Elective Node Radiation Appears More Effective for Nodal Recurrent Prostate Cancer

Elective nodal radiotherapy (ENRT) appears to reduce relapses better than stereotactic body radiotherapy (SBRT) in men with nodal oligorecurrent prostate cancer, according to a retrospective analysis. But ENRT is also more toxic, researchers reported online 19 July 2019 in the journal *European Urology*.

Following local therapy of prostate cancer, the most dominant sites of recurrence are lymph nodes, which can be targeted with focal SBRT or more comprehensively with ENRT. It remains unclear which of the treatments is better.

Dr. Elise De Bleser from Ghent University Hospital, in Belgium, and colleagues from 15 different centers reviewed differences in toxicity and efficacy between 309 men receiving SBRT and 197 receiving ENRT for oligorecurrent nodal prostate cancer.

The three-year metastasis-free survival (MFS) was 68% after SBRT and 77% after ENRT (P = 0.01). In multivariable analysis, ENRT resulted in significantly longer MFS than SBRT among men presenting with only one node, but not with more than one node at recurrence. Local progression was seen in 50 men following SBRT vs. only nine men following ENRT (P =0.001).

The three-year castration-resistant prostate cancer (CRPC)-free survival did not differ significantly between the treatment groups. During a median of 34 months of follow-up, 419 men remained free of CRPC.

There was no early or late grade-3-or-higer toxicity following SBRT, but there were five such events following ENRT. Early toxicity was significantly greater following ENRT (three cases of late toxicity was significantly greater following ENRT (three cases (Continued on page 8))
Validity of the Patient-Reported Outcome Measurement Information System (PROMIS) Sexual Interest and Satisfaction Measures in Men Following Radical Prostatectomy

Agochukwu NQ, Wittmann D, Boileau NR, et al.

J Clin Oncol 10 August 2019; Epub

Purpose: Patient-reported outcomes after radical prostatectomy (RP) have focused on erectile function (EF). To date, no studies have validated the Patient-Reported Outcome Measurement Information System (PROMIS) Sexual Interest and Satisfaction single item measures in patients with prostate cancer (PCa), nor have studies examined how these measures relate to EF. In addition, data are lacking with regard to the clinical responsiveness of these measures to treatment. We sought to validate and examine the clinical utility of these measures in men after RP.

Patients and Methods: We identified men who underwent a robotic RP from May 2014 to January 2016 in the Michigan Urological Surgery Improvement Collaborative. A single item from the PROMIS Global Satisfaction with Sex Life subdomain and a single item from the PROMIS Interest in Sexual Activity subdomain were administered. EF was also assessed. Differences between baseline and 24-month T-scores for both PROMIS interest and satisfaction were examined. Multilevel models examined change over time.

Results: A total of 1,604 men were included in the analysis. Convergent and discriminant validity of the PROMIS measures was supported. The mean PROMIS interest T-score decreased significantly from baseline to three months (P = 0.001) and significantly increased from three to 24 months in this cohort, with 24-month scores exceeding baseline scores (P < 0.001). The mean PROMIS satisfaction T-score declined from baseline to three months and increased from three to 24 months (P < 0.002).

Conclusion: PROMIS Global Satisfaction with Sex Life and Interest in Sexual Activity single-item measures are fundamental measures in PCa survivorship. Patients are interested in sex despite functional losses and can salvage satisfaction, thereby giving insight into attainable patient-centered survivorship goals for sexual recovery after RP.

Treatment-Related Toxicity Using Prostate Only Versus Prostate and Pelvic Lymph Node Intensity Modulated Radiation Therapy: A National Population-Based Study

Parry MG, Sujenthiran A, Cowling TE, et al.

J Clin Oncol 20 July 2019; Epub

Purpose: The effectiveness and toxicity of pelvic lymph node (PLN) radiotherapy (RT) for men with high-risk prostate cancer (PCa) is debatable. This study compared the toxicity of intensity-modulated RT (IMRT) to the prostate and the pelvic lymph nodes (PPLN-IMRT) with prostate-only IMRT (PO-IMRT).

Materials and Methods: Men with high-risk localized or locally advanced PCa treated with IMRT in the English National Health Service between 2010 and 2013 were identified by using data from the Cancer Registry, the National Radiotherapy Dataset, and Hospital Episode Statistics, an administrative database of all hospital admissions. Follow-up was available up to December 31, 2015. Validated indicators were used to identify patients with severe toxicity according to the presence of both a procedure code and diagnostic code in patient Hospital Episode Statistics records. A competing risks regression analysis, with adjustment for patient and tumor characteristics, estimated subdistribution hazard ratios (sHRs) by comparing GI and genitourinary (GU) complications for PPLN-IMRT versus PO-IMRT.

Results: Three-year cumulative incidence in the PPLN-IMRT (N = 780) and PO-IMRT (N = 3,065) groups was 14% for both groups for GI toxicity, and 9% and 8% for GU toxicity, respectively. Men receiving PPLN-IMRT and PO-IMRT had similar levels of severe GI (adjusted sHR, 1.00; 95% CI, 0.80 to 1.24; P = 0.97) and GU (adjusted sHR, 1.10; 95% CI, 0.83 to 1.46; P = 0.50) toxicity rates.

Conclusion: Including PLNs in radiation fields for high-risk or locally advanced PCa is not associated with increased GI or GU toxicity at three years. Additional follow-up is required to answer questions about its impact on late GU toxicity. Results from ongoing trials will provide insight into the antiserum effectiveness of PLN irradiation.
Doc Moyad’s What Works & What is Worthless Column — Also Known as “No Bogus Science” Column

“Boring B12 Testing & Vacuuming – Part 1?”

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.

Over 33 years I have witnessed the incredible verve for some companies and experts to come up with the ultimate nutritional blood test(s) for the general population (and cancer patients of course). Many of them were not cheap and most failed. I remember long ago when the beta-carotene blood test was exciting and then it turned out to not be that great. Next up, the selenium test and then nothing really happened. Lycopene? Sounds good, but offering it to the general population — Nope! And now there is the vitamin D test! Almost everyone is on that blood test bandwagon despite losing a few wheels along the way. Since it is Prostate Cancer Awareness Month I wanted, once again, to celebrate another unsung hero. I learned long ago that minimal money makers, or the really boring stuff, are precisely the kind of things we should really focus on when it comes to lifestyle changes (aka Moyad World). My point is the vitamin B12 blood test has been around as long as I have been around, and it has never been more important. Age, alcohol exposure, acid reflux drugs (OTC and Rx), metformin, some autoimmune diseases, some surgeries, etc. can cause B12 to drop to dangerously low levels!

This is not a good thing since B12 is responsible for so many functions from head (memory/cognition), to tippy toes (nerve function), and even to healthy blood cells (preventing a form of anemia). Furthermore, plant-based diets (especially vegans and vegetarians) are more popular than ever before (yeah!), but they tend to contain minimal-to-no B12 (unless fortified), and now there is new research suggesting that even weight gain could lower B12 levels in the body. Yikes (aka sad face emoji)! Ergo {in other words}, now you arguably have one of the most important and cheapest nutritional blood tests ever invented.

Please keep in mind that if your B12 appears low there are other supportive blood tests your doctor can run to determine the significance of this result. Best of all, even if you need to take a B12 pill because of a deficiency not solved by dietary/lifestyle changes, then they are some of the cheapest supplements ever invented! Yeah! Again, all this stuff will not cost you many clams (by the way clams are a good dietary source of B12).

Stay tuned! In the October 2019 issue of the Us TOO HotSHEET we will cover Part 2, vacuuming or the other unsung hero in my world! Oh, this is going to be great!

Reference:

DRE is Still a Prognostic Tool for Prostate Cancer (Continued from page 1)

all of my patients,” said study senior author William Hall, MD, also from the Medical College of Wisconsin, in an interview with Medscape Medical News. These findings reaffirm that PCa clinicians should be using DRE.

“At New York University in New York City, all urologists perform a DRE during initial patient visits,” said William Huang, MD, who was asked for comment. “In men with biopsy-proven PCa, the ability to palpate a tumor with a finger provides an inexpensive prognostic tool,” he stated. The study authors point out that tumor (T) stage, established via DRE, is part of the NCCN risk stratification system for PCa patients.

“However, DRE is not high on the list of such tools, which include PSA, Gleason grade, MRI, and genomic tests,” said Huang. Dr. Hall added, “But, anecdotally, clinicians are moving away from the inexpensive physical exam (i.e., DRE) and into more expensive high-tech tools to establish prognosis.”

NYU’s Huang also observed that, as a screening test, DRE has seen a drop in utilization as other more effective methods have emerged. Borkenhagen and colleagues also acknowledge the obvious: DRE is “invasive and undesirable” to many men. For their study, investigators identified a subset of 5,291 men in the National Cancer Database with high-risk clinical T2N0M0 PCa treated with external-beam radiotherapy (RT) and androgen deprivation therapies (ADT), with or without surgery in the latter part of the 2000s. High-risk was defined as having any of the following clinical factors at diagnosis: Gleason score >7, PSA >20 ng/mL or clinical stage T3a–T4.

As expected, this group also had a high percentage of men with ct2 disease, which is determined by physical exam (i.e., DRE). Hall explained that all of these men have organ-confined disease but are subclassified via DRE as ct2a, ct2b, and ct2c, based on the extent and location of their tumors, as detected by examination. At a median follow-up of 5.4 years, the proportion of deaths in each subclass were 22.5% for ct2a, 25.7% for ct2b, and 29.8% for ct2c. In multivariate analysis, the ct2a, ct2b, and ct2c subclassifications had prognostic significance, with increasing hazard ratios (HR) for death. Specifically, the values were 1.00 (reference) for ct2a; 1.25 for ct2b (P = 0.0046); and 1.43 for ct2c (P < 0.0001). The findings were independent of other known prognostic variables such as age and insurance type.

Given that DRE is such a subjective test, Hall was pleasantly surprised that the overall survival differences between the subclassification groups were spread out incrementally, as might be expected with a more objective test, with the ct2c subset having the worst outcome. “In the clinic, the findings of a DRE — and the related T subclassification — may influence
Darolutamide 600 mg (two 300-mg tablets) twice daily or placebo while continuing to receive androgen deprivation therapy (ADT). The results showed a significant improvement in MFS when darolutamide was added to ADT. The median MFS was 40.4 months for the combination, vs. 18.4 months for placebo plus ADT (P <0.0001). “The P value was highly significant,” commented lead investigator Karim Fizazi, MD, PhD, head of the Department of Cancer Medicine at the Institut Gustave Roussy, Villejuif, France, when he presented the trial results earlier this year. The rate of discontinuation because of adverse reactions in both treatment arms was 9%. The most frequent adverse reactions that required discontinuation in men receiving darolutamide were cardiac failure (0.4%) and death (0.4%). Adverse reactions that occurred more frequently in the darolutamide arm (≥2% vs. placebo) were fatigue (16 vs. 11%), pain in extremity (6 vs. 3%), and rash (3 vs. 1%). Darolutamide is awaiting approval in the European Union, Japan, and other countries. It was developed jointly by Bayer and Orion Corporation.

Commenting on the ARAMIS trial, Liaw said: “Additional follow-up will further define the adverse effect profile of darolutamide but, because it does not cross the blood-brain barrier to any significant degree, it may potentially be associated with less fatigue, falls, and seizure risk, as compared to apalutamide or enzalutamide.” The ARAMIS trial was a double-blind, placebo-controlled phase 3 trial that randomly assigned 1,509 men with nmCRPC to receive either darolutamide or enzalutamide.”

Obese men face higher odds of perioperative complications from radical prostatectomy (RP), according to findings from a database study published online 20 July 2019 in the journal *Urology*. Dr. Sophie Knipper of University Hospital Hamburg-Eppendorf, in Hamburg, Germany, and colleagues used data from the U.S. National Inpatient Sample database from 2008 to 2015 to investigate the effect of obesity (defined as a body mass index of 30 kg/m² or higher) on perioperative outcomes and total hospital charges associated with robot-assisted (RARP) or open radical prostatectomy (ORP).

Based on data from more than 53,000 men who underwent RARP (8.6% of them obese) and more than 35,000 who underwent ORP (6.9% of them obese), the overall complication rates were 13.1 vs. 7.9% of obese vs. nonobese RARP patients and 17.4 vs. 11.3%, respectively, of ORP patients. In multivariable analyses, obesity independently predicted 70% higher odds of overall complications, 70% higher odds of miscellaneous medical complications, 80% higher odds of cardiac complications, 60% higher odds of respiratory complications and 70% higher odds of genitourinary complications after RARP.

Obesity at RARP translates into fewer adverse perioperative outcomes compared to obesity at ORP,” the researchers note. “However, total hospital charges associated with RARP appear to be higher than those associated with ORP in obese patients. Thus, the resulting trade-off between higher cost and more favorable complication profile of RARP in obese patients suggests primarily considering RARP in these patients.”

*Reuters Health Information* 10 August 2019

Check out Us TOO web pages on maximizing quality of life after prostate cancer treatment:

**Sexual Health/Intimacy & Erectile Dysfunction**

[www.ustoo.org/intimacy](http://www.ustoo.org/intimacy)

**Urinary Incontinence**

[www.ustoo.org/incontinence](http://www.ustoo.org/incontinence)
**Radiation Therapy May Have a Role in Oligometastatic Prostate Cancer**

Radiation therapy (RT) can be effective for managing men with oligometastatic prostate cancer (OPCa), according to investigators at Johns Hopkins University School of Medicine in Baltimore, MD.

A team led by Phuoc T. Tran, MD, PhD, based that conclusion on a study of 156 men with OPCa (median age 65.5 years) who underwent stereotactic ablative radiation (SABR) therapy to 354 metastatic lesions (54.2% in lymph nodes, 49.2% in bone, and 2.9% in visceral sites). Median follow-up was 25 months.

“This study represents, to the best of our knowledge, the largest single institutional series of men with OPCa treated with definitive intent RT to oligometastatic lesions,” Dr. Tran’s team wrote in a paper published online ahead of print in the *International Journal of Radiation Oncology Biology Physics*.

At 24 months, the cumulative incidence of local failure was 7.4%. Median biochemical progression-free survival (bPFS) for the entire cohort between 2004-2009 were identified retrospectively from a cancer registry database and MRI reports. The mpMRI sequences comprised T2-weighted and dynamic contrast-enhanced series (2004-2005) with diffusion-weighted imaging 2006 onwards. Clinical outcomes were assessed up to July 2015 by review of subsequent pathology results, PSA levels and review of electronic patient records. The primary outcome was csPCa diagnosis by follow-up. We also estimated the sensitivity, specificity, PPV and NPV of all prostate mpMRI during the period.

502 mpMRI with a prior biopsy were included. 121 were in men with a prior negative systematic biopsy for cancer (median PSA 9.5; median age 60 years). Of these, 96% (70/73) of men with negative mpMRI remained free of csPCa at median follow-up of 6.7 years (range 2.6-10.7 years). The overall NPV and PPV of mpMRI in the entire cohort regardless of pre-mpMRI biopsy status was 86% (80-91%) and 54% (52-57%) respectively, during the time period. Prostate mpMRI has high clinical NPV. In men with pre-mpMRI negative biopsy and a negative MRI, the risk of developing clinically significant prostate cancer at median 6.7 years is extremely low.

**Men’s Testosterone Levels Largely Determined by Where They Grow Up**

Men’s testosterone levels are largely determined by their environment during childhood, according to new research.

The Durham University-led study suggests that men who grow up in more challenging conditions where there are a lot of infectious diseases, for example, are likely to have lower testosterone levels in later life than those who spend their childhood in healthier environments. The study, published in *Nature Ecology and Evolution*, challenges the theory that testosterone levels are controlled by genetics or race.

As high testosterone levels potentially lead to an increased risk of prostate enlargement and cancer, the researchers suggest that any screening for risk profiles may need to take a man’s childhood environment into account. The study found that Bangladeshi men who grew up and lived as adults in the UK had significantly higher levels of testosterone compared to relatively well-off men who grew up and lived in Bangladesh as adults.

*PROSTATE CANCER HELPLINE: 1-800-808-7866 WWW.USTOO.ORG*
Wilmot Cancer Institute scientists believe they have figured out why a commonly used drug to treat late-stage prostate cancer often stops working after four or five months and appears to have a dual function that later turns the cancer into a relentless aggressor.

By describing how the drug, enzalutamide, inadvertently causes the harmful transformation, corresponding author Chawnshang Chang, Ph.D., and colleagues believe they have also discovered a way to block it from occurring, at least in mice. The study, led by Jie Luo, a graduate student from the Department of Biology at the University of Rochester, was published in the journal Nature Communications.

“As more patients look to enzalutamide to extend their lives, even for just a few months, our goal is to find ways to make the drug work for longer periods and to block the dangerous pathways that lead to adverse side effects,” Chang said.

Prostate cancer is the second leading cause of cancer death in American men. Although some early-stage types with a low Gleason score can be treated with a “watch and wait” approach, other types are higher-grade cancers that require surgery and androgen deprivation therapy (ADT). The goal of this treatment is to lower the amount of male sex hormones (androgens) in the body, which fuel the cancer. An especially aggressive subtype of the disease is known as castration-resistant prostate cancer (CRPC), which keeps growing despite treatment.

For men who have this aggressive form of metastatic prostate cancer, and are no longer responding to chemotherapy, enzalutamide can extend survival by an average of five months. In 2018 the Food and Drug Administration also approved the drug to treat men who have CRPC that had not yet spread.

But enzalutamide, a pill, can cause side effects. One of the worst effects is neuroendocrine differentiation (NED), an increase of neuroendocrine cells in the prostate tumors. An abundance of NED cells makes tumors resistant to treatment.

Chang and Luo identified non-coding RNA-p21 as the main culprit for inducing neuroendocrine differentiation, by the fact that IncRNAp-21 can switch the function of a key gene, EZH2. They also showed that IncRNAp-21 is highly expressed in NED prostate tumors.

“Earlier, scientists believed that only a tiny percentage of advanced prostate cancer tumors underwent neuroendocrine differentiation. But recent studies estimate that 30 to 40 percent of patients have tumors containing aggressive neuroendocrine prostate cancer cells for which the average survival rate after detection is less than one year – making more patients vulnerable to the worst-case disease progression,” Chang said.

Edward Messing, M.D., a national and international authority in urologic cancers who treats patients at Wilmot and UR Medicine, said the latest discovery has the potential to impact men with challenging cases.

“Dr. Chang’s team has identified an important molecular mechanism that affects many of the thousands of men with advanced prostate cancer who will eventually succumb to their disease,” Messing said. “Understanding and reversing the ‘switch’ that causes neuroendocrine differentiation should prolong the lives of these men and significantly reduce their suffering.”

Although no treatments are available yet in clinical trials to block to molecular switch, Chang’s lab identified a small molecule drug that appears to work in mice; researchers elsewhere have revealed similar drugs, and further study is needed.

Provided by University of Rochester Medical Center.


Join Us for the 15th Annual SEA Blue Chicago Prostate Cancer Walk and Run
Sunday, September 15, 2019
8:00 am – 1:00 pm
1790 North Stockton
Chicago, IL

Register at:
seablueprostatewalk.org
Enter code HOTSHEET19 for $5 off registration

Can’t make it in person? Sign up as a Virtual Mover to help fundraise or create your own satellite SEA Blue event., OR
Consider a donation to help Us TOO provide support, education, and advocacy for the prostate cancer community, OR

Just help us spread the word via email, social media, and old fashioned word of mouth.

Thank you!
Doctor Chodak’s Bottom Line


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, “FDA Approval for…” An interesting development has occurred from the FDA regarding approval of new drugs to treat non-metastatic castrate resistant prostate cancer. They have issued another approval based on the drug’s effect on metastases rather than require the time-tested requirement of improving survival.

Darolutamide received this approval after it significantly improved metastasis-free survival (MFS). This drug is another oral androgen receptor antagonist, similar to enzalutamide and apalutamide. At this time, it remains unclear which of these three agents is best, or which one should be started first. Whether direct comparisons will be performed is unclear. Nevertheless, it is another important option for managing a rising PSA. Also, it will be interesting to see if survival eventually improves. If so, it will mean that this endpoint of MFS will become the new standard for obtaining an FDA approval.

The Bottom Line: Men now have another option for treating non-metastatic castrate resistant disease.

P1, “Elective Node RT…” Some of the men getting recurrent disease after radical prostatectomy (RP) do so in the pelvic lymph nodes that are not removed even if a lymph node dissection has been performed. The treatment options include stereotactic body radiotherapy (RT) or elective nodal RT. De Bleser, et al. compared the two retrospectively in over 500 men treated at 15 European centers. At three years, the MFS was slightly, but significantly higher in the elective nodal therapy group, having only one but not more than one node involved with cancer. Unfortunately, there are several biases in the study including the non-standard follow-up evaluation and variable use of androgen deprivation therapy. As stated by the authors, a randomized study would be needed to properly compare the two treatments.

The Bottom Line: Whether nodal recurrence after RP should be treated with stereotactic body RT or elective nodal RT remains unclear and more data are needed.

P1, “DRE is Still…” DRE or no DRE?, seems to be a debatable question. Its main value has been in detecting prostate cancer and simultaneously evaluating for possible rectal cancer. Lately it has been called into question, primarily for patient comfort, as some men really dislike the test and perhaps, doctors don’t like doing it.

A retrospective study by Borkenhagen, et al. provides additional support because it helps provide prognostic information. First, not doing it because it sometimes causes a few seconds of discomfort is not the reason to abandon it. Second, there are still about 15-20% of cancers that are suspected on DRE when the PSA is low. In other words, the PSA may miss some cancers.

The result of a DRE can also help with treatment decisions. For example, if a T2 or T3 cancer is found, then it may not be advisable to preserve the nerve on that side at the time of RP. I believe that recommending the DRE for prognostic information is the weakest argument because it really doesn’t help the individual. Instead, it provides data when evaluating groups of men undergoing a specific therapy.

The Bottom Line: Despite the growing number of tests available to counsel patients, the DRE should not be abandoned at this time.

P2, “Validity of Patient…” PROMIS (Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction measures (PROMIS SexFS) is a validated survey for assessing sexual function and satisfaction in men and women. Although RP may result in a decreased ability for sexual relations, it is unclear what men’s attitudes toward sex might become. Agochukwu, et al. used this survey to evaluate a large group of men treated by RP between 2014 and 2016. Although both interest and satisfaction declined in the three months after surgery, they then increased up to 24 months. This occurred despite decreases in sexual function. This is an important observation and should be part of counseling of patients despite their decreased ability to have an erection.

The Bottom Line: Although sexual function may decline post-RP, men seem to regain both interest and satisfaction from three to 24 months.

P2, “Treatment-Related…” Men with high-risk prostate cancer have an increased risk for cancer in their pelvic lymph nodes. Unfortunately, existing imaging may not be able to identify those areas. Therefore, doctors will often recommend RT to the nodes to eradicate potential disease. There are two questions that must be answered: First and most importantly, will RT to the lymph nodes improve survival, and second, how will the RT affect side effects?

To gain insight into the second question, Parry and co-workers reported on men in the English registry who received either of those treatments. At three years, they found no significant difference in either GI or GU toxicity. These findings suggest that adding the lymph node RT may not cause added harm. Unfortunately, since the study was not randomized, these findings do not prove equal safety. That will require a randomized study, which hopefully will be done. The same is true for assessing whether the added RT (Continued on page 8)

Video is Available from:
Prostate Cancer Pathways for Patients & Caregivers Webcast
With Content Specific to:
• Prostate Cancer and Sexuality
• Advanced Stage Disease and Immunotherapy
• Meditation
• Men’s Health
• Integrative Medicine
• Prostate Cancer 101
• Localized Disease
• And More...

Access direct links to video pertaining to each specific topic at:
https://ustoo.org/Pathways-EnglewoodNJ
Men’s Testosterone Levels Mazy Be Determined by Where They Grow Up

(Author) Dr. Mazy Be performed a study on testosterone levels in men born in different places. The study found that testosterone levels in men born in various countries are determined by the environment in which they were raised, rather than by their ethnicity or where they live as adults. The study included children born in Europe, the UK, and other countries, and found that the testosterone levels in these children were determined by their surroundings during childhood, not by their ethnicity or where they live as adults. The study suggests that the factors affecting testosterone levels in men are not fixed but can change depending on the environment in which they are raised. The study also found that obesity can affect testosterone levels, but more research is needed to confirm these findings. The study is significant because it challenges the idea that testosterone levels are fixed and not influenced by environmental factors. The study is published in the journal *Science Daily*.
Between the Sheets... September 2019

This column provides the platform for experts in the field to help men and women by providing answers to questions about sexual health and intimacy challenges that can result from prostate cancer treatment.

This column was compiled with the help of Dr. Jeffrey Albaugh, Director of Sexual Health at NorthShore University HealthSystem and at Jesse Brown VA Medical Center in Chicago, IL. Dr. Albaugh is a funded researcher, a board certified advanced practice urology clinical nurse specialist, and a board certified sexuality counselor. In addition to his many publications in peer reviewed journals and chapters in books on sexual dysfunction, Dr. Albaugh published Reclaiming Sex and Intimacy After Prostate Cancer Treatment. He has been quoted in media and publications as an expert in the treatment of sexual dysfunction, and is a member of the Us TOO Board of Directors.

QUESTION FROM PROSTATE CANCER SURVIVOR:
At age 71 I was diagnosed with prostate cancer and had seed implants which were effective. After healing from the implants, I had no erection problems for 6-7 years but then it slowly began to be a problem. Viagra and Cialis were helpful, somewhat, for a while but then even those did not help. The frustrating and strange thing is I still wake up numerous times at night with erections. Articles about ED seem to center around blood flow to the penis or psychological problems. Are sleep time erections created from blood flow or some other function? If blood flow, why the problem during sexual activities but not during sleep?

RESPONSE FROM DR. JEFFREY ALBAUGH:
Thank you for your question. All erections, including night time erections, are the result of blood filling the penis. Your penis literally works out while you sleep to keep erections in shape. It is a good sign you are still getting nocturnal erections, even though they might not happen as often or be as strong as when erections were working well. Erectile function requires nervous conduction (communication) between your brain and penis and blood flow to engorge the penis. You continue to struggle during sex with a partner with your erectile dysfunction and that is probably due to multiple factors. You are nearly 80 years old now and many medical conditions can impact erectile function as you age, including: high blood pressure, elevated cholesterol, coronary artery disease, diabetes, obesity, chronic spinal disc issues, neurologic disorders or sleep disorders. Most of the men in your age group have erectile dysfunction due to the many medical conditions that may occur by the time you are nearing 80 years old. In addition, the anxiety over possibly losing erections or pleasing a partner can negatively impact erections. If we were able to completely track your night time erections over the years, they have probably diminished in frequency and quality over time, along with the diminished erectile function with your partner. We have no way of knowing how the night time erections differ now versus when things were working right, but it is still a good sign you do get numerous night time erections. Blood is flowing to your penis, but the frustrating thing is that it is not consistently doing that when you are trying to have sex, and that is likely due to both physical and psychological factors. Keeping your mind focused and staying present with your partner, while not worrying, can be very important to erectile function with a partner. Enjoying sex regardless of erections can make a big difference. If you are not hard enough for intercourse, enjoy oral stimulation, manual stimulation and/or vibratory stimulation of the genitals together (outercourse). If you are hard enough, you can enjoy intercourse. The anxiety will bring down the erections with the blood going back into your body. There are also other treatments for erectile dysfunction, if and when pills are not working. I hope this information is helpful to you and others in the journey towards health.

You can access the new edition of my book or download a free copy of my original book at www.drjeffalbaugh.com.

Watch Dr. Albaugh’s presentation on sexual health and intimacy from the Prostate Cancer Pathways for Patients and Caregivers event recorded at NorthShore University HealthSystem in Skokie, IL on November 3, 2018 at https://www.youtube.com/watch?v=Hiq0dDEb1l0&t=4483s.

Read previous issues of Between the Sheets at www.ustoo.org/BTS.

Do you have a question about sexual health or intimacy? If so, we invite you to send it to Us TOO. We’ll select questions to feature in future Between the Sheets columns.

Please email your question to: ustoOBTS@ustoo.org

Or mail your letter to:
Us TOO International
Between the Sheets
2720 S. River Road, Suite 112
Des Plaines, IL 0018
Advancements in prostate cancer research provide hope for finding a cure and lead to the discovery of new treatments to minimize the impact of a man’s prostate cancer and maximize his quality of life. This regular Hot SHEET supplement includes some of the latest research from the Prostate Cancer Foundation (www.pcf.org).

The PCF is the world’s leading philanthropic organization funding and accelerating prostate cancer research. Founded in 1993, the PCF has raised more than $745 million and provided funding to more than 2,000 research programs at nearly 200 cancer centers and universities.

Aggressive Prostate Cancer and Our “Dark DNA”

Imagine you’re a scientist studying human genes, looking for a way to cure prostate cancer. You could learn many things by studying the genes that make the code that becomes proteins: our building blocks – or, you might say, our hardware.

These protein-coding genes make up just two percent of our human genome. The other 98 percent are non-coding. “Not too long ago, says PCF-funded investigator Hui Li, Ph.D., of the University of California-San Francisco, “scientists thought these genes were just ‘junk,’ the genetic equivalent of background noise.” But now, Li and an increasing number of scientists believe, “these non-coding genes play a very important role in many cellular processes, including the development and progression of cancer.”

These non-coding genes that don’t make proteins make something else that is important: RNA. “They’re like the hidden software of our bodies,” says medical oncologist and molecular biologist Jonathan Simons, M.D., CEO of the PCF. It turns out that these genes – our very own “dark matter,” or “dark DNA” – might not make the difference between getting cancer and not getting it, but they might make the difference between getting cancer that’s easy to cure and cancer that is much more likely to be lethal. “There’s a lot of genetic software running in the background,” adds Simons. “If you have a single letter wrong, it can set you up for trouble. Some of those changes in code might mean you have higher cholesterol, and then a higher chance of having a heart attack or stroke. But that one letter could also change the command for cancer to grow fast or grow slowly; if you have cancer, it could mean you have a much higher chance of having a bad one – one that will go at 75 miles per hour, instead of maybe 25.”

In research with his mentors, Felix Feng, M.D., and Peixuan Guo, Ph.D., Li has painstakingly looked at thousands of RNA-sequencing genes. “This kind of work wouldn’t have been possible, even a few years ago,” notes Li. “Because of the advancement of next-generation sequencing technology, we now have the bioinformatics and the ability to analyze these novel genes.”

Many genetics studies are like a game of “spot the misspelled word” – on steroids, a task akin to speeding through the Encyclopedia Britannica, one letter at a time, looking for something that is wrong or out of place.

Li’s work is more like a genetic game of, “Where’s Waldo?” Except he didn’t know what Waldo looked like. But he may have found Waldo, after all: a suspicious gene called SCHLAP1-AS.

SCHLAP1-AS is a long non-coding RNA gene that is “highly expressed in prostate cancer, and is highly prognostic for metastasis,” explains Li. It is “only guilty by its presence. We have identified that SCHLAP1-AS is more closely associated with the progression of prostate cancer than any other protein-coding or non-coding gene in our patient cohort.”

His studies have found that inhibiting this gene in prostate cancer cells causes them to become less oncogenic (less proliferation of cancer). One aim is to see whether this gene can be employed as a novel therapeutic target – to turn back the disease, or halt its progression. Li also believes it could become a prognostic biomarker. The presence of SCHLAP1-AS in prostate cancer when it is first diagnosed could tell doctors: This cancer is going to be aggressive. Don’t do active surveillance; treat it aggressively. Maybe it could even be looked for earlier, to indicate: This young man has a bad gene; he needs to start checking for prostate cancer at an earlier age, and he needs to be tested every year.

Li believes this is just the beginning of looking at RNA-coding genes in personalized medicine. “We think studying this gene, and learning how to block it, will enhance our understanding of prostate cancer biology in a subset of patients with aggressive disease.” And more: “The non-coding genome was considered undruggable before,” says Li. “If we can make a real breakthrough in this area – hit a previously unknown target – it may also mean a breakthrough in how we treat patients with other forms of cancer, like pancreatic cancer and brain cancer, which share some common traits with prostate cancer.”

For more information visit www.pcf.org, email info@pcf.org, or call 1-800-757-2873.