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Affected by Prostate Cancer?



SUPPORT - EDUCATION - ADVOCACY

Hot SHEET

Us TOO INTERNATIONAL Prostate Cancer Education and Support Network

Dose Intensified vs. Standard Salvage Radiation for Biochemically Recurrent Prostate Cancer after Prostatectomy

Initial results of a European phase III trial (SAKK 09/10), reported in the *Journal of Clinical Oncology* by Ghadjar, et al of the Swiss Group for Clinical Cancer Research, showed little difference in acute toxicity with salvage radiotherapy (SRT) of 70 vs. 64 Gy in men with biochemical recurrence (BCR) of prostate cancer after radical prostatectomy (RP). Quality-of-life (QoL) analysis showed greater worsening of urinary symptoms in the dose-

intensified group. Pirus Ghadjar, MD, of Charité Universitätsmedizin Berlin, Germany, is the corresponding author of the article published in the *Journal of Clinical Oncology* (Vol. 33, pp. 4158–4166, 2015).

In the trial, 344 men without evidence of residual disease from sites in Switzerland, Germany, and Belgium were randomized between February 2011 and April 2014 to receive RT at 70 Gy/35 fractions (n=175) or 64 Gy/32 fraction (n=169) using three-dimensional conformal RT or intensity-modulated RT/rotational techniques. The

primary endpoint was freedom from BCR. Secondary endpoints included acute toxicity and QoL assessed at up to three months after treatment. QoL was assessed by the European Organisation for Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire (QLQ) C30 and the prostate cancer module QLQ-PR25; urinary symptom score (QLQ-PR25) was the primary QoL endpoint.

Acute grade 2 and 3 genitourinary (GU) toxicity was observed in 16.6% and 1.7% of the 70-Gy group vs. 13.0%

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Vanderbilt Examines Risk Factors for Cardiovascular Disease in Prostate Cancer Survivors

The three million prostate cancer survivors in the US are likely to die from something other than cancer, thanks to early detection, effective treatment and the disease's slow progression. What survivors need to be more concerned with is heart disease, the most common non-cancer cause of death for men with prostate cancer, according to a paper published in the journal *Circulation*, authored by Vanderbilt physicians.

For this reason, Vanderbilt's Cardio-oncology program is focusing on modulating the risk factors for cardiovascular disease in men, especially those receiving androgen deprivation therapy (ADT) to treat their prostate cancer.

"While ADT greatly benefits many men with prostate cancer, it may also increase the risk of developing diabetes or having a heart attack or stroke. By collaborating with urology, medical oncology and the cardio-oncology program, we are better able to determine which men are most likely to benefit from hormones, and in those who do get hormones, how to better protect their cardiovascular system," said Eric Shinohara, MD, associate professor of medicine and medical director of the Vanderbilt Radiation Oncology Clinic.

ADT reduces serum testosterone, which can make prostate cancers shrink or

(Continued on page 4)

ASCO Endorses Active Surveillance for Prostate Cancer

The American Society of Clinical Oncology (ASCO) now recommends active surveillance (AS) instead of immediate treatment for most men with low-risk prostate cancer. The recommendation comes by way of an endorsement of guidelines from Cancer Care Ontario, which was published online February 16th in the *Journal of Clinical Oncology*.

"There is an increasing awareness that AS is an important approach to spare many prostate cancer patients from treatment that they don't need and that can cause lasting quality-of-life effects," lead author of the endorsement, Ronald C. Chen, MD, MPH, from the University of North Carolina Lineberger Comprehensive Cancer Center in Chapel Hill, said in a press statement.

Other organizations have recommended AS for some time. The National Cancer Comprehensive Network (NCCN) led the way in 2010, recommending AS for the sole management for low-risk prostate cancer. Recently, NCCN expanded its recommendation to include favorable intermediate-risk prostate cancer.

Estimates vary on how common AS is practiced in the US. In 2010 and 2011, just 12.1% of men with very low-risk prostate cancer were treated with AS, according to one study (*JAMA Intern Med* 2015; 175: 1569–1571). However, another study showed that 38.4% of men with low-risk disease were treated with either AS or watchful waiting.

In their endorsement, the ASCO team made some modifications to the Canadian guidelines, explained senior author Suneil Jain, MB, PhD, who is now a radiation oncologist at Queen's

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Clinical Significance of Prospectively Assigned Gleason Tertiary Pattern 4 in Contemporary Gleason Score 3+3=6 Prostate Cancer

Doshi C, Vacchio M, Attwood K, et al

The Prostate 16 February 2016; Epub

Objective: To determine the oncologic impact of prospectively assigned tertiary pattern 4 in contemporary Gleason score (GS) 3+3=6 radical prostatectomy (RP) specimens.

Patients and Methods: Oncologic outcomes were retrospectively reviewed for 720 consecutive patients from a single National Comprehensive Cancer Network (NCCN) center with at least six months follow-up after RP for GS 3+3=6 (GS6, N=222), GS6 with tertiary pattern 4 (GS6t4, N=62), or GS 3+4=7 (N=436) prostate cancer, as prospectively graded since 2006 using the 2005 International Society of Urologic Pathologists criteria. Preoperative NCCN risk category, RP pathology, progression-free survival (PFS) and me-

tastasis-free survival (MFS) were compared among the GS6, GS6t4, and GS3+4=7 groups using χ^2 , Kaplan-Meier, and log-rank analyses.

Results: The incidence of low NCCN preoperative risk classification for GS6t4 patients (63%) was less than that for GS6 patients (77%) while greater than that for GS3+4=7 patients (30%, $P < 0.001$). GS6t4 patients had RP pathologic features which were intermediate in risk between that of GS6 and GS3+4=7 based on extraprostatic extension (27% vs. 6% vs. 31%, respectively, $P < 0.001$) and mean percentage of prostate gland involvement (13% vs. 10% vs. 16%, respectively, $P < 0.001$). With a mean overall follow-up of 42 months, PFS for GS6t4 patients (5-year 85%)

was intermediate between that of GS6 (5-year 93%) and GS3+4=7 (5-year 76%) patients ($P < 0.001$). The 5-year MFS rate was 100% for GS6 and GS6t4 patients compared to 97% for GS3+4=7 patients ($P=0.07$).

Conclusions: This study provides the longest follow-up to date for RP patients with prospectively assigned GS6t4 and supports a risk for adverse RP pathology and postoperative disease progression that is intermediate between GS6 and GS3+4=7. Whether a tertiary pattern 4 in GS6 disease increases the risk of metastasis is uncertain and requires longer term study. Given favorable oncologic outcomes, less stringent postoperative surveillance for both GS6 and GS6t4 patients may be warranted.

New Consumer Advice on Prostate Cancer Includes 'Value'

Being confronted by a spectrum of treatment options can be bewildering, so a new initiative called Proven Best Choices™ has been launched to guide patients through the maze. These documents offer, for the first time, information to patients on the "relative value of treatment," notes Caitlin Morris, from Families USA, a nonprofit healthcare advocacy group that partnered with the Institute for Clinical and Economic Research (ICER), a nonprofit organization that evaluates evidence on the value of medical tests, treatments, and delivery system innovations to produce the guides.

One of the first of these guides, released last month, is aimed at men with low-risk prostate cancer. Medscape approached three experts to comment on it.

"I applaud these efforts to provide guidance to men regarding treatment options for low-risk prostate cancer, and for taking cost into consideration," said Stacy Loeb, MD, assistant professor of urology and population health at New York University in New York, NY. But she pointed out that the document missed a very important consideration – the patient's life expectancy.

Another expert was not impressed. Marc B. Garnick MD, Gorman Brothers clinical professor of medicine at Harvard Medical School and the Beth Israel Deaconess Medical Center in Boston, MA, and editor in chief of the HMS Annual Report on Prostate Diseases, said the guide is "overly simplified."

This is one of the "most controversial areas of clinical

medicine and urologic oncology – that of providing concise advice to aid the bewildered patient when selecting therapies for low-risk prostate cancer," he commented. Overall, the guide "does little to advance the complexities of decision-making for our patients," he said.

Dr. Garnick is concerned that "the advice is misleading and sanitized; there is no place for nuances related to a patient's specific circumstances." And he objected to the use of the word "proven" in the trademarked name for these guides, saying it is misleading. "I only wish that we did have 'proven' choices for this disease, which is so complicated and in need of significantly more research to get to the true 'proof,'" he said.

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Doc Moyad's What Works & What is Worthless Column, Also Known As "No Bogus Science" Column

"Legume – The Tenzing Norgay of the Prostate Cancer World?!"

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.

Bottom Line:

A new extensive dietary study within a randomized trial of dietary supplements to prevent cancer and heart disease found a significant reduction in prostate cancer risk with a greater intake of legumes! It is time to talk LEGUMES and Tenzing Norgay people before or after a prostate cancer diagnosis to keep things moving smoothly and regularly in your life so you can achieve your goals!¹

In one of the only and largest looks at specific dietary items in a randomized trial and risk of prostate cancer after a median follow-up of 12.6 years (that is more than three Olympics!) and a total of 139 prostate cancers from 3,313 male participants from a famous French clinical trial called "SU.VI.MAX" (a French word meaning "SU.VI.MAX"), a significant 44% reduction in prostate cancer risk was

found for a greater legume intake! Fruits, other veggies, and tomato products showed nada (that means "nothing" in Moyad vernacular). How could this be? What is a legume? Well it has the letters "UM" in it so it must mean something powerful, gorgeous and fabulous (get it-UM like University of Michigan – shameless plug whenever the opportunity presents itself). Think BEANS, LENTILS, PEAS, and more and these are legumes!

The Legume group of foods is not only ridiculously healthy due to low or insignificant sodium content and lots of nutrients, but also due to high dietary FIBER content (and protein)! Oh yeah! You remember fiber – it's your daily ticket for ensuring a smooth and non-turbulent plane ride (get my drift?). In fact, in one of the only other extensive dietary post-analysis from this trial on prostate cancer risk

these researchers found a potential reduction in risk with greater intakes of insoluble fiber and the legume is high in insoluble fiber! Whether it is because legumes can increase friendly bacteria counts in the gut, or improve male hormone metabolism, lower cholesterol, lower inflammatory markers, reduce insulin resistance...

Soybeans are also in the legume group but interestingly when researchers excluded soy intake, the results still stood strong. In other words, a diversity of beans or legumes appeared to be beneficial. One thing for sure is that Legumes = HEART HEALTHY! I have felt for a long time that legumes are the unsung heroes of the diet world because they have consistently been shown to be associated with heart-healthy and prostate-healthy benefits, but you never see enough education or commercials on the health

benefits of the bean. In other words, legumes are like the Tenzing Norgay of the diet world. Tenzing Norgay was the Sherpa that showed Sir Edmund Hillary to the top of Mount Everest and although many people know Hillary as the first person to get to the top of this mountain, most folks believe that Norgay was the first and without him, Sir Edmund Hillary would not have even been able to get anywhere near the summit.

Regardless, this is why legumes remind me of Tenzing Norgay because they do all the work and others in the diet world get all the credit! Not anymore my friends! Viva Legumes! Viva Legumes! Viva Legumes! Notice how I repeated that three times so you would never forget it! Oh, and Viva Tenzing Norgay!

Reference

1. Diallo A, Deschasaux M, Galan P, et al. Br J Nutr 7 March 2016; Epub.

The Clinical and Economic Impacts of Skeletal Related Events among Medicare Enrollees with Prostate Cancer Metastatic to Bone

McDougall JA, Bansal A, Goulart BH, McCune JS, Karnopp A, et al et al

The Oncologist 10 February 2016; Epub

Background: Approximately 40% of men diagnosed with metastatic prostate cancer (mPCa) experience one or more skeletal-related events (SREs) – a pathological fracture (PF), spinal cord compression, or surgery or radiotherapy to the bone. Accurate assessment of effects on survival, health care resource utilization (HCRU), and cost may clarify value of preventive interventions for SREs.

Materials and Methods:

Men older than age 65 years with PCa and bone metastasis diagnosed between 2004

and 2009 were identified from linked SEER-Medicare records. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk for death associated with SREs were calculated by using Cox regression. HCRU and costs (in 2013 US dollars) were evaluated in a propensity score-matched cohort by using Poisson regression and Kaplan-Meier sample average estimators, respectively.

Results: Among 3,297 men with Pca metastatic to bone, 40% experienced ≥ 1 SRE (median follow-up, 19

months). Compared with men who remained SRE-free, men with ≥ 1 SRE had a two-fold higher risk for death (HR, 2.3; 95% CI, 2.1-2.5). PF was associated with the highest risk for death (HR, 2.8; 95% CI, 2.4-3.2). Among men with ≥ 1 SRE, emergency department (ED) visits were twice as frequent (95% CI, 1.8-2.3) and hospitalizations were nearly four times as frequent (95% CI, 3.2-4.4). Attributable cost of ≥ 1 SRE was \$21,191 (≥ 1 SRE: \$72,454 [95% CI, \$67,362-\$76,958]; SRE-free: \$51,263 [95% CI, \$45,439-\$56,100]).

Conclusions: Among men with PCa metastatic to bone, experiencing ≥ 1 SRE is associated with poorer survival, increased HCRU, and increased costs. These negative effects emphasize the importance of SRE prevention in this population.

Implications for Practice:

This study confirms the substantial adverse clinical and economic effects of SREs in men with PCa. Compared with men who have PCa metastatic to the bones and no SREs, men with PCa meta-

(Continued on page 5)

Recommendations against PSA Test Taken to Heart by Primary Care Practitioners (PCPs)

PCPs in the US appear to have taken recent task force guidelines to heart, virtually halving their use of PSA tests for routine screening for prostate cancer (PCa).

In contrast, US urologists reduced PSA testing by only a fraction during the study period, new research shows.

In late 2011, the US Preventative Services Task Force (USPSTF) issued a recommendation against PSA screening for all men in 2012, citing concerns that widespread screening identified indolent tumors that did not require treatment and for which treatment could have adverse consequences.

The new study compared PSA testing in 2010 and 2012 to assess the impact of the new recommendations. The findings were reported in a research letter published online 8 February 2016 in *JAMA Internal Medicine*.

"Definitely we should not be ordering as much prostate cancer screening testing as we are ordering now," said Charles Vega, MD, health sciences clinical professor of family medicine, University of California, Irvine. He was not involved in the study.

"But at the same time, the study did not delve into any detail as to why the tests were ordered, and anyone in a urologist's office may have more advanced reasons to be there — they may be symptomatic, and these are the men who actually need the PSA as a diagnostic test for potential PCa," he added.

"So I think the types of patients seen in a urologist's office vs. primary care can be quite different, so that's one
(Continued on page 5)

Cardiovascular Disease in Prostate Cancer Survivors (Continued from page 1)

grow more slowly. In 2010, the American Heart Association released a statement about the possible association between ADT and adverse cardiovascular events.

Specifically, there appears to be an association between ADT and increased low-density lipoprotein and triglyceride levels, increased fat and decreased lean body mass, increased insulin resistance and decreased glucose tolerance, and a general metabolic state similar to metabolic syndrome, the authors report.

"Aggressive treatment of these altered cardiovascular risk factors can be an important step to decrease the risk of heart attack and stroke in men treated with ADT," said senior author Javid Moslehi, MD, assistant

professor of Medicine and director of Vanderbilt's Cardio-oncology program. "In general, cardiovascular wellness is an important aspect of care for all of the nearly 230,000 men newly diagnosed with prostate cancer each year in the US."

Cardiovascular disease is the number one killer of all men in the US whether they have prostate cancer or not, so it's important for men to understand the elevated risk associated with ADT, said David Penson, MD, MPH, the Paul V. Hamilton, M.D. and Virginia E. Howd Professor of Urologic Oncology, and an author of the *Circulation* paper.

Vanderbilt's Cardio-oncology program is rare in its collaborative, multi-specialty care of men with prostate cancer, said Moslehi, who helped

develop the Vanderbilt ABCDE paradigm for cardiovascular health in cancer survivors, an algorithm that is now being adapted as part of national cancer survivorship guidelines by National Comprehensive Cancer Network (NCCN).

The ABCDE algorithm for prostate cancer survivors includes awareness and aspirin; blood pressure monitoring; cholesterol management and cigarette avoidance; diet and diabetes; and exercise. Patient education is a shared responsibility of the multiple specialists who comprise the cardio-oncology program.

"Collaboration among subspecialties in medicine is critical to maintaining the health of our patients. No

(Continued on page 5)

ASCO Endorses AS for Prostate Cancer (Continued from page 1)

University Belfast in Northern Ireland. Dr. Jain and his coauthors state that "for most patients with low-risk (Gleason score 6) localized prostate cancer, AS is the recommended disease management strategy."

However, they add a qualifying statement to the Canadian guidance: "It is known that there is heterogeneity within this population and therefore factors such as younger age, high-volume Gleason 6 cancer, patient preference, and/or African American ethnicity should be taken into account in this recommendation. Young patients (younger than age 55 years) with high-volume Gleason 6 cancer should be closely scrutinized for the presence of higher-grade cancer, and definitive therapy may be warranted for select patients."

These men have a "higher likelihood for disease progression during their life-

time," the authors report.

The ASCO team does "not wish to indicate that patients with the above factors should not be considered for AS, but that clinicians and patients should keep the risk for disease progression in mind when making a decision," Dr. Jain told *Medscape Medical News*.

Select men with low-volume, intermediate-risk (Gleason 3+4=7) prostate cancer can be offered AS, according to the endorsement. However, active treatment (radical prostatectomy or radiation therapy) is recommended for most men with intermediate-risk (Gleason score 7) localized prostate cancer, the ASCO team writes.

AS protocols should include a PSA test (drawn every three to six months), a digital rectal examination (performed at least every year), and serial prostate biopsies. At the least, the biopsy should be a

12-core confirmatory transrectal ultrasound-guided procedure (including anterior directed cores) within six to 12 months, and then serial biopsy every two to five years thereafter.

Investigational ancillary radiologic and genomic tests could be used in men with discordant clinical and/or pathologic findings, the report indicates. Men who are reclassified into a higher-risk category (Gleason score ≥ 7) or experience a significant increase in tumor volume on follow-up biopsies should be offered active therapy, the authors state.

The ASCO team does not endorse any medical specialty as being best suited to manage AS, but does state that a "multidisciplinary team approach should be taken when a change to active treatment is considered."

Medscape Medical News
3 March 2016

Consumer Advice on Prostate Cancer Includes 'Value' *(Continued from page 2)*

The new document says there are three “best proven choices” for low-risk prostate cancer – active surveillance (AS), radical prostatectomy (RP), and brachytherapy (BT), which involves inserting radioactive seeds into the prostate. The guide then lists intensity-modulated radiation therapy (IMRT) and proton-beam RT as “lower value options.”

There are large cost differences between these three types of RT, Dan Ollendorf, PhD, chief scientific officer at ICER, explained to Medscape Medical News. Typical costs are around \$10–15,000 for BT, \$25–\$30,000 for IMRT, and more than \$50,000 for proton-beam RT. BT involves a single visit for inserting the radioactive seeds, whereas the other two involve a series of visits for a course of RT. However, he also noted that BT is not widely used, and that its use varies geographically across the US. “IMRT was, in the past, the second most commonly used treatment after RP, which accounted for about 60% of treatments,” he said. But management in recent years has changed, and registry data from last year show that AS increased sharply from 2010–2013, now accounting for about 40%. RP still accounts for about 50%, and the other 10% is for other forms of RT.

Dr. Garnick said the guide does a disservice by placing IMRT in the unfavorable position of a lower value option, which he said is a “truly arbitrary designation.” In addition, he said that the information on BT “is devoid of any discussion regarding side effects, which in this case can be debilitating and cumulative over years.”

Another expert also questioned the comments on RT. David Penson, MD, MPH, professor of both urologic

oncology and urologic surgery at the Vanderbilt University Medical Center in Nashville, TN, said that, overall, the guide is “reasonable and accurate,” but added: “That being said, in certain patients, external-beam RT (EBRT), i.e., IMRT or proton beam, may still be of high value. I wouldn’t completely dismiss those treatments in low-risk patients. Simply put, different patients are going to have different preferences, such that the value may vary from patient to patient,” Dr. Penson stated. “That being said, these recommendations make sense on a population level.”

Dr. Garnick said that the guide had many inaccuracies, including one in the AS section, which indicates that this involves undergoing a prostate biopsy every year. “While this may be true for the first year, most AS programs call for biopsies every two to three years,” he said, and “there is no mention of the emerging and important studies of genomic testing to help drive decision making.”

Dr. Loeb, in her reaction, also homed in on the same point of yearly biopsies, pointing out that some programs space the biopsies at longer intervals, and also that many AS programs are also beginning to integrate newer tests, such as multiparametric MRI to help guide the timing. But she said she is very pleased to see this option highlighted.

Countering these comments, Dr. Ollendorf said that the section on AS sets out “the most conservative approach” that the patient may expect, and he agrees that the frequency of biopsies varies, for example from one institution to another, and depends on specific individual circumstances. He also said that the data on genomic tests so far

are preliminary, and these tests are not proven.

Dr. Loeb elaborated about the importance of considering the patients’ life expectancy when selecting treatment for low-risk prostate cancer. She cited NCCN guidelines, which state that for men with a life expectancy under 10 years, observation is the preferred option. For men with a life expectancy of 10 to 20 years, AS is the preferred method. NCCN lists choices such as RP, AS, and RT only for men with a life expectancy greater than 20 years. This is similar to the choices outlined in the Families USA/ICER document, except that it comments on the value of different types of RT.

Medscape Medical News
15 February 2016

Against PSA Test

(Continued from page 4)

limitation of the study,” Dr. Vega commented.

Under lead author Michael Zavaaski, MD, Brigham and Women’s Hospital, Boston, MA, investigators used the National Ambulatory Medical Care Survey to examine the use of PSA testing in 2010 before the guidelines took effect and again in 2012 after they had been issued.

The investigators included all visits for men aged 50 to 74 years who presented to urologists (1,222) or primary care providers (1,109) for a preventive care visit.

The weighted sample that was subsequently analyzed included 27 million visits in 2010 and 2012. Of these, 800,000 examinations were provided by urologists, and 26.2 million were provided by primary care providers.

Between these two time points, PSA testing dropped

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Dose of Salvage RT

(Continued from page 1)

and 0.6% of the 64-Gy group (P=0.2). Acute grade 2 and 3 gastrointestinal (GI) toxicity was observed in 15.4% and 2.3% vs. 16.0% and 0.6% (P=0.8). Early changes in QoL were minor. Men receiving 70 Gy had a greater and clinically relevant worsening in urinary symptoms (P=0.02).

Authors concluded, “Impact of dose-intensified [SRT] on QoL was minor, except for a significantly greater worsening in GU symptoms.”

The ASCO Post
10 February 2016

Costs of SREs

(Continued from page 3)

static to the bones experiencing ≥ 1 SRE had a twofold increase in the risk for death, a twofold increase in the number of ED visits, and a fourfold increase in the number of hospitalizations; they also incurred an additional \$21,000 in direct medical costs attributed to SREs. Strategies to prevent SREs are potentially of high value in this patient population.

ABCDE Algorithm

(Continued from page 4)

one is simply a prostate or a heart, and the treatments we use to treat one illness or another can dramatically affect the well-being of other parts of a patient. Bringing together a comprehensive team that addresses all facets of a patient’s health allows us to provide the best medical care there is,” said oncologist Alicia Morgans, MD, MPH, assistant professor of Medicine, also an author of the *Circulation* paper.

Vanderbilt Univ. Med. Center,
11 March 2016

Stereotactic Body Radiation Therapy Becomes a Standard of Care for Prostate Cancer

By Susan Thompson, Senior Director, Patient Access, Accuray, Incorporated

On April 1st, National Government Services (NGS), one of the largest Medicare contractors in the country, will be implementing a Medicare policy in 10 states (NY, IL, MA, WI, MN, CT, NH, RI, ME, and VT) covering a form of prostate cancer treatment called stereotactic body radiation therapy (SBRT). While there is nothing new about a Medicare contractor implementing an SBRT coverage policy, what is new is how they determined the coverage for the treatment of prostate cancer.

SBRT, often delivered with a machine called the CyberKnife® System, is a type of prostate cancer RT administered in four to five treatments over one week rather than conventional treatments (such as Intensity Modulated RT) that are typically delivered in 40 to 45 treatments over eight to nine weeks. In the past 10 years, SBRT has gone through an evolution in how it is viewed by the medical, insurance, and patient communities. Initially performed at Stanford University in the early 2000s, the treatment was only available to men who had heard about it and were willing to try something new.

What intuitively made sense to many men and their clinicians was the unique robotic maneuverability and real-time image guidance of the CyberKnife, which allowed it to track and adjust the beam to account for patient or tumor motion during treatment.

Medicare and most private payers require data that would only become available if clinicians have the opportunity to treat patients to understand the benefits and risks of the new treatment. This unfortunate road block commonly develops during coverage decisions with

many new treatments and creates a classic Catch-22: Coverage decisions cannot be made without data, which can only be gathered by conducting treatment procedures that are not covered by insurance.

In response, the prostate cancer community tapped into an idea that originated in the late 2000s when patients and clinicians came together at the local level and proposed an interim solution known as “coverage with evidence development,” or “CED.” Medicare contractors agreed to allow access to SBRT for patients willing to enroll in registries. Faced with the option of no access at all, many clinicians and patients gladly agreed to take the extra steps to make sure a promising therapy remained an option for those who felt it was the right treatment to pursue. The Registry for Prostate Cancer Radiosurgery was established in 2010 and has since enrolled more than 3,000 men in over 20 states. A paper recounting this novel approach to solving the coverage Catch-22 for the first 2,000 patients enrolled was published last year (<http://journal.frontiersin.org/Journal/10.3389/fonc.2014.00369/full>).

Also noteworthy is that while the Medicare contractors were adopting their CED policies, commercial payers (who often lag behind Medicare), began to realize the economic and clinical benefits of covering SBRT and began liberalizing their policies without requiring patients to enroll in registries. As Blue Cross Blue Shield (BCBS) of N. Carolina put it in their July 2013 policy revision: “Based on the biologic response of prostate cancer to radiation (low α/β ratio),

SBRT (high dose per treatment) is potentially more effective than long-course IMRT at 1.8-2 Gy per fraction. SBRT is a less costly treatment, and available data suggest that SBRT is at least as effective as IMRT with no worse side effects at five to six years.” Most of the large national payers including Aetna, Anthem Wellpoint, CIGNA, Humana, and United Healthcare; and many of the regional payers such as Blue Shield of California and BCBS of Texas and Illinois also agreed with the conclusion by BCBS of N. Carolina, and began covering prostate SBRT.

The NGS Medicare policy that becomes effective this month eliminates the requirement for registry enrollment. In their summary of public comments on the draft policy, NGS quoted the major medical professional specialty society, the American Society for Radiation Oncology (ASTRO), who updated their model SBRT policy back in 2013 and stated, “It is ASTRO’s opinion that data supporting the use of SBRT for prostate cancer have matured to a point where SBRT could be considered an appropriate alternative for select patients with low- to intermediate-risk disease.”

While SBRT is not for everyone, stakeholders, including payers, came together to ensure that patients were able to consider SBRT as another effective treatment option for prostate cancer.

Editors note:

The content of this article was reviewed and edited for inclusion in the Us TOO Hot SHEET, but should be recognized as information provided by Accuray Incorporated about their CyberKnife treatment. Side effects of CyberKnife treatment are usually

mild and temporary, may include nausea, fatigue, and skin irritation, and may vary from patient to patient. As with any radiation treatment, the side effects can also be severe in some patients and lead to permanent injury or even death, and results may vary from patient to patient.

PET CT Plus MRI May Aid Salvage RT for Recurrent Prostate Cancer to Nodes

Men with nodal recurrent prostate cancer (PCa) after radical prostatectomy (RP) may benefit from extended salvage radiotherapy (RT) directed by positron emission tomography/computed tomography (PET/CT) and magnetic resonance imaging (MRI), a study found.

The study included 25 PCa patients who experienced nodal or nodal plus locally recurrent PCa confirmed by choline-PET/CT and MRI after primary RP or salvage RT. Following extended salvage RT (esRT) at the sites of recurrence, the cohort had a mean follow-up of 2.9 years.

Of the 25 men, 21 (84%) had PCa recurrence only in pelvic nodes, three had recurrence in retroperitoneal nodes only, and one had recurrence in both pelvic and retroperitoneal lymph nodes. Researchers led by Hans Christian Rischke, MD, of Albert-Ludwigs University Hospital of Freiburg in Germany, and colleagues found that esRT resulted in complete biochemical remission in seven

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Affected by Prostate Cancer?

 SUPPORT - EDUCATION - ADVOCACY

Doctor Chodak's Bottom Line *(Page number and first few words of article title)*

Gerald Chodak, MD, Author, *Winning the Battle Against Prostate Cancer*, Second Edition <http://www.prostatevideos.com/>

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

P1, "ASCO Endorses AS" As active surveillance (AS) grows in popularity, guidelines could be helpful to standardize management. In response to guidelines developed in Canada, ASCO has reviewed those recommendations and adopted some, but not all of them. It is quite interesting to see that the standard of care for Gleason 3+3=6 cancer is AS. Surprisingly, there is no further separation according to number of cores, amount of cancer, etc. Also, they recommend serial biopsies but do not specify a range of intervals. Importantly, they also did not make a recommendation for the use of a 5-alpha reductase inhibitor (e.g., Proscar or Avodart) for men on AS, which is a good thing since the long-term impact on survival is unknown.

The Bottom Line: AS is gaining increased acceptance and now major oncology societies recommend it as first line treatment for low-risk prostate cancer.

P1, "Dose-Intensified" Men with a rising PSA after radical prostatectomy (RP) often undergo salvage radiation therapy (RT). However, only a small percentage appear to benefit when lower dose RT (60–64 Gy) is used. An important question is whether a higher dose would prove more effective without significantly increasing side effects. A European randomized study did a trial comparing the standard RT dose with 70 Gy. Overall, the higher dose was well tolerated, although the authors did identify a significantly higher incidence of urinary side effects. Longer follow-up is needed to determine if this higher dose does improve overall survival. Until that is

available, men offered the higher dose should be made aware of the higher risk.

The Bottom Line: Using 70 Gy instead of 64 Gy to treat a rising PSA after RP is associated with a small, but significantly higher, risk of urinary side effects. At this time, the impact of the higher dose on overall survival is unknown.

P1, "Vanderbilt Physicians" Over the past ten years, clinicians have gained considerable knowledge about the wide range of potential side effects from androgen deprivation therapy (ADT). However, no formal guidelines to address these side effects are currently available. Now, a paper from the University of Tennessee describes their approach to this issue using a system they call ABCDE. The authors did not conduct a study to determine if their system would impact survival. But at a minimum, it can heighten awareness about the important risk factors of ADT in the minds of the physicians that prescribe it.

The Bottom Line: Systems are needed to ensure that men get proper monitoring and treatment for the variety of side effects that can develop during ADT. The ABCDE method appears to offer one reasonable option.

P2, "Clinical Significance" Gleason score remains one of the most important criterion for assessing a man's risk from prostate cancer. Doshi, et al suggests that a new classification should be made to distinguish men from those with pure Gleason 3+3=6 and 3+4=7 cancers. In some cases, a small amount of Gleason pattern 4 cells may be seen in a biopsy, but not enough to justify classifying the tumor as

Gleason 3+4=7. The new term is called GS6t4. From this moderate sample size, the authors were able to show that progression free survival for men in this group was slightly better than those in the Gleason 3+4=7 group, but not as good as men in the Gleason 3+3=6 group. More data is needed to confirm this finding, but it is conceivable that this might prove to be helpful for identifying certain men with Gleason 3+3=6 prostate cancer may not be the best candidates for AS.

The Bottom Line: A finding of any Gleason pattern 4 cancer cells in a biopsy with predominant Gleason 3+3=6 prostate cancer might prove to be useful for identifying those men at higher risk of recurrence following AS.

P2, "New Consumer" One of the disappointing aspects of treating early stage prostate cancer is the lack of proof that one treatment is better than another. Now it appears a new guide has been developed called "Best Proven Choices" to helping patient counseling. This *Hot SHEET* contains an article in which three clinicians comment on the guide. One extremely important critique points out that the guide uses the word "proven," which is, of course incorrect. Another problem relates to RT, which the article classified as "lower value." Here too, there are no data to justify that this statement. Undoubtedly, a helpful guide could benefit men facing this decision. However, it would appear that this particular guide is misleading.

The Bottom Line: "Best Proven Choices" may mislead in at least two ways, greatly compromises its value.

P3, "The Clinical and" Doctors have known for years that pathological fractures (PF) have severe health consequences. However, concern has been raised about the high costs associated with treatments to prevent initial and future "skeletal related events" (SREs) in men with metastatic prostate cancer. Now, a paper by McDougal and coworkers quantifies the costs and mortality associated with having more than one SRE. Compared to men without a SRE, the authors found that occurrence of one SRE doubled the risk of death, doubled the risk of a visit to the ER, quadrupled the hospitalization rate, and resulted in significantly higher medical expenses.

The Bottom Line: Therapies that reduce the risk of SREs have important health benefits and are associated with lower medical costs. For those reasons, they should be given to men at risk of developing SREs.

P4, "US Recommendations" The controversy over screening for prostate cancer continues. Based on its review of the various studies done, the Agency for Health Care Policy has recommended against screening asymptomatic men with PSA. Zavaaski, et al looked at the impact this recommendation had on clinical practice. Among general practitioners, the authors found that orders for PSA tests dropped from 36% of the visits in 2010 to 16.4% in 2012. Only a slight decrease occurred among urologists. Of potential concern in the future will be legal issues when men are diagnosed with prostate cancer

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Recommendations against PSA Testing

(Continued from page 5)

by 57% in visits to primary care providers, from 36.5% in 2010 to 16.4% in 2012 (P=0.009). In contrast, PSA testing dropped by only about 4% in urology visits, from 38.7% in 2010 to 34.5% in 2012 (P=0.09).

The difference between the two groups of physicians administering PSA tests during the study years was statistically significant (P <0.001).

"There is a great deal of controversy about if, and how, we should screen for prostate cancer," senior author Quoc-Dien Trinh, MD, Brigham and Women's Hospital, Boston, MA, stated.

"Moving forward, [our] findings emphasize the need to continue interdisciplinary dialogue to achieve a broader consensus on PCa screening," Trinh, et al stated.

He explained that there are many forms of "dialogue," of which national recommendations or consensus state-

ments are the first step.

"If the CMS or private payers start incentivizing or penalizing the use of certain tests for certain individuals, this will ultimately lead to more uniform practice patterns, for better or for worse," she said.

Dr. Vega supported the 2012 USPSTF recommendations. "I believe and stand by the recommendations, given the failure of any major trial to really demonstrate any change in the risk in overall mortality associated with PCa screening," he said.

"The PSA screening test doesn't have to be thrown out entirely, but if a middle-aged male comes in and their PSA is very low, the risk of them developing PCa is actually quite low, so I don't think screening every single year has merit. It's wasteful and exposes people to unnecessary harm," Dr. Vega added.

Medscape Medical News
11 February 2016

RT for PCa to Nodes

(Continued from page 6)

men (28%) at the latest follow-up, according to a report in *Advances in Medical Sciences* (2016;61:212-218). Median time to PSA progression for the entire cohort was 19.6 months, but it was significantly longer for patients with 1-2 PET-positive lymph nodes than for those with three or more PET-positive lymph nodes (median 34.9 vs. 12.7 months).

Patients experienced mild to moderate acute and late toxicity and no grade 3 adverse events, according to the investigators.

The authors concluded that PET/CT- and MRI-directed RT of nodal recurrent PCa with or without local recurrence after RP is feasible and may have the potential to prolong PSA progression in patients with one to two PET-positive lymph nodes with a low acute and late toxicity.

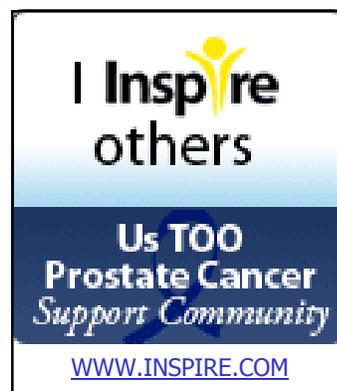
Renal & Urology News
25 February 2016

The Bottom Line

(Continued from page 7)

and have not had a PSA.

The Bottom Line: More attention should be paid to the possible legal consequences of telling doctors that routine screening for prostate cancer is not recommended. One hopes doctors have done due diligence in counseling men about the pros and cons of screening and they have documented the conversation.



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