Gleason Score 8 Prostate Cancer Diagnosed at Biopsy Frequently Downgraded

Almost half of patients with clinical Gleason Score 8/Grade Group 4 (cGG4) prostate cancer (PCa) diagnosed on transrectal biopsy experience pathologic Gleason Score downgrading at radical prostatectomy (RP), according to a study presented at the 2019 American Urological Association (AUA) annual meeting. In addition, researchers identified biopsy-based risk factors that can predict the likelihood of downgrading.

“If these risk factors for downgrading are validated, they can be used to tailor patient counseling regarding risk of truly having Gleason 8 disease vs. less significant PCa,” said lead investigator Vignesh T. Packiam, MD, of Mayo Clinic in Rochester, Minnesota, told Renal & Urology News.

Dr. Packiam and his collaborators identified 244 men with cGG4 PCa who underwent RP from 2006 to 2017. Pathologic examination of RP specimens resulted in the downgrading of 118 (48%) patients. Of these, 73 were pathologically downgraded to GG3, 42 to GG2, and three to GG1.

Downgraded patients were significantly more likely to have a lower percent of GG4 cores in the total (23 vs. 37%) and positive (58 vs. 80%) cores than men not downgraded. Increasing number of cores of GG4 was associated with decreased odds of downgrading. On multivariable analysis, each additional GG4 core was significantly associated with 15% decreased odds of downgrading, whereas each additional GG1-GG3 core was significantly associated with 17% increased odds of downgrading.

(Continued on page 8)
Clinical Utility of Circulating Tumour Cell Androgen Receptor Splice Variant-7 Status in Metastatic Castration-Resistant Prostate Cancer

Eur Urol 27 April 2019; Epub ahead of print

Detection of androgen receptor splice variant-7 (AR-V7) mRNA in circulating tumour cells (CTCs) is associated with worse outcome in metastatic castration-resistant prostate cancer (mCRPC). However, reports rarely compare CTC counts and result of biopsy AR-V7 protein expression.

Purpose: To determine the reproducibility of AdnaTest CTC AR-V7 testing, and associations with clinical characteristics, CellSearch CTC counts, tumour biopsy AR-V7 protein expression and overall survival (OS).

Methods: CTC AR-V7 status was determined for 227 peripheral blood samples, from 181 mCRPC patients with CTC counts (202 samples; 136 patients) and matched mCRPC biopsies (65 samples; 58 patients).

Results: CTC AR-V7 status was associated with clinical characteristics, CTC counts, and tissue biopsy AR-V7 protein expression. The association of CTC AR-V7 status and other baseline variables with OS was determined.

Of the samples, 35% were CTC+/AR-V7+, CTC+/AR-V7+ samples had higher CellSearch CTC counts (median CTC; interquartile range [IQR]: 60, [19-184] vs. 9, [2-64]; Mann-Whitney test p<0.001, a statistically significant difference) and biopsy AR-V7 protein expression (median H-score, [IQR]: 100, [63-148] vs. 15, [0-113]; Mann-Whitney test p=0.004, a statistically significant difference) than CTC+/AR-V7- samples. However, both CTC- (63%) and CTC+/AR-V7- (62%) patients had detectable AR-V7 protein in contemporaneous biopsies. After accounting for baseline characteristics, there was shorter OS in CTC+/AR-V7+ patients than in CTC-.

Research Evidence on High-Fat Diet-Induced Prostate Cancer Development and Progression

Narita S, Nara T, Sato H, Koizumi A, Huang M
J Clin Med 30 April 2019; Epub ahead of print

Although recent evidence has suggested that a high-fat diet (HFD) plays an important role in prostate carcinogenesis, the underlying mechanisms have largely remained unknown. This review thus summarizes previous preclinical studies that have used prostate cancer (PCa) cells and animal models to assess the impact of dietary fat on PCa development and progression. Large variations in the previous studies were found during the selection of preclinical models and types of dietary intervention. Subcutaneous human PCa cell xenografts, such as LNCaP, LAPC-4, and PC-3 and genetic engineered mouse models, such as TRAMP and Pten knockout, were frequently used. The dietary interventions had not been standardized, and distinct variations in the phenotype were observed in different studies using distinct HFD components. Use of different dietary components in the research models is reported to influence the effect of diet-induced metabolic disorders. The proposed underlying mechanisms for HFD-induced PCa were divided into (1) growth factor signaling, (2) lipid metabolism, (3) inflammation, (4) hormonal modulation, and others. A number of preclinical studies proposed that dietary fat and/or obesity enhanced PCa development and progression. However, the relationship still remains controversial, and care should be taken when interpreting the results in a human context. Future studies using more sophisticated preclinical models are imperative in order to explore deeper understanding regarding the impact of dietary fat on the development and progression of PCa.
**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.

Okay, I would bet anyone reading this column knows the jaded, boring and often recited phrase “breakfast is the most important meal of the day.” BORING! I never believed that phrase because there was not enough strong evidence to support it, and now we are surrounded by the most calories in human history, and an obesity epidemic that is not good and getting worse. In fact, the last time I ate a full breakfast was years ago, and when I talk to a number of colleagues, they now tell me they feel better skipping breakfast. They have more energy and they have lost some weight. Keep in mind that breakfast is a relative term since I have a coffee or tomato juice many mornings and each is essentially my “mini-breakfast.” Anyway, what the heck do I know? So, along comes a meta-analysis from my good friend (relative endeavors research term—I do not actually know them), in Melbourne, Australia that examined 13 previous randomized trials from high-income countries. They basically concluded that “breakfast might not be a good strategy for weight loss in adults, as it could have the opposite effect.” I could not agree more since humans need to find a way to live with less and skipping breakfast or minimizing it could be one path to success. When you consume some foods in the morning it can cause you to become more tired later that same morning. One argument against skipping breakfast is that humans will just end up consuming more calories at lunch or dinner and ultimately will still consume the same number of total daily calories. However, this recent review suggests that this is not necessarily the case for some folks.

Regardless, obesity or weight gain appears to increase the risk of aggressive cancers (including prostate) and simply makes the prostate get bigger in some men, so it is not a urologic- or urinary-friendly thing. When I began skipping breakfast years ago, it took about a week and then I no longer missed it (kind of like high school).

Whatever works for you, but I love studies that challenge common health advice that was never adequately tested in the first place. This is one problem with nutrition and even some over the counter pills that were never tested enough, and yet people want to generalize about the advice; because I believe there are some financial forces behind it.

My goal is to change the common breakfast phrase to: “breakfast, oh well, heck I can do with or without it...no big deal.” Who is with me on this one? Perhaps I will organize a rally near you, and after we are done marching in the early morning we can all meet for lunch?

**Reference:**

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**Clinical Validation of IsoPSA™, a Single Parameter Structure-Based Assay for Improved Detection of High-Grade Prostate Cancer**


J Urol 1 June 2019; Epub ahead of print

**Purpose:** Current PSA markers to detect prostate cancer are limited by low specificity for high-grade disease. IsoPSA™ is a blood based, structure-focused assay, which predicts risk by partitioning the isoforms of PSA that are linked to cancer in an aqueous two-phase reagent system. We validated the clinical performance of this assay for identifying high-grade disease in a new contemporary biopsy cohort.

**Materials and Methods:** We performed a multicenter prospective validation in 271 men scheduled for prostate biopsy at a total of seven academic and community centers who were enrolled between May 2017 and March 2018. Blood samples were obtained for assay prior to biopsy. The discrimination power of the assay to detect high-grade prostate cancer (Gleason 7 or greater) was evaluated by Receiver Operating Characteristic (ROC) curve analysis and compared to prior results. Clinical performance was further improved by comparison with multiparametric magnetic resonance imaging-ultrasound vs. transrectal ultrasound guided biopsies.

**Results:** The assay AUC was 0.784 for high-grade vs. low-grade cancer/benign histology, which was superior to the AUCs of total PSA and percent free PSA. If 1,000 patients were biopsied, the assay would have reduced the number of unnecessary biopsies from 705 to 402 (43%) with only 22 missed high-grade cancers, of which seven would have been Gleason sum 4 + 3 or higher. Subset analysis of multiparametric magnetic resonance imaging-guided biopsy produced a substantial improvement of the AUC to 0.831.

**Conclusions:** Validation of the structure based IsoPSA assay demonstrated statistical concordance with previously reported results and verified its superior performance vs. concentration-based PSA and the free-to-total PSA ratio. The assay improvement in detecting high-grade prostate cancer using multiparametric magnetic resonance imaging ultrasound guided biopsy may help define a new diagnostic paradigm.

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**PROSTATE CANCER HELPLINE: 1-800-808-7866 WWW.USTOO.ORG**
Packing a PUNCH in Prostate Cancer Chemo, ADT & Surgery (Continued from page 1)

comes – including overall survival (OS) – are worth discussing with men with high-risk localized prostate cancer. “I think [urologists] should have a conversation with their patients about the benefits of this approach,” he told Medscape Medical News in an exclusive interview.

Such patients are those with Gleason scores of 8-10 who have a high probability (>40% on a nomogram) of biochemical recurrence (BCR) within five years after RP (which was the PUNCH population). “Patients, rather than going to surgery immediately, should consider a neoadjuvant approach first,” added Eastham. “The neoadjuvant CHT approach consisted of androgen deprivation therapy (ADT) plus docetaxel. This should now be a standard of care in this setting,” Eastham suggested.

However, another prostate cancer expert dismissed the trial – and the treatment approach used for this group of patients – as not being proven to be helpful. “The basic idea behind PUNCH is a good one,” suggested Eric A. Klein, MD, Glickman Urological and Kidney Institute at Cleveland Clinic, who was approached for comment.

“More aggressive cancers need more aggressive treatments,” he stated. “We have known for some time that we could cure men with early-stage [localized] prostate cancer with single-modality therapy,” he continued. “But that has not been completely true for high-risk localized disease,” he added.

“Thus, the world of prostate cancer research conducted a string of trials testing more aggressive strategies in this setting. None has succeeded. The new results do not alter that,” said Klein. “Does this [PUNCH trial] change the standard of care?” he asked. “Absolutely not. They didn’t meet their primary endpoint,” he concluded.

The failure of PUNCH to meet its primary endpoint is an involved tale. Part of the complexity stems from the fact that about 40% of men received salvage radiotherapy, ADT, or both prior to meeting the study’s definition of BCR. During the course of the long study, “there was a change in clinical practice to initiate salvage therapy earlier,” said Eastham.

He also pointed out “there is a statistically significant improvement in bPFS over the course of the study,” referring to the entire study period (P = 0.02), not just the three-year bPFS, which was the primary outcome. Median follow-up was just over five years in the study.

Eastham also championed the OS findings. In his oral presentation at AUA, he said “although the confidence interval covers 1, there is strong evidence for a survival benefit stemming from neoadjuvant CHT.” This was a reference to the OS data, which were not statistically significant (P = 0.06).

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<th>Treatment</th>
<th>3-year</th>
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<td>RP alone</td>
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<td>RP plus CHT</td>
<td>98</td>
<td>94</td>
<td>87</td>
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The survival benefit “happened earlier than we thought,” Eastham said. “The question then becomes, is it worth it?” He was questioning if the toxicity of the treatment is worth the possibility of modest benefit later.

Cleveland Clinic’s Klein was not impressed. He pointed out that at eight years, there were data on only eight men in the surgery-alone arm and 11 men in the neoadjuvant arm. The confidence intervals were also “fairly wide,” he added. “This doesn’t move the bar. This does not change the standard of care,” Klein told Medscape Medical News.

Eastham presented the AUA audience with a different conclusion: “These data support neoadjuvant chemohormonal therapy plus RP as a standard option for at least delaying bPFS in men with clinically high-risk prostate cancer.”

Presented at the AUA 2019 Annual Meeting: Abstract LBA12.
Medscape Medical News 7 May 2019

Prostate Cancer Metastases at Diagnosis on the Rise

Investigators have documented a sustained and definite increase in the incidence of prostate cancer distant metastases at diagnosis, according to a study presentation at the 2019 American Urological Association (AUA) annual meeting. “The incidence of distant metastases at prostate cancer diagnosis increased gradually from 130.1 to 157.3 per million men aged 50 to 74 years from 2007 to 2015, following a slight decline from 2005 to 2007,” Neal Patel, MD, of Weill Cornell Medical College in New York, reported. The incidence increased from 451 to 586.1 per million men aged 75 years or older from 2011 to 2015 after a progressive decline from 2004 to 2011.

The incidence of distant metastases increased significantly from 451 to 504 per million men from 2011 to 2012. Among men aged 75 years or older, the incidence increased from 532.3 to 586.1 per million men from 2014 to 2015.

In contrast, from 2004 to 2015, the incidence of nonmetastatic prostate cancer decreased from 4,618 to 2,977 per million among men aged 50 to 74 years and from 6,919.3 to 3,221.1 per million among men aged 75 years or older.

“Potential causes of the risk in metastatic disease at presentation among men aged 75 years and older include an evolution in imaging for prostate cancer staging, including the use of positron emission tomography/computed tomography, magnetic resonance imaging, and prostate-specific membrane antigen imaging as well as shifts in PSA screening,” Dr. Patel told attendees.

Presented at the 2019 AUA meeting, Abstract PD30-10.
Renal & Urology News 4 May 2019

Visit the Us TOO Prostate Cancer Clinical Trial Finder at www.ustoo.org/HCP-ClinicalTrials
Guy’s. No men underwent transrectal ultrasound (TRUS) guided biopsy.

“The TP-only biopsy strategy, which was facilitated by the novel PrecisionPoint Transperineal Access System (Perineologic), was indeed feasible,” Stroman reported. TP biopsy provided low complication rates, including 0.16% for sepsis (that required hospital admission and intravenous antibiotics). Also, urologists in the study carried out 58% of TP biopsies under local anesthesia, which enables an in-office procedure and would be a boon to wider adoption of the method.

Step one of Trexit was this feasibility study, which started as planned at Guy’s on September 1, 2017. The hospital has not performed a TRUS biopsy since that day.

Step two was to implement the TP change in nearby hospitals and the entire Southeast London Cancer Network before March 7, 2019, a couple of weeks ahead of the now-passed Brexit deadline.

“Mission accomplished,” said Stroman. “We challenged ourselves to beat the time of Brexit and we did,” he said.

Step three of the Trexit project is to enact the switch at various—and then all—centers throughout the UK, which hopes to be the first country to fully retire TRUS biopsies. There is no target completion date at this time, but the effort is supported by a National Health Service innovation program.

However, Jan Philipp Radtke, MD, University Hospital Essen, Germany, claimed that the biopsy-method switch is not novel. “Multiple European medical centers have made the switch—some as long as eight years ago,” he said.

“The reported complication rates with TP biopsies are near zero. They are very, very good,” said Radtke, who co-moderated the podium session that included the Trexit presentation.

In the United States, the PrecisionPoint system used in the new UK study has been FDA approved since 2016 and is in use at American centers, including Johns Hopkins in Baltimore, MD, Anderson in Houston, and Rush University in Chicago, according to the company website.

“Developed by urologist Matthew Allaway, MD, the system does not require extensive training,” said Stroman. "The learning curve has been quick," he said. After assisting on 14 cases, he went "solo."

“The term Trexit is not currently being used outside the UK,” said Stroman. It was coined by Tim O’Brien, MD, the incoming president of the British Association of Urologic Surgeons.

The session moderator, an American, had fun with British presenter Stroman. "I notice Teresa May is not a coauthor on this," quipped Kevin Loughlin, MD from Harvard Medical School in Boston, immediately triggering audience laughs.

Historically, TRUS has been used to perform prostate biopsies and is still the most commonly used method. TP biopsies, on the other hand, have required general or spinal anesthesia to allow men to tolerate multiple needle passes through the perineal tissue.

However, in the new study, the PrecisionPoint tool allowed for local anesthesia, including in the office setting, which, as stated, could lead to wider use of TP biopsies.

The Guy’s Hospital team also used a single dose of antibiotics prior to each procedure. The median age of men in the study was 60.5 years.

One of the 678 men (0.16%) had sepsis requiring hospital admission and intravenous antibiotics. A total of four men (0.5%) had urinary retention, but none needed surgery. No complications were Clavien 3 or higher.

Biopsy under general anesthesia was completed in 205 men (30%) and under IV sedation in 78 (11%). Systematic biopsies with/without additional targets were completed in about 40% of cases.

Presented at the AUA 2019 meeting, abstract PD64-03. Medscape Medical News, 9 May 2019

Prevalence Predictors and Implications for Appropriate Use of Active Surveillance Among Black Men Diagnosed with Low-Risk Prostate Cancer

Taku N, Narayan V, Wang X, Vapiwala N

J Clin Oncol 29 April 2019; Epub ahead of print

Consensus guidelines recommend active surveillance (AS) be considered for managed men with low-risk prostate cancer (LRPC). The objective was to evaluate the prevalence and predictors of an AS approach in black men (BM) diagnosed with LRPC after inclusion of AS in LRPC consensus guidelines.

BM and white men (WM) diagnosed with LRPC (PSA ≤10 ng/mL, Gleason score [GS] ≤6, clinical stage T1-T2a) between 2010 and 2013 were identified from the National Cancer Database. Logistic regression models were used to assess the likelihood of AS over time and to examine associations between sociodemographic characteristics (SDCs) and the receipt of AS. A subanalysis was performed to assess the likelihood of GS upgrading on radical prostatectomy (RP) specimens for cases that received RP treatment.

Overall, 9% of BM (15,242) with LRPC were managed with AS. The likelihood of BM undergoing AS increased from 2010 and for all subsequent years of the study period (P<0.001). Uninsured BM were twice as likely as those with private insurance to undergo AS (odds ratio [OR]=1.97; 95% confidence interval [CI], 1.51-2.58; P<0.001). BM were less likely than WM (86,655) to receive AS (OR=0.82; 95% CI, 0.77-0.87; P<0.001). However, on multivariate analysis adjusted for SDCs, there was no significant difference in AS utilization between the two race groups. Nearly half of BM (47.5%) treated with RP had a post-RP GS≥7, and BM were 17% more likely to experience post-RP upgrading to GS≥7 when compared with WM (OR=1.17; 95% CI, 1.08-1.26; P<0.001).

The utilization of AS for BM with LRPC seems to be increasing, is influenced by SDCs, and may not differ from AS utilization among WM. Careful consideration of prostate biopsy technique and sampling as well as SDCs at time of treatment planning may be necessary to ensure adequate evaluation of prostate disease and appropriate disease management for BM with LRPC.
Sipuleucel-T Could Be More Widely Used for Advanced Prostate Cancer

More men with advanced prostate cancer could benefit from immunotherapy with sipuleucel-T, according to researchers who found use of the drug was influenced by income and other factors.

“Prostate cancer is a disease that affects men of every race, income level, and in every part of the country,” Dr. Megan V. Caram of the University of Michigan, in Ann Arbor, told Reuters Health by email. “Therefore, it is important that future work be done to investigate and identify disparities in use of therapies for prostate cancer. Identifying disparities is an important first step in working toward ensuring that treatment of patients is based on their disease and not their income, race, the doctor that they see, or where they live.”

Sipuleucel-T was approved by the U.S. FDA in 2010 for use in metastatic castration-resistant prostate cancer (mCRPC) with minimal or no symptoms. It met with considerable initial skepticism as the first treatment of its kind, and its use remains controversial despite evidence of its efficacy and safety.

Dr. Caram’s team used data from the Clininformatics Data Mart Database to investigate patient, physician and regional factors associated with the adoption of sipuleucel-T. Among the 7,272 men included in the study who received treatment for mCRPC, only 730 (10.0%) received sipuleucel-T, a fraction that increased from 0.6% in 2010, peaked at 15.1% in 2012, and then fell to 8.6% by 2016.

“Most patients who received sipuleucel-T (69.0%) received it as first-line treatment, and most (68.2%) received subsequent therapies,” the researchers report in JAMA Network Open, online April 19. Nearly 10% of men treated with sipuleucel-T received it concurrently with other therapies, which is a non-evidence-based practice.

After adjusting for all other variables, Hispanic ethnicity and living in the Pacific region were independently associated with lower odds of receiving sipuleucel-T. Meanwhile, higher household income, having preferred provider organization insurance and treatment by a urologist were independently associated with higher odds of receiving the drug.

“In my opinion, the most important take-home point is the difference in use of sipuleucel-T at different income levels,” Dr. Caram said. “This difference may be explained by an element of financial toxicity since many patients are still required to pay a significant amount out-of-pocket for this therapy. It’s also possible that patients of lower income do not have access to centers that offer sipuleucel-T, or are not being offered this therapy by their provider. Future studies will help elucidate the reason behind the income level difference.”

“It is encouraging that we found most providers are using sipuleucel-T as first-line therapy in patients, the period of their disease when we would expect most patients would have the fewest symptoms and the lowest volume of their disease,” she said. “However, it is still unknown when the optimal time will be and in which patients sipuleucel-T will provide the most benefit.”

‘Fake News’ in Urology: Evaluating the Accuracy of Articles Shared on Social Media in Genitourinary Malignancies


BJU International 13 May 2019; Epub ahead of print

The objective of this study is to evaluate the accuracy of the most popular articles on social media platforms pertaining to genitourinary malignancies and to identify the prevalence of misinformation available to patients.

The 10 most shared articles on popular social media platforms (Facebook, Twitter, Pinterest, and Reddit) were identified for prostate cancer, bladder cancer, kidney cancer, testis cancer, and PSA testing using a social media analysis tool (August 2017 and August 2018).

Articles were reviewed for accuracy by comparing the article information against available scientific research and consensus data. Each article was classified as accurate, misleading or inaccurate. The Mann-Whitney U-test was used for statistical comparison.

Articles pertaining to prostate cancer were the most shared across all social media platforms (399,000 shares), followed by articles pertaining to kidney cancer (115,000), bladder cancer (17,894), PSA testing (8,827) and testicular cancer (7,045).

The prevalence of inaccurate or misleading articles was high: prostate cancer, 7/10 articles; kidney, 3/10 articles; bladder, 2/10 articles; testis, 2/10 articles; and PSA testing, 1/10 articles.

There was a significantly higher average number of shares for inaccurate (54,000 shares; P <0.01) and misleading articles (7,040 shares; P <0.01) than for accurate articles (1,900 shares).

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 Us TOO web page for important information on recognizing and managing anxiety, depression and prostate cancer.

www.ustoo.org/anxiety-and-depression
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, “Packing a PUNCH...”** The timing of using chemotherapy for prostate cancer is slowly changing. High-risk men with metastatic disease appear to have a benefit from receiving chemotherapy at the outset rather than waiting until disease progression. Now a study from Memorial Sloan Kettering raises the possibility of using chemotherapy prior to radical prostatectomy in high-risk men. Although the study did not reach its primary objective, the lead author still believes that some men will benefit from receiving early chemo/hormone therapy. A well-recognized prostate cancer expert criticized the author’s conclusion, arguing that proof of benefit was not achieved, so its use should be restricted to clinical trials.

The **Bottom Line:** Chemo/hormone therapy prior to radical prostatectomy in men with high-risk disease does not yet show a benefit.

**P1, “Gleason Score 8 PCa...”** Men with high-risk prostate cancer (Gleason >7) are at higher risk for disease progression and are often given combination therapies to maximize their likelihood of survival. Given they need more aggressive therapy, it is critical to make sure that a patient does indeed have high-risk disease. The study by Peckiam and co-workers quantified the proportion of men whose initial biopsy showed Gleason 8 disease were downgraded after undergoing radical prostatectomy. Results showed that nearly one-half of all men were downgraded. Further analyses were done to determine factors more likely to predict downgrading.

The **Bottom Line:** Men with Gleason 8 disease on biopsy have nearly a 50% chance their cancer will be downgraded on the final pathological section so caution is needed to insure they are properly graded before proceeding to treatment.

**P1, “Transrectal Exit...”** Should transrectal biopsies become a thing of the past? That opinion might be evolving in the UK where more and more clinicians are performing prostate biopsies via the transperineal approach. In a feasibility study involving 678 men, the complication rate using transperineal prostate biopsies was very low. In particular, the rate of sepsis (bacterial infection in the blood) was about 0.2%, which is much lower than the approximate 3% rate reported with transrectal biopsies. Although a large percentage of men were biopsied under general anesthesia, researchers believe that use of a local anesthesia may vary considerably exposing more patients to discomfort.

The **Bottom Line:** A movement is developing to promote widespread acceptance of the transperineal biopsy in place of the transrectal approach.

**P4, “Prostate Cancer...”** Is prostate cancer becoming a more aggressive disease? The findings by Patel and co-workers raise that possibility. They found that the incidence of metastatic disease increased from 2007-2015 and the incidence of non-metastatic disease declined during that time. One possible explanation is that improvements in imaging, such as the greater sensitivity of PET scans could be an explanation; and the other is changes in the approach to screening for the disease. A third explanation is that environmental changes are making more aggressive cancers. Hopefully, nothing really has changed other than that doctors are able to find early metastatic disease sooner than they used to.

The **Bottom Line:** The percentage of men found to harbor metastatic disease at diagnosis is increasing.

**P6, “Sipuleucel-T...”** Since its approval, sipuleucel-T has not been widely accepted. One reason is that its efficacy hasn’t been widely accepted. Approval, sipuleucel-T. Regardless of the obstacle, physicians have a responsibility to tell their eligible patients of this treatment.

The **Bottom Line:** Social media is used to disseminate medical information, however it is frequently inaccurate or contains misinformation; therefore, doctors should communicate to their patient their concerns about using social media as a source of medical information.

**Video is Available from:**

Prostate Cancer Pathways Educational Event and Webcast

With Content Specific to:
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- Advanced Stage Disease and Immunotherapy
- Meditation
- Men’s Health
- Integrative Medicine
- Prostate Cancer 101
- Localized Disease

Access direct links to video pertaining to each specific topic at: [https://ustoo.org/Pathways-EnglewoodNJ](https://ustoo.org/Pathways-EnglewoodNJ)
A novel ablative technology for prostate cancer (PCa) doesn’t leave much of the gland behind after a typical treatment, reducing prostate size by 90% (41 to 4 cm³), according to a new study reported at the 2019 American Urological Association (AUA) annual meeting.

“Magnetic resonance-guided transurethral ultrasound ablation (TULSA) is a relatively new procedure for localized PCa,” said lead author Scott Eggener, MD, urologist, University of Chicago, at an AUA press briefing.

The new phase 2 study was done at 13 institutions in five countries. TULSA is done in an MRI suite, under general anesthesia, with a team that includes a urologist and radiologist. The cancer and prostate are mapped via a transurethral probe.

The median pre-treatment PSA was 6.3 (range 4.6-7.9) ng/mL and median age was 65 years. Seventy-two (63%) of 115 men had Grade Group 2 (GG2) PCa, also known as Gleason score 3+4 or higher. The median post-treatment PSA was 0.34 ng/mL, which is “really darn low, and 96% of men met the primary endpoint of ≥75% PSA reduction.” Eggener acknowledged that other technologies that fully ablate the prostate have yielded PSA reductions “in this ballpark.”

Median treatment duration was 51 minutes. That impressed Alan Priester, PhD, urology researcher, University of California, Los Angeles. “Radical prostatectomy (RP) takes hours, as do many MR-guided interventions such as high-intensity focused ultrasound (HIFU) or laser ablation,” he said.

The reported treatment time did not account for the time spent on patient prep and MR localization. Nonetheless, Priester said, “It is still an impressive reduction in procedure time, which could help lower procedure costs and improve safety.”

Grade 3 adverse events occurred in nine (8%) men, including infections (4%), urethral stricture (2%), urinary retention (2%), urethral calculus and pain (1%), and urinary (1%), all resolved. There were no rectal injuries or Grade 4 or higher events. Of 112 men with one-year continence data, 1% were incontinent (more than one pad/day), daily leakage increased 4%, and 8% wore a pad. Median International Prostate Symptom Score was unchanged at one year.

At one year, 20% of men had Grade 2 erectile dysfunction. However, 69/92 (75%) men maintained erections sufficient for penetration. Presented at the 2019 AUA meeting: Abstract LBA26.

Medscape Medical News 10 May 2019

Downgrading

(Continued from page 1)

The median follow-up duration among survivors was 5.8 years. Downgraded men had significantly improved oncologic outcomes, including 10-year biochemical recurrence-free (66 vs. 29%), progression-free (75 vs. 51%), and PCa-specific (97 vs. 84%), and overall survival (86 vs. 74%).

Dr. Packiam noted that characterization of risk factors for pathologic downgrading of cGG4 disease potentially can allow men to be managed with intermediate-risk radiation therapy/androgen deprivation therapy (ADT) protocols. For example, Dr. Packiam said a man with risk factors for downgrading may benefit from four-to-six months of ADT (intermediate-risk protocol) rather than 18 to 36 months of ADT (high-risk protocol). However, this approach would require prospective validation.

Presented at the 2019 AUA meeting, Abstract MP09-11.

Renal & Urology News 3 May 2019

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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.

Between the Sheets...

June 2019

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:

My partner and I are struggling with our changing sex life because of my lack of erection rigidity after my prostate surgery during sex. We have been together for more than 20 years and over the year since my surgery, I have begun to get partial erections, but they are still not hard enough for sex, even with the pills. Any advice on how we can continue to enjoy sex, given my lack of erection rigidity?

RESPONSE FROM DR. JEFFREY ALBAUGH:

I think you are not alone in your feelings of frustration in dealing with a lack of an erection rigid enough for sex. It is very frustrating to not be able to do the sexual things you enjoy. I think it is most important for you and your partner to communicate and discuss sex (outside the bedroom and away from the times you are having sex together). What are your goals in terms of sex together? It will help to discuss the underlying goals of sex. Many enjoy the connectedness with their partner that occurs with intimacy and sex, as well as the pleasure of giving and receiving sexual stimulation together. Determining your mutual goals can help you determine necessary steps for the future in terms of treatments.

If you need to be rigid enough for penetration to reach your goals with sex, you need to consider the various treatment options carefully. The oral agents are not working for you, so you need to determine which of the other options you are willing to try given the pros and cons of each option. Local therapies, such as the vacuum device and penile injections, often work better than oral agents after prostate cancer treatment. The vacuum device is non-invasive and can work in up to 90% of patients with lots of practice and patience, but it is cumbersome and awkward, and you have to wear a ring during sex. The injections give you a more natural feeling erection without needing a ring to hold the hardness, but you have to inject the penis each time you want to have sex, and some people get side effects. Side effects of injections may include pain, bleeding/bruising, priapism (prolonged erection) and scarring. If medical treatments are not satisfactory and/or not something you want to do, and you have eventually completed any recovery of erectile function after surgery (which can take an average of 2 years and up to 5 years), the penile implant is a surgical option. The implant is completely internally placed in the operating room. It has pros and cons, as with any treatment, and you need to understand them completely. The main complaints I hear are pain (which does get better over time, but it is a sensitive place to have surgery) and shortening (they have to leave some tissue at the end of the penis as a cushion for the device, so it doesn’t erode through the end of the penis). There are many other things to consider, and the placement of the implant cylinders in the penis will permanently change the structures within the penis.

If you and your partner do not need to have a hard erection to enjoy connectedness, pleasure and orgasms together, you can continue to enjoy non-penetrative sex. Either way, I would highly encourage you to enjoy your intimate time together by being fully present with each other and embracing the connection you share along with the pleasure. You should be able to orgasm regardless of erection hardness through oral, manual or vibratory stimulation. It might be helpful for you and your partner to work with a sexuality counselor or therapist to further explore ways to maximize pleasure during sex.

You can access the new edition of my book or download a free copy of my original book at [www.drjeffalbaugh.com](http://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](https://www.youtube.com/watch?v=Hiq0dDEb1l0&t=4483s).

Read previous issues of Between the Sheets at [www.ustoo.org/BTS](http://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
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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.

A New Standard of Care for Low-Volume Metastatic Prostate Cancer
Men diagnosed with metastatic prostate cancer will often not undergo local treatments, such as surgery or radiation, of the primary prostate tumor. Primary hormone therapy (also known as androgen deprivation therapy or ADT) has long been the standard of care, although recently the addition of docetaxel or abiraterone to ADT has become a standard of care option. In March, the National Comprehensive Cancer Network (NCCN) released its 1.2019 version of guidelines for prostate cancer. For men with low-volume metastatic disease who have not previously been treated with hormone therapy, there is an important update: the option of radiation therapy (RT) to the prostate in addition to ADT (unless medically contraindicated).

Digging Deeper Into Trial Results
This update is based on results of a large randomized controlled trial called STAMPEDE. But before STAMPEDE, there was another trial called HORRAD, the first study adding RT to ADT in patients with metastatic prostate cancer. In the analysis of all 400+ patients in the HORRAD trial, there was no difference in overall survival. Taken at face value, adding RT “didn’t work.” Case closed?

Not so fast … because, when researchers looked at a small subset of patients who had a low number of metastatic disease sites, they saw a suggestion of a survival benefit.

A Large European Trial
STAMPEDE is a very large multi-arm, multi-stage trial conducted in Europe that is comparing the efficacy of several different treatment regimens in men with prostate cancer who are starting long-term ADT. Within the overall trial, one “arm” looked specifically at the benefit of adding RT to ADT in patients with metastatic disease. There were two treatment groups (ADT, and ADT + RT), each with more than 1000 patients. Eighteen percent of the patients in each group also took docetaxel and, prior to the trial, the groups were similar to each other in other important ways.

Once again, as in the HORRAD trial, when looking at the entire patient cohort, no benefit was seen with RT to the prostate added to ADT. However, when analyzing only the patients with a low metastatic disease burden, the researchers saw a 32% reduction in the risk of death. More patients in the RT group (81%) were alive after 3 years, compared to the group that received only ADT (73%).

This is why the “random” assignment of patients to treatment groups is so important: We know that it’s very likely that the RT group survived longer than the no-RT group because of the addition of RT, not because the RT group had less severe disease or was otherwise in better shape.

But wait … what about side effects of radiation? The study also assessed toxicity, and found no difference in rates of severe events between the two treatment arms.

Based on this large, well-designed trial, the National Comprehensive Cancer Network (NCCN) guidelines were updated in March 2019 to recommend RT to the prostate in combination with ADT as the new standard of care for men with low-volume metastatic prostate cancer who have no contraindications to RT. Talk to your doctor about whether this approach is right for you.


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