that are usually as good as – or significantly better than -- the best outcomes of the other primary therapies such as radical prostatectomy and radiotherapy. Such published outcome measures of success include: 5- and 10-year "Biochemical Disease-Free Survival" (BDFS) or "10-year cancer-specific survival," and "10-year metastasis-free survival."

In addition, both HIFU systems have improved complication profiles with respect to return of urinary continence (94%+), reduced urethral stricture or stenosis (both treatable), and preservation/return of sexual function. HIFU treatments have lesser complication rates (e.g., pad-free continence of 94-100%; and returned potency of 80-90%) than whole gland ablation (88-97%; and 40-70%, respectively).

Both systems can be used for "salvage" (rescue) treatment after another therapeutic approach has failed; however, as expected, in these cases post-salvage procedure outcome profile may be less ideal.

Direct comparison of the two systems is challenging due to differences in patient selection, facility, equipment, and clinical experiences; however, the data presented in summary tables suggest that, at present, *Ablatherm* may be edging ahead somewhat.

(Editor's note: Dr. Glover accompanied his remarks with series of slides comparing the efficacy of HIFU to the traditional therapies for prostate cancer. Other slides compared the two HIFU systems, *Sonablate* and *Ablatherm*.)

QUESTIONS AND ANSWERS

Q: How does HIFU compare to "Cyberknife"?

A: "Cyberknife" doesn't involve a knife! It is the proprietary name for external beam irradiation as used by some prostate cancer treatment centers to distinguish their equipment and procedure for recognition in the medical marketplace.

Q: How available is the HIFU procedure around the country?

A: Given the recent FDA approval, many facilities and urologists are starting to use it or consider its use. They and their patients' favorable experience is prompting rapid expansion of HIFU availability. However, it is not yet approved for Medicare and some other insurance reimbursements. By the way, HIFU ablation is being tried in select medical centers for brain cancer and it may eventually find application in other cancer therapies beyond prostate cancer.

Q: How often is segmental (focal) ablation performed by HIFU compared to total prostate ablation?

A: My usual preference has been to perform total prostate ablation because prostate cancer can arise in multiple areas of the prostate and treating only one area might leave other areas untreated. For example, traditional breast cancer therapy favored complete mastectomy: however, nowadays "lumpectomy" surgery in breast cancer is increasingly in vogue. So I am gradually accepting the proposition that segmental prostate ablation may be sufficient in many cases.

Q: In comparing cumulative data from historically standard treatments with the HIFU ablation, are there features of patient selection or variations in patients' interpretation of follow-up evaluations (impotence, incontinence) that make direct comparisons difficult.

A: Yes, but there are useful comparisons that can be made now with the large amount of both non-US data and large US studies done under the FDA's required conditions for HFU clinical research. It is worth noting that the massive US-wide (Medicare-based) database that has been ongoing for approximately four decades (SEER database) enables the urologist to see that the overall rate of major complications (strokes, heart attacks and pulmonary emboli) associated with radical prostatectomy is about 20%. In addition, the perioperative death rate is about 1.5%. In this context, the HIFU ablation is notably better.

Q: Are measures of loss and return of sexual potency comparable across studies?

A: Not precisely. However, the trends are favorable for HIFU ablation. Do remember that aging males have other causes for loss of sexual function with time. The incidence of these –

such as diabetic neuropathy or peripheral vascular diseases affecting blood flow in the pelvis and penis – are increasing with the age of the patient irrespective of the procedure being performed.

Q: Do other therapies play a role to enhance the likelihood of long-term successful outcome measures of freedom from return of prostate disease, perhaps later appearing as a metastasis?

A: Yes, one seemingly advantageous therapeutic approach is to recognize that cancer-positive prostatic biopsies are accompanied – repeated studies have now shown – by cancer cells circulating in the peripheral blood. To prevent those cells from lodging in the bone marrow and providing a later focus of metastatic disease, I offer the patient several weeks of pharmacologic "androgen deprivation" using agents like Lupron to block the normal effect of male testosterone on prostate cells. The result seems to be that the disseminating cells are starved and are less likely to set up "colonies" in the bone marrow or elsewhere.

CLOSING

It has been my pleasure tonight to share with you my HIFU experience. No doubt, you will be hearing more about HIFU as a definitive alternative to the traditional therapies for prostate cancer.

INTENTIONALLY BLANK

♦ WRNMMC US TOO COUNSELORS ♦

(As of November 1, 2016)

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

SURGERY

Tom Assenmacher	Kinsvale, VA	(804) 472-3853	
Jack Beaver	Falls Church, VA	(703) 533-0274	1998 (Open RP)
Rob Calhoun	Annapolis, MD	(410) 293-6635	2011 (Robotic Surgery)
Gil Cohen	Baltimore, MD	(410) 367-9141	
Richard Dorwaldt	San Antonio, TX	(210) 310-3250	(Robotic Surgery)
Michael Gelb	Hyattsville, MD	(240) 475-2825	(Robotic Surgery)
Robert Gerard	Carlisle, PA	(717) 243-3331	
Tony Giancola	Washington, DC	(202) 723-1859	2008 (Radical Prostatectomy)
Ray Glass	Rockville, MD	(301) 460-4208	
Monroe Hatch	Clifton, VA	(703) 323-1038	
Tom Hansen	Bellevue, WA	(425) 883-4808	1998 (Robotic Surgery)
Bill Johnston	Berryville, VA	(540) 955-4169	
Dennis Kern	San Francisco, CA	(415) 876-0524	
Sergio Nino	Dale City, VA	(703) 590-7452	
Ed Postell	Collegeville, PA	(610) 420-6765	(Robotic Surgery)
George Savitske	Hellertown, PA	(703) 304-3081	2000 (Open RP)
Artie Shelton, MD	Olney, MD	(301) 523-4312	
Jay Tisserand	Carlisle, PA	(717) 243-3950	

PROSTATE CANCER AND SEXUAL FUNCTION

James Padgett	Silver Spring, MD	(301) 622-0869
George Savitske	Hellertown, PA	(703) 304-3081

RADIATION

Leroy Beimel	Glen Burnie, MD	(410) 761-4476	1987 (External Beam Radiation)
Bob Bubel	Grand Junction, CO	(970) 263-4974	2010 (Proton Beam Radiation)
Harvey Kramer	Silver Spring, MD	(301) 585-8080	1998 ((Brachytherapy)
Joseph Rosenberg	Kensington, MD	(301) 495-9821	2009 (Brachytherapy)
Barry Walrath	McLean, VA	(571) 969-8269	2001 (Brachytherapy)

WATCHFUL WAITING

Tom Baxter	Haymarket, VA	(703) 753-8583	Active Surveillance

SPOUSE SUPPORT

Renate Bubel	Fairfax, VA	(703) 280-5765
Karen Collins	Mechanicsburg, PA	(717-766-6464
Betty Kramer	Silver Spring, MD	(301) 585-8080
Ellen Rosenberg	Kensington, MD	(301) 495-9821
Nancy Wallrath	McLean, VA	(703) 915-8108

OTHER THERAPIES/MULTIPLE THERAPIES

Howard Bubel	Fairfax, VA	(703) 280-5765	1995,1996 (Hormonal, Cryosurgery, Sexual Function
Arthur E. Clough	Kerryville, TX	(830) 896-8826	1993 (Surgery and Radiation)
Pete Collins	Mechanicsburg, PA	(717) 766-6464	2007, 2009 (Surgery, Radiation, Hormonal)

♦ MEETING ANNOUNCEMENT ♦

THURSDAY, NOVEMBER 3, 2016

7:00 - 8:30 PM

AMERICA BUILDING (BLDG 19, 2D FLOOR) ROOM 2525
(DIRECTLY ABOVE THE LAB/PHARMACY)

WALTER REED NATIONAL MILITARY MEDICAL CENTER

♦ SPEAKER ♦

CAMILLE McCANN WILLIAMS, MD

RADIATION ONCOLOGIST, WRNMMC

♦ TOPIC ♦

"RADIATION THERAPY TREATMENT OPTIONS FOR PROSTATE CANCER:

UNDERSTANDING THE BASICS"

Gate/Parking: If you enter the base through South Gate (Gate 2) off Rockville Pike/Wisconsin Avenue, take the first right (Palmer Road South). On your left will be the Emergency Room. Continue to follow signs to the America Building and the America parking garage.

Security: A military ID card is required to get on base. Persons without a military-related ID card who are attending the meeting are required to register in advance in order to gain entry. To register, contact the CPDR front desk at 301-319-2900 <u>at least four business days prior to Thursday, 2016, to arrange entry.</u> Have a photo ID card ready when arriving at the gate.