Brachytherapy Boost Tops Surgery for Prostate Cancer

Lower Disease-Specific Mortality in Those with Gleason 9-10 Tumors

Patients with a particularly aggressive form of prostate cancer treated with extremely dose-escalated external beam radiotherapy (EBRT) plus androgen deprivation therapy (ADT) achieved better clinical outcomes than those treated with radical prostatectomy (RP), a retrospective study indicated.

"EBRT plus brachytherapy was associated with significantly lower prostate cancer–specific mortality (PCSM) than either EBRT alone (cause-specific hazard ratio [HR] 0.41, P=0.002) or RP (HR 0.38, P=0.001), with a better adjusted five-year PCSM rate (3%) compared with EBRT alone (13%) or RP (12%)," reported Amar U. Kishan, MD, of the University of California Los Angeles, and colleagues in the Journal of the American Medical Association (JAMA Vol. 319, pp. 896-905, 2018).

EBRT plus brachytherapy also yielded better adjusted five-year incidence rates of distant metastasis (8%) compared with EBRT alone or RP (24% each), with a significantly lower rate of distant metastasis compared with EBRT alone (propensity-score-adjusted cause-specific HR 0.30, P<0.001) or RP (HR 0.27, P<0.001).

"I would present extremely dose-escalated RT as an option to all patients I see," Dr.

(Continued on page 4)

Imaging Agent Can Change Plans for Recurrent Prostate Cancer

When men with prostate cancer experience biochemical recurrence (BCR), the rise in levels of PSA suggests that the disease may have spread. This is distressing both for clinicians and patients, because it suggests that curative-intent primary therapy has not succeeded.

It also prompts immediate questions: What is the extent of local recurrence and metastases? And what should be done next therapeutically? At present, there is uncertainty as to how to address these issues, because when patients experience BCR, the PSA level rises, but there is no visual evidence of disease on conventional scans.

A new study shows that adding an imaging agent to the scans provides more information, and this has a "substantial impact" on clinical decisions for such patients. The imaging agent, 18F-fluciclovine, was used in conjunction with positron-emission tomography (PET)/CT scanning. The results from the new study, known as FALCON (Fluciclovine [18F] PET/CT in Biochemical Recurrence of Prostate Cancer), were presented at the Genitourinary Cancers Symposium (GUCS) 2018.

"For 52 of 85 men enrolled in the study (61%), clinical management was changed after 18F-fluciclovine PET/CT imaging," reported Eugene Jueren Teoh, MBBS, an oncologist at Oxford University Hospital in the United Kingdom. For some patients, management

(Continued on page 6)
No Definitive Link Found Between Physical Activity and Prostate Cancer

A large meta-analysis was unable to find a conclusive relationship between levels of physical activity and the risk of prostate cancer, though some suggestion of reduced risk was seen for occupational activity and for some specific cancer subtypes. There was also indication that physical activity after diagnosis of prostate cancer might have a protective effect.

“Knowledge about prostate cancer risk factors is limited, complicating the formulation of appropriate strategies for the prevention of prostate cancer,” wrote study authors led by Daniela Schmid, MSc, of the University of Regensburg in Germany. “The role of potential modifiable risk factors for the development of prostate cancer such as obesity, smoking, poor diet, and physical activity is less well understood.”

The authors conducted a meta-analysis and review of studies of physical activity and prostate cancer, including 48 cohort studies and 24 case-control studies incorporating a total of 151,748 cases of prostate cancer. The mean age of the participants at baseline was 61 years. Results were published in the *Annals of Oncology*.

The primary analysis relating physical activity to prostate cancer revealed an association that was close to null, with a relative risk (RR) of 0.99 (95% Confidence Interval [CI], 0.94-1.04) comparing the highest and lowest categories of activity. The same held true when case-control and the cohort studies were examined separately.

They then stratified by the domain of physical activity, and found a significant inverse association between long-term occupational activity and total prostate cancer incidence, with an RR of 0.83 (95% CI, 0.71-0.98) and a borderline association with short-term occupational physical activity with an RR of 0.85 (95% CI, 0.72-1.00). However, the long-term significant RR did not remain so after removal of individual studies from the analysis.

When stratifying by both type of physical activity and subtypes of prostate cancer, further associations were seen. However, inverse associations between long-term recreational physical activity and prostate cancer were only seen with two studies. There was no association seen between pre-diagnosis physical activity and death due to prostate cancer. However, there was an inverse association between physical activity after diagnosis and prostate cancer mortality among survivors, with an RR of 0.69 (95% CI, 0.55-0.85), based on four studies.

“These associations may represent an indication for a potential protective effect of long-term activity on prostate cancer incidence,” the authors wrote. “However, our findings must be interpreted with caution.” The analysis’s sensitivity to removal of individual studies, and the small number of studies that revealed some of the significant results, make interpretation difficult.

“Despite a growing body of literature on physical activity and prostate cancer incidence, evidence for a link between overall physical activity and risk of prostate cancer remains elusive.”

*Cancer Network*  
1 March 2018

Novel PET Imaging Agent Detects Prostate Cancer Recurrence Early

**Targets Copper Accumulation in Tumors**

An Italian study featured in the March issue of *The Journal of Nuclear Medicine* (Vol. 59, pp. 444-451, 2018) demonstrates that a novel nuclear medicine imaging agent targeting copper accumulation in tumors can detect prostate cancer (PCa) recurrence early in patients with biochemical relapse (BCR, i.e., a rising PSA).

Copper tends to be more concentrated in tumors, making it a good imaging biomarker. For this study of 50 patients, researchers conducted PET/CT scans comparing the new imaging agent, copper-64 chloride (64CuCl2), with fluorine-18-choline (18F-Choline). Multi-parametric magnetic resonance imaging (mpMRI) was also conducted. In addition to calculating the detection rate of each imaging modality, the biodistribution, kinetics of the lesions and radionuclide dosimetry of 64CuCl2 were evaluated.

“This is the first time this novel agent has been compared with 18F-Choline-PET/CT in a considerable number of PCa patients with BCR,” explains Arnoldo Piccardo, of E.O. Ospedali Galliera in Genoa, Italy. He points out, “Early detection of PCa relapse may improve the clinical management of patients, for example implementing early salvage radiotherapy.”

The effective dose of 64CuCl2 was determined to be 5.7 mSv, similar to those of other established PET tracers (although higher than for 18F-Choline, which is 4 mSv).

(Continued on page 5)
Doc Moyad’s What Works & What is Worthless Column – Also Known as “No Bogus Science” Column

“Low-Fat vs. Low-Carb, & the Winner is You & Your Wallet!”

Mark A. Moyad, MD, MPH, University of Michigan Medical Center, Department of Urology

Editor’s Note: Us TOO invites certain physicians and others to provide information and commentary for the Hot SHEET to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

After one year, weight loss was similar with a low-fat or low-carb diet regardless of genetic and personal differences between subjects, so is it probably time to pick a cheap diet that fits your personality and basic (not technical) medical profile?

Diet battles are getting boring. But at least with more and more research we are learning that there is really little to no difference from one fad diet to the other, primarily when it comes to the amount of weight-loss over time. Additionally, many study subjects in longer-term dietary clinical trials actually end up eventually moving toward moderation anyway by ignoring the strict rules of the diet they are being asked to adhere to over a year or two. And we are also learning that, apart from weight-loss, there are at least some unappreciated basic measurement differences with certain diets that should be discussed because it might sway the decision about what diet you should try this year.

So, along comes this wonderful Stanford University (you know the university that used to have Harbaugh as their coach) study of 609 overweight adults, and cutting to the chase (I just made up that saying) both groups lost approximately 12 pounds over the one-year diet that they were placed in.¹ Not bad! Yet, these researchers thought that certain genotypes (genetics) and personal insulin levels might help some do better on low-fat (lower insulin levels) or low-carb (those with higher insulin resistance). In other words, perhaps researchers can personalize a diet based on genetic tests! Not yet (aka “nope”)! That did not happen! What did happen was a reminder that when going low-fat (like past Dr. Ornish research) one can see a large drop in LDL (“bad cholesterol”) similar to some low-to-moderate dose statin drugs! Yeah! And, when going low-carb one can see a large drop in triglycerides (fat in the blood) and an increase in HDL (“good cholesterol”) as good as and safer than many medications/supplements. Yeah again! And, this is exactly what happened in this current clinical trial!

So if I want my LDL to drop I should consider a low-fat diet, and if I want my triglycerides to drop and HDL to increase then I should consider low-carb (with other factors of course). Ultimately, the major goal is to lose weight with a diet that is the right fit for the individual’s personality. Heck I like reruns of Star Trek and Star Wars, but we are not yet living in that kind of diet future. I wish expensive personalized or even moderately priced genetic testing could be matched with a diet.

So, in the meantime, you still need to follow the dietary basics in general to lose weight/waist, which means “consume less to lose more” (Moyad Circa 1998 to 2018). BORING? Yes, but cost-effective – “diet cheap baby” just how I like it!!

Reference:

Single Screening PSA Test Fails to Reduce Deaths (Continued from page 1)

Localized disease (stage T1 or T2 cancer) was diagnosed at a more frequent rate in the screened (2.6%) vs. control group (1.9%); in turn, fewer cases of advanced-stage cancer were diagnosed in this group (0.5% vs. 0.6% in the control group).

In the all-cause mortality analysis, 25,459 men died in the intervention group compared with 28,306 in the control group for a RR of 0.99 (P=0.49). Of the 549 men who died of prostate cancer in the screening group, only 188 had visited the clinic for PSA testing. Lethal cancer was diagnosed in 59 of 188. Of the remaining 129 men:

- Four men had a benign biopsy.

Screening for prostate cancer using PSA tests remains controversial, as the potential benefits of disease detection in its early stages can be outweighed by harms from overtreatment.

In 2012, the U.S. Preventive Services Task Force (USPSTF) recommended against routine PSA screening for men of any age, but in 2017 adjusted this recommendation and now support an individualized approach to screening for men ages 55 to 69.

“It has been hypothesized that screening men in their early 50s may be more effective than at a later age,” the authors wrote. “However, we did not find statistical evidence to support this.”

In terms of adherence to screening, 75,707 (40%) of 189,386 men assigned to the intervention arm attended the clinic for PSA testing; 67,313 of these men underwent PSA testing. High PSA levels – 3.0 ng/mL to 19.9 ng/mL – were detected in 6,857 patients and 5,850 underwent a biopsy.

In an accompanying editorial Michael J. Barry, MD of Harvard Medical School and Massachusetts General Hospital wrote: “A key question is whether the findings from the CAP trial should swing the pendulum further in the direction of not offering screening PSA tests. Based on these results, an offer of a single PSA screen in a population of men aged 50 to 69 years is ineffective, and given the higher risk of a prostate cancer diagnosis this approach engenders, likely does more harm than good.”

Barry, who is a member of the USPSTF, added that while further follow-up from CAP could potentially reveal benefit, based on the evidence so far “that eventualty seems unlikely.”

MedPage Today
6 March 2018
Kishan told MedPage Today, “The data, albeit retrospectively, are compelling.”

This cohort study included 1,809 men with Gleason score 9-10 prostate cancer treated from 2000 to 2013 at 12 tertiary centers. Patients were grouped into three cohorts based on definitive therapy received: extreme dose escalation of EBRT plus a brachytherapy boost (n=436; median age 67.5), EBRT alone (n=734; median age 67.7), or RP (n=639; median age, 61). PCSM was the primary endpoint.

ADT is generally recommended among men receiving EBRT, but may be contra-indicated for medical reasons — men who did not receive ADT were not excluded.

Adjusted 7.5-year all-cause mortality rates were 10% with EBRT plus brachytherapy, 18% with EBRT alone, and 17% with RP. By 7.5 years of follow-up, EBRT plus brachytherapy was associated with significantly lower all-cause mortality compared with EBRT alone (cause-specific HR 0.61, P=0.002) and RP (HR 0.66, P=0.03). But these differences did not remain statistically significant beyond 7.5 years.

Use of EBRT plus brachytherapy declined over the years among the men studied, mostly in favor of RP. From 2000 to 2005, 31% of men received EBRT plus brachytherapy. This dropped to 25% from 2006 to 2010 and to 15% from 2011 to 2013. During these same years, frequency of RP use rose from 24% to 53%.

“I would also stress that, should patients move forward with standard RT, they consider the importance of receiving at least high-dose RT, along with a long duration of ADT,” said Kishan, noting that outcomes were better in the subgroup that received ADT.

“For patients receiving RP, early postoperative RT (potentially with ADT at that point), may be superior to just RP,” he said. “I think the important theme is that many patients with Gleason score 9-10 disease need a multimodality strategy that includes both intense local treatment and some form of systemic treatment.”

Some of the limitations of the study include its retrospective nature, though a randomized trial in this population would likely not be feasible due to the relative rarity of the disease, according the authors — only 7% to 10% of prostate cancer cases are Gleason score 9-10 on biopsy. Due to the aggressive nature of this disease, however, this comparative outcomes analysis was able to achieve statistical power within a contemporary treatment period.

Patient-reported outcomes or toxicity profiles by treatment type were not available for the researchers to analyze. In the ASCENDE-RT trial, EBRT plus brachytherapy resulted in poorer urinary and physical function as reported by patients compared with EBRT alone. “This is an important point,” said Kishan. “Extremely dose-escalated RT may not be appropriate for patients with severe urinary symptoms, very large prostates or high-risk of bleeding that could make the brachytherapy procedure difficult.”

Other limitations of the study were a short median follow-up time, not all centers providing data on the three treatment modalities, and only 41% of EBRT-treated patients receiving both RT doses of 70 Gy or greater and ADT for a duration of two years or longer — suggesting a tolerance issue with the combination.

MedPage Today
6 March 2018

New Resources Address Anxiety, Depression and Prostate Cancer

Many men who are diagnosed with prostate cancer, or are managing the disease, experience some level of anxiety and/or depression. Caregivers may also be affected. The psychosocial challenges surrounding treatment choices and side effect management can have a negative impact on the prostate cancer journey. Anxiety and depression aren’t always effectively treated, in part because the symptoms may not be recognized.

We encourage you to visit the new Us TOO web page for information on recognizing and managing anxiety, depression and prostate cancer.

www.ustoo.org/anxiety-and-depression

Current PSA Monitoring Ignores Risk to Some Prostate Cancer Survivors

Researchers Hope Their Study will Encourage New Guidelines That Take a More Patient-Focused Approach to Monitoring

Prostate cancer survivors make up the largest group (41 percent) of male cancer survivors. In these survivors, early detection of recurrence can lead to life-saving interventions; but in older men who survived low-risk cancer and have limited life expectancy, those same interventions may do more harm than good.

However, when UC San Francisco researchers analyzed current monitoring practices, they found that doctors use a one-size-fits-all approach to monitoring—performing the same frequency of testing regardless of a survivor’s health and prognosis. In a new study, the researchers recommend that doctors individually tailor how often older prostate cancer survivors who have undergone curative treatment are monitored for disease recurrence.

“This is the first study suggesting a need for guidelines to encourage prostate-specific antigen (PSA) monitoring that considers life expectancy, risk of recurrence, and the values and preferences of cancer survivors rather than a one-size-fits-all approach,” said senior author Louise Walter, MD, chief of the UCSF Division of Geriatrics and geriatrician at the affiliated San Francisco VA Health Care System. The study was published online 8 February 2018, in the Journal of General Internal Medicine.

After surgery or radiation, some data suggest the interventions given just after early detection of recurrence based on elevated PSA levels may improve survival. But PSA monitoring may lead to complications from invasive diagnostics or treatment and surrounding treatment choices and side effect management can have a negative impact on the prostate cancer journey. Anxiety and depression aren’t always effectively treated, in part because the symptoms may not be recognized.

We encourage you to visit the new Us TOO web page for information on recognizing and managing anxiety, depression and prostate cancer.

www.ustoo.org/anxiety-and-depression

Brachytherapy Boost Tops Surgery (Continued from page 1)
Liquid Biopsies Not Ready for Prime Time
Not Enough Evidence, Too Many Questions, Panel Concludes

“Not ready for prime time” might best describe the current state of liquid biopsies in oncology, according to a review by a panel of oncology and pathology experts. Too little evidence has emerged to say with any certainty whether most tests that measure circulating tumor (ct) DNA should be used outside the setting of a clinical trial. Too many questions remain about the accuracy, reliability, and reproducibility of the tests.

“There is not enough evidence, at this time, to support the routine use of ctDNA tests for early-stage cancer, making treatment decisions, monitoring how well a treatment is working, finding remaining cancer cells, or for cancer screening, except screening for participation in, or during, a clinical trial,” according to a statement from the American Society of Clinical Oncology (ASCO) and the College of American Pathologists (CAP).

The finding came from a review of literature and data by a panel representing the two organizations – the Journal of Clinical Oncology and Archives of Pathology and Laboratory Medicine.

“Like all new things in medicine, the use of ctDNA assays in routine cancer care requires evidence of clinical utility,” panelist Daniel F. Hayes, MD, immediate past president of ASCO, said in the statement. “At present, there is insufficient evidence of clinical validity and utility for the majority of ctDNA assays in advanced cancer, including those that interrogate a panel of genes.”

Beginning with the publication of early results, liquid biopsies have attracted widespread attention in professional and consumer media. To date, only the COBAS blood test to detect Epidermal Growth Factor Receptor (EGFR) mutations associated with non-small cell lung cancer has received FDA approval. However, multiple types of tests have been developed and made available for use in clinical practice.

“This is an area of great interest to both pathologists and oncologists,” said panel co-chair Jason D. Merker, MD, PhD, representing CAP. “It’s also an area where we see a lot of commercial advertisement, and a lot of enthusiasm from the public. We thought it was a good time to look at the literature and take an evidence-based approach to various uses for ctDNA assays.”

The review encompassed 77 articles published from January 2007 to March 2017. The panel limited the review to analyses of sequence and gene copy number variants in ctDNA associated with solid tumors.

Aside from finding insufficient evidence to support widespread clinical use of liquid biopsies in general, the review showed inconsistency between results with liquid biopsies and pathological findings obtained from tumor specimens. Lack of consistency between different tests was borne out in a recent independent comparison of two commercially available liquid biopsies for evaluation of patients with prostate cancer.

A Double-Blind, Randomized Trial on the Efficacy and Safety of Hyperbaric Oxygenation Therapy in the Preservation of Erectile Function After Radical Prostatectomy

Chiles KA, Staff I, Johnson-Arbor K, et al.
J Urol 199: 805-811, 2018

Purpose: We evaluated the efficacy and safety of hyperbaric oxygenation therapy to preserve erectile function (EF) as part of penile rehabilitation after robot assisted bilateral nerve sparing radical prostatectomy (RABNSRP) for prostate cancer.

Materials and Methods: We performed a prospective, randomized, double-blind study from January 2009 to April 2013. Men 40 to 65 years old who underwent RABNSRP were randomized 1:1 to the control or the treatment group. Participants were exposed to air as the control or to 100% oxygen as the treatment in hyperbaric conditions. Primary outcome was EF at 18 months as measured by IIEF (International Index of Erectile Function). Secondary outcomes were 12-month urinary symptoms, and 18-month sexual, urinary, bowel and hormonal-related symptoms as measured by EPIC-26 (Expanded Prostate Index Composite-26). Adverse events and long-term cancer outcomes were monitored. Primary and secondary outcomes in the groups were compared by the independent group t-test, the Wilcoxon rank sum test and the chi-square test of proportion.

Results: A total of 109 potent men were randomized to hyperbaric therapy or the control group. A total of 43 men in the air group and 40 in the hyperbaric oxygenation therapy group completed the 18-month follow-up. No statistically significant differences were observed between the two groups on any outcome measure.

Conclusions: This study revealed no difference in erectile recovery in men treated with hyperbaric oxygenation therapy vs. placebo. Larger studies involving more diverse comorbidities and different hyperbaric oxygenation therapy regimens are needed to further evaluate the usefulness of hyperbaric oxygenation therapy for penile rehabilitation after RP.
Imaging Agent Can Change Plans for Recurrent Prostate Cancer (Continued from page 1)

was changed to “provide a better chance at cure or to avoid possibly futile salvage therapy,” Teoh told the audience. He also pointed out that 18F-fluciclovine is a synthetic amino acid that is taken up by amino acid transporters that are “massively” upregulated in many cancers, including prostate cancer.

“It is already approved in the US and the European Union for PET/CT imaging in cases of biochemical recurrence of prostate cancer. In the US, costs are reimbursed by insurance through the Centers for Medicare & Medicaid Services,” Teoh said.

Sumanta Pal, MD, a urologic oncologist from the City of Hope Cancer Center in Duarte, CA, said the rate of management change in the study was thought provoking. “I think 60% is awfully impressive. If I had any other diagnostic test that changed my management more than half of the time, I would definitely implement it,” said Pal, who was asked for comment. He also placed the results in the context of currently used technology. “We realize that many patients with localized disease [and rising PSA levels] may actually have brewing metastasis. But we just don’t have the technology with current modalities, such as CT scans and technetium bone scans, to detect these areas of disease spread,” said Pal.

Study Details
In the FALCON study, the investigators recorded the intended management plan for patients being considered for radical salvage treatment after the patients experienced initial BCR; the investigators subsequently recorded newly recommended plans following scanning with 18F-fluciclovine. “The primary objective was assessment of the clinical impact of the scanning agent on patient management. Post-scan changes to treatment modality, such as a change from salvage radiotherapy (RT) to systemic therapy, were classified as ‘major,’ changes within a modality (e.g., modified RT fields) were classified as ‘other,’” said Teoh.

Of the 52 men for whom changes in management were made, 31 underwent a major change (for 18 men, planned salvage treatment was changed to systemic non-curative therapy; for 13 men, planned salvage treatment was changed to watchful waiting). For 21 men, management changes were classified as “other” (planned RT was modified to include a boost to a positive lesion or a widening of the field to include the whole pelvis).

For the 85 enrolled patients, the mean period following initial diagnosis was 4.8 years; the patients’ median age was 67 years. Most (56; 65.9%) had previously undergone radical prostatectomy (RP), and 27 had received RT (± other therapy). For 12 men (14.1%), the Gleason score was ≤6; for 60 (70.6%), the score was 7; and for 13 (15.3%), the score was ≥8. Notably, the median PSA level among the men was 0.63 ng/mL. That median PSA level worried a clinician in the GU CSC audience.

Daniel Lin, MD, a urologist at the University of Washington in Seattle, said, “I would put someone forward for salvage RT much before PSA got to 0.6.” Lin wondered whether waiting for disease spread to show up on a scan, even with highly sensitive 18F-fluciclovine PET/CT imaging, might result in “missing the window for cure.”

“In the study, not all the scans were positive. Among men who had already undergone prostatectomy and whose PSA level was <0.5 ng/mL, there was a 25% detection rate upon scanning. That would have triggered salvage RT at my institution at Oxford,” Teoh said. “In addition, it was a multicenter study, and ‘hypersensitive’ PSA tests were ‘heterogeneously’ used in the study,” Teoh noted in explaining the relatively high trigger point for progressing to salvage RT.

“There is a need for ‘robust’ criteria for employing 18F-fluciclovine scanning,” Teoh admitted. “It’s not for everyone,” he commented. “But I do believe there will be a subset [of patients], particularly post-prostatectomy, who will benefit.”

Teoh also said there is no cutoff PSA value with regard to not performing the scan. “I would scan patients with a fast doubling time whose PSA level was ≥0.1 ng/mL,” he said. The inclusion criteria for the study was a PSA level >0.1 and a doubling time <15 months or a PSA >1.0 ng/mL, regardless of doubling time. “Enrollment in the UK trial was stopped after this interim analysis with 85 patients,” said Teoh, “because of ‘overwhelming efficacy.’” More research is needed. Currently, follow-up is underway to assess whether men in the current study experienced clinically-related outcomes – PSA dropping/stabilizing or increasing – after 18F-fluciclovine scanning. Teoh said, “Long-term studies are needed to determine the impact of this tool on disease outcomes.”

“18F-fluciclovine is well established as a diagnostic tool for detecting sites of recurrent prostate cancer,” he added. However, a member of the Dana Farber Cancer Institute in Boston, MA, who attended GU CSC, told Medscape Medical News that the cutting-edge center had added 18F-fluciclovine scanning only in the past six months.

Pal was under the impression that the technology was still mostly limited to use in major academic centers. “If we continue to see compelling trends like these – namely, fluciclovine changing patient management upwards of 60% of the time – we may see greater clinical implementation,” he added. “This modality can be used in the confines of most existing radiology practices.”

“This is an important step for this imaging agent,” he suggested. “Assessing the rate of change in management is really key, as opposed to simply identifying the additional sites of metastases that you can pick up with fluciclovine above and beyond standard modalities.”


Medscape Medical News
13 February 2018
Doctor Chodak’s Bottom Line
Gerald Chodak, MD, Author, Winning the Battle Against Prostate Cancer, Second Edition
http://www.prostatevideos.com/

Editor’s Note: Us TOO has invited certain physicians and others to provide information and commentary for the Hot SHEET to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

P1, “Single PSA Test Fails…”
Well, here we go again. In the largest randomized prostate screening study ever done involving over 400,000 men, a British study found no difference in survival at ten years following a single PSA screening test. In fact, the study found more low-risk Gleason 6 cancers in the men screened vs. the control group, so there is the potential for doing more harm by treating men who might not have needed it. But, before thinking the PSA screening controversy is over, let’s look more closely at this particular study to see if there are any problems that may have influenced the findings. There are two issues that clearly stand out:

First, among the men assigned to the screening group, less than one-third actually had the test done. Second, only 85% of the men who were advised to have a biopsy based on their PSA result actually had it done. These two problems could invalidate the conclusions UNLESS we know more details about the men in the screened group who died of their disease. For instance:

- If a significant percentage of the deaths occurred in men who did not adhere to the screening or biopsy recommendation, then a significant bias could have occurred in favor of the control group.
- But, if those men who died of prostate cancer had indeed been screened and biopsied appropriately, then the conclusion would remain valid.

So it would seem that more information is needed and it may be in the full paper, which I did not review. However, even if it turns out that the study is entirely valid, it does not prove that screening should be abandoned. All it would prove is that doing a single PSA screening test may do more harm than good whereas doing repeat exams may offer a greater chance for benefit, even if that benefit is quite small. Also, as more years go by, these results could still change.

The Bottom Line: A one-time screening test may do more harm than good but further analysis is needed and longer follow-up could change the results.

P1, “Brachytherapy Boost…”
Are we getting a better idea how to treat aggressive, localized prostate cancer? Data from a study by Kishan and co-workers addresses this clinical scenario and is certainly interesting. They conducted a retrospective analysis of over 1,800 men with Gleason 9 or 10 cancers who were treated either by radical prostatectomy (RP), radiotherapy (RT) or RT plus brachytherapy boost. The authors found better cancer-specific survival, lower mortality and delayed time to metastases with the combined therapy compared to external RT or RP. Although not randomized, the results are certainly interesting. But, as with all non-randomized studies, we must be cautious about the interpretation. Questions needing answers are the following: It appears that no central review was conducted for the pathology specimens so it is entirely possible that some of the cancers may have been overgraded, which potentially could have biased the findings. A second and extremely important question is how androgen deprivation treatment was administered to the men treated with RT, particularly in the group that did not have a brachytherapy boost. Randomized studies of high-risk prostate cancer, including T3 disease showed that at least 18 months of ADT is appropriate. Since the study was not randomized, the dose of ADT is likely to have varied considerably, and this too could have created a bias. It would be interesting to find out more about these two issues. Despite the fact that the study results are encouraging, they do not provide definitive proof that adding the brachytherapy boost is the best approach. A randomized study would provide data that could be discussed with patients.

The Bottom Line: External beam RT with a brachytherapy boost plus ADT may offer the best survival, but further analysis or, ideally, a randomized study is needed.

P1, “Imaging Agent Can…”
An important change is occurring in the management of a rising PSA after local therapy. Whereas doctors have previously relied upon the results of the bone scan and CAT scan, those two tests are not very reliable at low PSA levels. PET scanning with various agents is proving to be more sensitive in detecting disease for detecting.

(Continued on page 8)

Inclusion for Prostate Cancer Trials Inadvertently Excludes Blacks
Almost half of clinical trials for prostate cancer use criteria that disproportionately exclude black men, according to a research letter published online in JAMA Oncology.

Noting that clinical trial eligibility criteria may disproportionately prevent black patients from participating due to racial variations in laboratory values, Marie E. Vastola, from the Dana-Farber/Brigham and Women’s Health Cancer Center and Harvard Medical School in Boston, and colleagues examined clinical trials in prostate cancer. Trial characteristics were compared for 401 interventional prostate cancer clinical trials with an end point of overall survival.

The researchers found that 47.9% of these trial used serum creatinine (sCr) alone instead of race-adjusted measurements for renal function and/or required participants to have an absolute neutrophil count (ANC) of 1.5 × 10⁹ cells/L or higher, which excludes men with benign ethnic neutropenia. Trials sponsored by academic investigators or cooperative groups versus industry more often used sCr alone and/or an ANC cut-off level of 1.5 × 10⁹ cells/L or higher. These trials were also more often phase 1 or 2 versus phase 3, had lower accrual, or had at least one treatment arm that was considered high toxicity.

“While adopting race-based differences in trial criteria may add slight logistical challenges when ensuring that patients meet trial eligibility, these adjustments would prevent healthy individuals from being excluded solely because of race-related benign laboratory differences.”

Renal & Urology News
13 February 2018
Current PSA Monitoring (Continued from page 4)

may even be unnecessary in older men with a history of low-risk cancer or limited life expectancy.

In the study, Walter and her colleagues examined the national VA and Medicare data of 13,397 men age 65 or older diagnosed with prostate cancer between 1 January 2003 and 31 December 2008, and treated with radiation or radical prostatectomy. All participants were followed for four years after their one-year treatment anniversary date.

Men with limited life expectancy treated for low-risk cancer are least likely to experience disease recurrence in their lifetime, making them the most likely to experience harms of PSA monitoring without benefit. However, these men received only marginally fewer PSA tests per year compared to men with longer life expectancy treated for high-risk cancer, the group most likely to benefit from monitoring. The researchers note that the most consistent predictor of monitoring frequency was time since treatment, slightly decreasing every year, rather than any patient characteristic. “The narrow range of PSA monitoring frequencies across patient and tumor characteristics indicates little individualization in how clinicians currently monitor for prostate cancer recurrence in older men,” Walter said.

Most of the men received approximately two PSA tests per year – consistent with current guidelines. The researchers hope their study will encourage new guidelines that take a more patient-focused approach to monitoring for prostate cancer recurrence.

University of San Francisco (UCSF) News Center
12 February 2018

Liquid Biopsies (Continued from page 5)

“There is very significant potential for many different applications of ctDNA tests in the future,” said Merker. “However, we need to make sure clinical trials are done to develop the body of evidence needed to support these applications in various tumor types.”

ASCO and CAP will continue to monitor the evolution of liquid biopsies and the accumulation of associated evidence, including evidence from clinical use of the tests. The organizations pledged to develop recommendations for use of the tests when sufficient evidence exists to support formal clinical statements or guidance.

“What is promising is that this area of research is rapidly evolving, so there should be enough evidence soon to formulate evidence-based guidance for a variety of clinical scenarios,” said Hayes.

The Bottom Line: PET scans are becoming the new standard of care to evaluate men with a rising PSA after local therapy.

The new Us TOO call-in caregiver support group, A Forum for Her, was established for the women behind the men affected by prostate cancer. To register for upcoming calls, email terril@ustoo.org or call 877-978-7866.

The Bottom Line (Continued from page 7)

US TOO INTERNATIONAL PROSTATE CANCER EDUCATION & SUPPORT

US TOO INTERNATIONAL, 2720 S. RIVER ROAD, SUITE 112, DES PLAINES, IL 60018