Incidence of Aggressive Prostate Cancer Diagnoses Declining in the United States

High Gleason score prostate cancer in the US is declining in incidence among all races, according to findings presented at the 17th Annual Meeting of Society of Urologic Oncology (SUO). Using the Surveillance, Epidemiology and End Results (SEER) database, a team at Saint Louis University in Missouri led by Sameer Siddiqui, MD, examined the effect of the 2008 and 2012 guidelines issued by the US Preventive Services Task Force (USPSTF) stating there was insufficient evidence to support prostate cancer screening. The study included 337,504 men diagnosed with prostate cancer from 2008 to 2013 having an average age range of 65 to 74 years. The investigators categorized Gleason score (GS) as low (GS 2–6), intermediate (GS 7), and high (GS 8–10). Low, intermediate, and high GS were recorded for 42%, 36%, and 16% of the men, respectively. The GS was unknown for 6% of the patients.

From 2008 to 2013, the incidence of GS 8–10 disease (per 100,000 men) decreased from 21.7 to 19.4 among white men, 39.5 to 33.7 among black men, 22.8 to 19.0 for Hispanic men, and 17.7 to 13.8 among Asian/Pacific Islanders. The trend suggests decreased diagnosis of aggressive prostate cancer following issuance of the USPSTF guidelines, stated the investigators. Over the six-year study period, black men had the highest cumulative incidence of low GS cancer (76.2 per 100,000), followed by white men (52.9 per 100,000), the researchers reported in a poster presentation. The cumulative incidence of high GS cancer was 21.0 per 100,000 for black and (Continued on page 8)

Physicians Continue to See Merits of PSA Testing

Although about two fifths of all of physicians (40%) in a recent Medscape poll said they believe the PSA test is overused, a huge majority (90%) said the benefits of the test always, often, or sometimes outweigh the risks, and many frequently recommend a baseline diagnostic for their male patients. The poll results reflect the minefield detection of significant cancer at the time of the repeat biopsy,” Dr. Rosenkrantz said. Prostate MRI, when used, should done in accordance with the guideline.

(Continued on page 5)

FEBRUARY 2017

INSIDE
AUA Consensus Statement Says Use MRI for Prostate Biopsy
Incidence of Aggressive Prostate Cancer Diagnoses Declining in US
Physicians Continue to See Merits of PSA Testing for Screening
HIFU vs. Robotic Prostatectomy to Manage Unilateral Prostate Cancer
Inherited Mutations in Three Genes Predict Aggressive Prostate Cancer
Doc Moyad’s No Bogus Science: “Turmeric/Curcumin Supplements?!”
Extraprostatic Extension Rare in Prostate Score 6 Prostate Cancer
Light Therapy ‘a Huge Leap Forward’ for Early Prostate Cancer
Effect of Longer vs. Standard Dosing Intervals of Zoledronic Acid
Prostate Cancer Patients on AS May Benefit from MRI/Fusion Biopsy
Doctor Chodak’s Bottom Line

PROSTATE CANCER HELPLINE: 1-800-808-7866 WWW.USTOO.ORG

AUA Consensus Statement Says Use MRI for Prostate Biopsy

Men with suspected prostate cancer who have had a prior negative biopsy should undergo high-quality prostate magnetic resonance imaging (MRI) instead of, or before, a repeat biopsy if the technology and interpretative skills are available, according to a consensus statement from the American Urological Association (AUA) and Society of Abdominal Radiology published in the December issue of The Journal of Urology.

The recommendation is based on the results of a literature review by Andrew B. Rosenkrantz, MD, from the New York University Langone Medical Center, New York City, and colleagues, which showed that prostate MRI and subsequent MRI-targeted cores are more effective than standard repeat biopsies alone for detecting prostate cancer in this population.

“This guideline is a departure from current clinical practice,” Dr. Rosenkrantz said in an interview with Medscape Medical News.

“Currently, if a patient has a systematic negative prostate biopsy and there is persistent concern for prostate cancer, another biopsy may again be done in a systematic, non-targeted, fashion,” he explained. “This new joint statement encourages an MRI before the repeat biopsy to help find suspicious areas in the prostate missed by the first biopsy, so as to provide a target during the repeat session.”

Available data indicate that targeting the MRI-defined areas will increase the detection of significant cancer at the time of the repeat biopsy,” Dr. Rosenkrantz said. Prostate MRI, when used, should done in accordance

(Continued on page 6)
Comparing High Intensity Focal Ultrasound Hemiablation to Robotic Radical Prostatectomy in the Management of Unilateral Prostate Cancer: A Matched-Pair Analysis
J Endourol 30 November 2016; Epub

Introduction: Although still experimental, focal treatment is being increasingly implemented in the management of prostate cancer (PCa). The aim of the current study was to compare functional and oncologic outcomes of high-intensity focal ultrasound (HIFU) hemiablation of the prostate to robot-assisted laparoscopic prostatectomy (RALP) in the management of unilateral PCa.

Materials: Fifty-five men with unilateral, clinically localized PCa underwent HIFU hemiablation of the affected prostatic lobe between 2007 and 2015. All patients were found to have unilateral disease on the basis of full concordance between multiparametric magnetic resonance imaging (MRI) and MRI-guided biopsies. These patients were matched 1:1 with patients who underwent RALP for PCa in which pT2a-b disease (unilateral) was found on final pathologic analysis. Matching criteria were Gleason score, prostate specific antigen (PSA), and clinical stage. Treatment failure was defined as the need for salvage external beam radiotherapy or systemic androgen deprivation therapy (ADT) due to disease progression. Kaplan-Meier curves and log-rank tests were constructed to assess differences in salvage treatment-free survival across surgical techniques.

Results: Matching was effective with no significant differences across the two groups, although men treated with HIFU were older (p < 0.001). Median follow-up was 36 months (interquartile range 16-56). HIFU was associated with better and faster recovery of continence, with most men (82%) showing no signs of urinary incontinence even right after surgery. Moreover, the risk of de novo erectile dysfunction was significantly lower after HIFU. No significant difference was found in the need for salvage external beam radiation therapy or ADT across the two surgical approaches: 7/55 men underwent salvage therapy in the HIFU vs. 6/55 in the RALP group (p = 0.76). Nonetheless, seven more patients in the HIFU arm required a complementary treatment on the contralateral lobe during follow-up, after developing a contralateral PCa. No patient died of PCa on follow-up, while six men died of other causes (five HIFU vs. one RALP, p = 0.11).

Conclusion: In this matched pair analysis, HIFU hemiablation was comparable to RALP in controlling localized unilateral PCa, with no significant differences in the need for salvage therapies. HIFU was also associated with significantly better functional outcomes. Accurate patient selection remains vital, and larger prospective trials are needed to confirm our findings.

Inherited Mutations in Three Genes Predict Aggressive Prostate Cancer

Summary: A new study of three genes associated with the development of prostate cancer found that men with inherited mutations in these genes are more likely to develop aggressive forms of the disease and die from prostate cancer at an earlier age than those without the mutations. The findings affirm previous studies and could have important implications in screening and treatment protocols for prostate cancer. The study published online ahead of print in the journal European Urology looked at germline mutations in the ATM and BRCA1/2 genes and represents important progress on the goal of being able to predict which men are more likely to develop a lethal form of prostate cancer versus an indolent one.

“Study results have an important translational impact because they clearly demonstrate that germline mutations in these three well-established genes can be used to predict risk for lethal prostate cancer and time to death,” said Jianfeng Xu, MD, DrPH, vice president of translational research at NorthShore University Health System (NorthShore) and director of the Program for Personalized Cancer Care. “This confirms major findings from previous studies and provides further direct evidence of the important role of genetic testing in prostate cancer screening and treatment.”

The study was a collaboration of NorthShore, the Johns Hopkins University School of Medicine (William Isaacs, PhD, et al.), and Fudan Institute of Urology, Fudan University (Qiang Ding, MD, et al.), in Shanghai, China. It is a retrospective case study of 313 patients with lethal prostate cancer and 486 with indolent prostate cancer in men of European American, African American and Chinese ancestry.

(Continued on page 4)
One of the hottest supplements in the US is turmeric and/or one of the potentially active ingredients in the spice known as “curcumin.” It is an anti-inflammatory darling with preliminary data showing that it fights cancer, arthritis, depression and blah blah blah. However, it may increase the risk of kidney stones (especially turmeric supplements); it did not work in one recent prostate cancer study, and has other issues. Well, you could call this objective reporting or just real life.

Turmeric contains a compound that is responsible for the yellow color of this spice and it has some ingredients (in theory) that seem to have anti-inflammatory effects. And, the name of that compound is “curcumin.” As a part of a supplement to reduce PSA it showed some preliminary activity in men with localized prostate cancer. Also, it was recently combined with chemotherapy for castrate resistant prostate cancer (CRPC) in a new small study. Importantly, this is preliminary research and results DO NOT convincingly demonstrate that curcumin is having this impact because it has been combined with drugs or other compounds. In addition, preliminary research studies suggest that it could help in the treatment of depression and even treat different types of arthritis. Yet, it is really tough to find someone or something that tells you the catch with turmeric and/or curcumin. And, I have learned in this life that if something wonderful does NOT come with a catch then something is really wrong. Heck, everything in life comes with some kind of catch! That of course excludes me, my wife, kids, dog, and Michigan Football – they/we are all perfect with no flaws (now clearing of my throat).

So, then what is the catch with turmeric supplements? They are high in soluble oxalates, which means they absolutely could increase the risk of kidney stones (curcumin not as much but this has not been well tested and studied). And, in another recent study of prostate cancer patients receiving radiation treatment, curcumin appeared to have no impact (aka did nothing), but this is also preliminary short-term research.

And, in most of these other cancer studies the dosages being used are no joke, for example 6,000 mg a day with chemotherapy (that equates to 12 CAPSULES PER DAY, in some cases more, and in some cases slightly less). So, there is definitely the potential for toxicity with these dosages. Oral intake can cause nausea and diarrhea and intravenous administration may potentially cause a change in blood cells. This has caused some cancer trials to be stopped early or dosages to be reduced because of side effects.

I am excited about seeing what curcumin could do at 500, 1,000 or 1500 mg – similar to the doses being tested for other medical conditions outside of cancer. Failing to mention the potential catches does not do anyone any favors except some folks that sell turmeric/curcumin supplements that claim it is the greatest thing since sliced pizza. Don’t get me wrong, I am excited about the role of curcumin in some areas of medicine but I am not overly excited that it causes me to fail to mention the catches!

I’ve got to go eat some sliced pizza! Hope this story spiced up your life (pun intended).
Light Therapy ‘a Huge Leap Forward’ for Early Prostate Cancer Treatment

Results of a phase III clinical trial suggest that light therapy may be an effective, non-surgical therapy for men with low-risk prostate cancer (PCa), after finding that almost half of study participants with PCa went into complete remission after the novel treatment procedure.

In a study of more than 400 men with localized PCa, researchers reveal that the new treatment – called vascular-targeted photodynamic therapy (VTP) – can kill PCa cells, without damaging the healthy surrounding tissue. Furthermore, VTP was found to significantly reduce the need for radical therapy.

VTP was developed by the Weizmann Institute of Science inIsrael, in collaboration with STEBA Biotech. Lead investigator Prof. Mark Emberton MD, dean of medical sciences and a consultant urologist at University College London, U.K., and colleagues reported their findings in Lancet Oncology.

For men with localized PCa – active surveillance (AS) is often the first port of call. This is where the cancer is closely monitored through PSA tests, digital rectal exams, or prostate biopsies, and it is only treated if it becomes more severe. If PCa does worsen, treatment may involve radical prostatectomy (RP) or radiation therapy (RT). These procedures can pose a number of side effects, including bowel issues, incontinence, and lifelong erectile dysfunction.

Dr. Emberton suggests that VTP could reduce the need for such treatments. The treatment involves the injection of a light-sensitive drug called WST11 – derived from bacteria found at the ocean floor – into the bloodstream. Upon activation with a laser, the drug releases free radicals that destroy PCa cells in the prostate gland.

For their phase III trial, researchers Emberton and colleagues enrolled 413 men from 47 sites across 10 European countries, all with early localized PCa and under AS. Of these, 206 were randomized to receive VTP, and the other 207 continued AS (as the control group).

Men were followed-up for two years and assessed for PSA change, urinary and erectile functions every three months, plus annual prostate biopsies. After two years, 49% of men treated with VTP had entered complete remission, compared with only 13.5% that received AS.

Researchers also found that only 6% of men treated with VTP required radical therapy vs. 30% in the control group. The team also reports that VTP-treated men were three times less likely to have their PCa progress, and VTP was found to double the average time to progression from 14 months to 28 months. Noting the side effects of VTP, the researchers report that some men experienced urinary and erectile problems, but these resolved within three months of treatment initiation. At two years, no significant side effects were present.

The researchers believe that the findings of their phase III trial indicate that VTP is a promising nonsurgical approach to the treatment of localized PCa. “These results are excellent news for men with early localized PCa, offering a treatment that can kill cancer without removing or destroying the prostate,” notes Dr. Emberton.

He points out that PCa can

Inherited Mutations (Continued from page 2)

nese ancestry.

“Our aim is to find genetic markers among men who are at high risk of developing an aggressive prostate cancer,” said Dr. Isaac, the William Thomas Gerrard, Mario Anthony Duhon and Jennifer and John Chalsty Professor of Urology at the Johns Hopkins Brady Urological Institute and member of the Johns Hopkins Kimmel Cancer Center.

“Mutations in these genes, particularly BRCA2 and ATM, have been linked to aggressive prostate cancer, and this study provides important estimates of the frequency of mutations in men dying at different age ranges.”

The study found that the frequency of gene mutations in lethal prostate cancer patients (6.07%) was significantly higher than that observed in localized cancer patients (1.23%). Mutation carrier status was also significantly associated with more advanced prostate cancer at time of diagnosis, and among lethal prostate cancer patients an earlier death (67 years vs. 72 years in non-carriers). In addition, the median survival time after diagnosis was significantly shorter in carriers (four years) than the non-carriers (eight years). In contrast, no mutations were observed in 49 men dying from prostate cancer over the age of 80.

Study authors say the results have important clinical implications, and recommend that mutation carrier status be included as an important factor as clinicians make treatment decisions. Men who have their prostate removed may experience significant side effects, including incontinence and erectile dysfunction.

“We have made great progress in identifying molecular factors in prostate cancer development in recent years but what remains elusive is being able to distinguish cancers that are particularly aggressive versus ones that are likely to remain indolent, maybe for years,” said Brian Helfand, MD, a NorthShore urologist and an author of the study. “This is absolutely vital information to have when considering whether to aggressively treat a patient’s cancer or take an approach of active surveillance.”

Authors acknowledged the rate of mutations in these three genes in men with lethal prostate cancer is relatively low, pointing to the need for further studies that investigate other DNA repair genes. Members of this same research group have conducted similar such studies and recently had a letter published in the New England Journal of Medicine about the potential role of the DNA repair gene CHEK2 in prostate cancer and lethal prostate cancer.

Science Daily
15 December 2016

Do you know an outstanding volunteer in the Us TOO support group network who has shown exemplary, dedicated service to helping prostate cancer survivors and their families?

Recognize this special person with a nomination for an Us TOO Edward C. Kaps Hope Award.

Nominations are now open and will be accepted until Feb 9th.

For details, visit http://bit.ly/2isnKxg
Effect of Longer Interval vs. Standard Dosing of Zoledronic Acid on Skeletal Events in Men with Bone Metastases: A Randomized Clinical Trial

Himelstein AL, Foster JC, Khatcheressian JL, et al.

JAMA 3 January 2017; Epub ahead of print

Zoledronic acid (ZA), a third-generation aminobisphosphonate, reduces the incidence of skeletal-related events (SREs) and pain in patients with bone metastases. The optimal dosing interval for ZA is uncertain.

Trials were conducted to determine whether ZA administered every 12 weeks is noninferior to ZA administered every four weeks.

Randomized, open-label clinical trials conducted at 269 academic and community sites in U.S. Patients (n = 1,822) with metastatic breast cancer, metastatic prostate cancer, or multiple myeloma who had at least one site of bone involvement were enrolled between May 2009 and April 2012; follow-up concluded in April 2014.

Patients were randomized to receive ZA administered intravenously every four weeks (n = 911) vs. every 12 weeks (n = 911) for two years. The primary end point was the proportion of patients having at least one SRE (defined as clinical fracture, spinal cord compression, radiation to bone, or surgery involving bone) within two years after randomization and a between-group absolute difference of 7% as the noninferiority margin. Secondary endpoints included the proportion of patients with at least one SRE by disease type, pain as assessed by the Brief Pain Inventory (range, 0-10; higher scores indicate worse pain), Eastern Cooperative Oncology Group performance status 0-4 (where higher scores indicate worse disability), incidence of osteonecrosis of the jaw, kidney dysfunction, skeletal morbidity rate (mean number of SREs per year), and, in a subset of 553 patients, suppression of bone turnover (assessed by C-terminal telopeptide levels).

Among 1,822 randomized patients, (median age, 65 years; 980 [53.8%] women; 855 with breast cancer, 689 with prostate cancer, and 278 with multiple myeloma), 795 completed the study at two years. A total of 260 (29.5%) patients in the ZA every 4-week dosing group and 253 patients (28.6%) in the every 12-week dosing group experienced at least one SRE within two years of randomization (risk difference of -0.3% [one-sided 95% CI, -4% to +1%]; P <0.001 for noninferiority). The proportions of SREs did not differ significantly between the every-four-week vs. the every 12-week dosing groups for patients with breast cancer, prostate cancer, or multiple myeloma. Pain scores, performance status scores, incidence of jaw osteonecrosis, and kidney dysfunction did not differ significantly between treatment groups. Skeletal morbidity rates were numerically identical in both groups, but bone turnover was greater (C-terminal telopeptide levels were higher) among patients who received ZA every 12 weeks.

Among patients with bone metastases due to breast cancer, prostate cancer, or multiple myeloma, the use of ZA every 12 weeks compared with the standard dosing did not increase the risk of SREs over two years. This longer interval may be an acceptable treatment option.

Clinicaltrials.gov Identifier: NCT00869206

Physicians Continue to See Merits of PSA Testing

(Continued from page 1)

The Medscape poll showed that, despite the controversy, physicians are still recommending baseline PSA testing to their male patients. When asked how often they recommend such a baseline test, a quarter (26%) of the poll’s 680 respondents said “always,” while 61% said they “often” or “sometimes” urge the baseline. Only a small percentage of doctors said they “rarely” or “never” recommended a baseline PSA.

“It is only by following the changes from a known early baseline without interference from [benign prostatic hyperplasia] etc., that we can assist our patients to make informed decisions about their care, including watchful waiting, active surveillance (AS), or definitive Mx (medical treatment),” said Dr. Jan Sheringham, a family medicine specialist, in comments on the poll. “Yes, do no harm is our watchcry, but I believe we can actually cause harm by not doing this test appropriately and according to our current knowledge,” she wrote.

Internists and family practice specialists who took the poll seemed a tad less enthusiastic than urologists about PSA testing, but still embraced the diagnostic. Slightly more urologists said the benefits of testing “always” outweigh the risks — 14%, compared with 9% of internists and 11% of family medicine physicians. Forty-one percent of urologists said testing’s benefits “often” outweigh risks, compared with 26% of internists and 30% of family medicine specialists.

About a third (30%) of urologists said they “always” recommend a baseline PSA, compared with 21% of internal medicine specialists and 21% of family medicine doctors. Colleagues in hematology/oncology responded similarly, with 21% saying they always urge the baseline; more than half (59%) said they only “sometimes” recommend it.

“Screening for prostate cancer with a PSA and a [digital rectal exam] is fairly innocuous, and it entails only a blood test, and a very brief exam,” said James Benton, MD, an oncologist, in commenting on the poll.

Dr. Benton said screening is not the issue. “It is what one does with the information that is the real issue,” he said. “Medical bureaucrats should not be the arbiters of decisions to screen or not screen,” said Dr. Benton, adding, “A man in conjunction with his family and doctor should have an unstructured right to know if he has a cancer and make an informed decision as to how he will proceed with various treatment options — from AS, to radiation or surgery.”

General practice physician Chris Blair said it was perhaps just a matter of time before the proper balance was found with PSA testing. “Not so long ago, an increased PSA often lead to surgical removal by enthusiastic surgeons,” he wrote. “Now watchful waiting and AS, with other sophisticated diagnostics, is included in the discussion,” said Dr Blair.

“The pendulum oscillates from one extreme to another, and hopefully we learn, and the world becomes a better place.”

Medscape Medical News
16 December 2016
with Prostate Imaging Reporting and Data System, Version 2 (PI-RADS V2), guidelines, according to the consensus statement. The authors advise that men receiving a PI-RADS assessment category of 3 to 5 undergo repeat biopsy with image-guided targeting.

Further, practices that integrate prostate MRI into their patient management protocols “are advised to implement quality assurance programs to monitor targeted biopsy results,” the authors write. They note that the MRI techniques are relatively new and that the lack of standardization of image quality and variation in individual radiologists’ interpretation abilities can influence outcomes.

The motivation for the consensus guidelines was the “common and challenging clinical problem” of men with a prior negative biopsy who continue to have elevated or rising levels of PSA, the authors write. “Although general guidelines exist regarding the need for repeat biopsy, well-recognized consensus guidelines are lacking, and decisions are often driven by individual or local practice patterns.”

For example, current American Urological Association guidelines provide indications for the performance of the initial prostate biopsy only. The National Comprehensive Cancer Network recommends repeat biopsy after a negative biopsy when certain criteria are met and advises the consideration of MRI with additional MRI-targeted cores after at least one negative biopsy, but does not recommend MRI use explicitly.

The most recent European Association of Urology guidelines similarly list indications for repeat biopsy and suggest MRI with MRI-targeted cores in the case of persistent clinical suspicion after negative biopsies to rule out an anteriorly located tumor. The most recent imaging recommendations for prostate cancer diagnosis and staging from the American College of Radiology indicate that prostate MRI is usually appropriate when cancer is clinically suspected after negative biopsies.

On the basis of their literature review, the authors observed that the cancer detection rate for clinically significant cancer on MRI-targeted biopsy in the rebiopsy setting ranges from 11% to 54%, which is a greater yield than that achieved using standard systematic sampling alone.

The consensus statement, collaboratively developed by a panel of urologists and radiologists aimed “to generate as clinically relevant and practical a paradigm as possible,” according to Dr. Renscrazt. They hope it can help change how prostate cancer is diagnosed and monitored by providing more reliable biopsies, more accurate risk assessment, and potentially improved treatment options.

“The decision to perform MRI in this setting must also take into account results of any other biomarkers, cost of examination, as well as availability of high-quality prostate MRI interpretation,” the authors stress.

“If MRI is done, it should be performed, interpreted, and reported in accordance with PI-RADS V2 guidelines.”

Other recommendations are:

- The use of cognitive (visual) targeting by a skilled practitioner in the absence of advanced technologies, such as transrectal ultrasound–MRI fusion or in-bore MRI targeting;
- Obtaining at least two targeted cores from each MRI-defined target;
- Making case-specific decisions whether to also perform concurrent systematic sampling, because multiple studies have shown that MRI-targeted cores miss a proportion of clinically significant cancers;
- Performing solely targeted biopsy only when quality efforts have validated the performance of prostate MRI interpretations with results consistent with the published literature;
- Use of ancillary biomarkers in men with a negative or low-suspicion MRI, PI-RADS assessment category of 1 or 2, respectively) to determine whether or not repeat systematic biopsy is warranted; and
- Continuing clinical and laboratory follow-up in low-suspicion MRI patients in whom repeat biopsy is deferred, and possibly incorporating repeat MRI into the surveillance regimen.

Medscape Medical News
12 December 2016

Prostate Cancer Patients on Active Surveillance May Benefit from MRI/Fusion Biopsy

MRI/fusion targeted prostate biopsy may improve detection of clinically significant tumors in cancer patients on active surveillance (AS) undergoing confirmatory biopsy, researchers reported at the Society of Urologic Oncology (SUO) 17th Annual Meeting in San Antonio, TX.

“Seventy percent of AS patients have MRI-detectable lesions, most of which are consistent with low-grade disease,” senior author J. Kellogg Parsons, MD, MHS, of UC San Diego, told Renal & Urology News. “MRI/fusion targeted biopsy in PI-RADS 4/5 lesions was superior to systematic biopsy for detecting clinically significant disease, suggesting that MRI and selective, targeted biopsy of PI-RADS 4/5 lesions should be considered in AS.”

First author Zachary Hamilton, MD presented the study results. MRI/fusion targeted biopsy (TB) was compared to standard ultrasound-guided systematic biopsy (SB) for detecting Gleason 3+4=7 or higher disease in 356 AS patients. A total of 195 (58%) men underwent prostate MRI after the initial biopsy. Of these, 138 (71%) had MRI-detectable prostate lesions. After TB implementation, 42 AS patients underwent confirmatory MRI/fusion TB: nine (21.4%), 19 (45.2%), seven (16.7%), and seven (16.7%) with PI-RADS 2, 3, 4, and 5 lesions, respectively. MRI-guided biopsy of the 14 men with PI-RADS 4/5 lesions upgraded 12 (85.7%) men. By comparison, of 106 men who underwent confirmatory SB, 30 (28.3%) had an upgrade.

The study revealed a significantly higher rate of disease upgrading associated with PI-RADS 4-5 lesions when compared with PI-RADS 1-3 lesions (85.7% vs. 14.3%) and TRUS-guided SB (85.7% vs. 28.3%). Additionally, PI-RADS 4-5 lesions were significantly and independently associated with 16-fold increased odds of upgrading on repeat biopsy. Upgrading of disease was significantly associated with nearly 5.8-fold increased odds of progression to definitive local therapy.

Presented at the 17th Annual SUO Meeting, San Antonio, TX; Poster 95
Renal & Urology News
4 December 2016
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, “AUA Consensus...” To MRI or not to MRI, that is the latest question? The AUA has issued a new recommendation for men with one negative prostate biopsy and are advised to have a repeat biopsy due to a change in condition. Rosenkranz and co-workers showed that MRI had a higher detection rate for clinically significant disease (CSD), which they defined as a Gleason score of 7 more. If the clinical suspicion was low, the chances of missing CSD were low. However, MRI does miss a small percentage of significant cancers. Therefore, appropriate follow-up is needed and other biomarkers may help determine if another biopsy should be done. While not standardized, guidelines for performing and interpreting MRIs have been established, so going forward, higher quality imaging should be forthcoming.

The Bottom Line: AUA now recommends MRI to guide a second biopsy where the first one was negative.

P1, “Incidence of...” In 2012, the USPTF concluded that routine screening was no longer recommended because they believe the harms outweigh the good. Many people are concerned that, without screening, the prostate cancer mortality will begin to rise. Recent surveys show that screening has indeed declined along with prostate cancer detection. Now we have a report by Siddiqui who looked at the SEER database and found that there has been a drop in the detection of high-grade disease among all ethnic groups. One may conclude that this is a result of decreased screening. If concerns about not screening are correct, we may see a rise in the detection of men with metastatic disease over the next few years among men that might have been detected earlier with routine screening. Everyone should realize that without screening, mortality may rise by a small percentage. However, the task force recommendation was based on what is best for society rather than what is best for individuals. Despite finding more cancers at an earlier time, screening still resulted in too many men being harmed by diagnosis and treatment. As greater effort is made in NOT treating low-risk disease, this balance may shift back toward screening. Despite the recommendation, a significant percentage of internists and urologists continue to believe that screening should be done and they get a baseline for their patients.

The argument is that screening is not the problem but overtreatment of non-life threatening cancers is the problem. Time will tell which approach is better.

The Bottom Line: High-grade disease is being diagnosed less often since the new USPTF guideline. More time is needed to see if a greater proportion of advanced cancers are diagnosed and if prostate cancer mortality begins to rise again.

P2, “Comparing High...” Another article on HIFU is included in this issue and again the problem is the information is too short-term to know what it means. Albisinni, et al. conducted a case matched evaluation of 55 men receiving HIFU hemi-ablation and compared them to men undergoing radical prostatectomy (RP). With only 36 months follow-up, the authors found that a second treatment to cancer on the opposite side of the gland as needed in more men treated with HIFU. There are extensive limitations of this analysis. First, the abstract does not define the percentage of men with Gleason 6 cancer, most of whom might have never needed therapy. Also, 36 months is far too early to assess relative efficacy. Finally, regardless of the long-term results, this study will be unable to prove if hemi-ablation with HIFU is an appropriate alternative to whole gland therapy.

The Bottom Line: The value of HIFU hemi-ablation will remain unknown for years to come unless a properly designed study is conducted.

P3, Extraprostatic...” How dangerous is Gleason 6 prostate cancer? Some argue that it lacks the ability to metastasize, which is why AS is a reasonable option. Supporting this concept is the study by Anderson and co-workers who found that the risk of finding extracapsular extension following RP for a pathologically-confirmed Gleason 6 was less than 1%. Seminal vesicle invasion was not found in this large cohort. What is difficult to assess from this report is whether, left untreated, this cancer would transform and invade outside the gland. It certainly adds strength to the need to weed out those men who harbor higher-grade disease. Longer follow-up of men with Gleason 6 disease on AS who do get treated will help further define the risk of this grade of disease. The key is to make sure from the outside that only Gleason 6 is present in a man’s prostate before proceeding to AS.

The Bottom Line: The risk of finding extracapsular disease in a man with only Gleason 6 cancer is extremely small, which makes active surveillance a very appropriate treatment option.

P4, “Light Therapy...” An interesting new treatment called vascular targeted photodynamic therapy (VTP), developed in Israel, uses a laser to activate a drug injected into the bloodstream. The laser then affects blood vessels in the prostate leading to cancer cell death. The latest report is very encouraging, although more data will be needed. In the present study, VTP was compared to AS and the percentage of men that needed definitive therapy was determined. In other words, mostly low-risk men were being treated. If it only offered men an alternative to AS, would that be enough to justify the high cost? Theoretically, it could be used for higher-grade disease and, if that is attempted, we will need to see how well it compares to surgery or radiation. For now, it is exciting to see something that has low morbidity for men with a low risk of disease progression.

The Bottom Line: VTP therapy is a new therapy for men with low-risk disease but longer follow-up is needed to determine if disease recurrence will occur.

P5, “Effect of Longer...” Men with metastatic prostate cancer are at risk of developing a skeletal related event (SRE); e.g., bone pain, fractures, and cord compression. Two drugs are currently approved to reduce this risk, (Continued on page 8)
**The Bottom Line** (Continued from page 7)

denosumab and ZA. Currently, denosumab does not require routine testing for renal function before administration and it can be given subcutaneously, whereas ZA is given intravenously and requires prior kidney function testing. The two have not been compared directly with one another. So which one should we choose? The large randomized study reported by Himelstein, et al. provides data showing that giving ZA every two months is not inferior to monthly dosing for which it was initially approved. This decreased frequency does add one advantage to using it, but if that is enough to overcome the injection method and need to undergo regular blood work will be an ongoing discussion between patient and doctor.

**The Bottom Line:** Administering ZA every two months is no less effective than monthly dosing and may make it a more acceptable alternative to denosumab.

P6, “Prostate Cancer...” The decision to offer AS to a man with low-risk disease always presents a risk that undergrading may occur. For that reason, many clinicians recommend a repeat biopsy to confirm the Gleason score before advising their patients. A study by Hamilton and co-workers looked at MRI-fusion biopsy compared to standard biopsy and found that MRI was less likely to miss a higher-grade cancer. Authors suggest that confirmatory biopsies be used when a man is considering AS. This study has similar findings to the report on using MR for repeat biopsies after the first biopsy is negative and provides growing support for replacing standard biopsy in these settings. More reports will likely follow comparing standard and MRI biopsies for first time procedures to determine if routine MRI should initially be used.

**The Bottom Line:** Use of MRI-fusion biopsies is better than standard biopsy for determining if men should proceed with AS.

---

**Light Therapy**

(Continued from page 4)

now be identified using magnetic resonance imaging (MRI) and targeted biopsies, meaning that it is possible to identify men who are most likely to benefit from VTP and therefore deliver more precise therapy.

“With such an approach we should be able to achieve a significantly higher remission rate than in the trial and send nearly all low-risk localized PCa’s into remission,” he adds. “We also hope that VTP will be effective against other types of cancer – it should be translatable to other solid cancers including breast and liver cancer.”

VTP is currently being reviewed by the European Medicines Agency for the treatment of PCa. However, the researchers say that it is likely to be a number of years until VTP becomes widely available.

*Medical News Today* 20 December 2016

---

**High GS Cancer**

(Continued from page 1)

white men, respectively. The annual percentage change (APC) declined significantly among all races for low GS cancer (-8.9% for whites, -8.6% for blacks, -8.6% for Hispanics, and -8.7% for Asian/Pacific Islanders) and intermediate GS cancer (-8.6%, -6.5%, -9.2%, and -9.9% respectively). The APC for high GS cancer declined significantly for blacks and Hispanics (-3.5% and -4.4%, respectively), but did not change significantly among whites and Asian/Pacific Islanders.

Presented at the 17th annual SUO meeting in San Antonio, TX; Poster 98

*Renal & Urology News* 12 December 2016

---

**Hot SHEET Personal Subscriptions Available**

We can deliver the *Hot SHEET* newsletter right to your home or office. Support the creation and distribution of the *Hot SHEET* with a suggested annual subscription donation of $35 for 12 issues (includes shipping and handling). To obtain an order form or to order online, go to: www.ustoo.org/Hot_Sheets.asp, or Call 1-800-808-7866 (1-800-80-USTOO).