Updated Guideline on Brachytherapy in Prostate Cancer

The American Society of Clinical Oncology (ASCO) and Cancer Care Ontario have issued a joint clinical practice guideline update on the use of brachytherapy (BT) for prostate cancer patients. The new guideline was published online in the *Journal of Clinical Oncology* on March 27th.

BT involves the implantation of radioactive seeds into the prostate gland. It is “now the nonsurgical standard of care for the majority of patients with prostate cancer – either by itself or as part of a combination approach,” said Andrew Loblaw, MD, FRCP, co-chair of the expert panel that developed the guideline update, who was representing ASCO.

“BT is also more convenient than external-beam radiation (EBRT) and has a much higher chance of curing the disease,” said Dr. Loblaw in a statement. “However, not every patient should have BT, and not all treatment centers are experienced in delivering high-quality BT.”

“For the urologist, who is most often the gatekeeper in terms of first contact with men with prostate cancer, this guideline update provides new information they can incorporate into patient counseling and treatment decision making,” said Joseph Chin, MD, FRCS, co-chair of the expert panel that developed the guideline update and represented Cancer Care Ontario.

“By optimizing treatment selection, which may or may not be BT for a particular patient, outcomes should ultimately be improved,” said Dr. Chin in a statement.

(Continued on page 4)

Vessel-Sparing Radiotherapy Preserves Erectile Function in Prostate Cancer

In a phase II study published online in *European Urology* on February 21st, vessel-sparing radiotherapy (RT) preserved erectile function (EF) in most men with localized prostate cancer.

“We would hope that physicians understand there is a new standard of successful treatment for prostate cancer – cure with quality of life,” stated Dr. Patrick W. McLaughlin from University of Michigan in Ann Arbor. “In the past, men seeking cure would potentially have to lose function to accomplish cure, but this study suggests that with close attention to mapping of critical adjacent structures, both cure and quality of life can be accomplished in the majority of men diagnosed with prostate cancer.”

Dr. McLaughlin and colleagues developed vessel-sparing RT with the intention of delivering the prescribed RT dose to the prostate with maximal sparing of the bilateral corpus cavernosum and internal pudendal artery. They reported five-year patient-reported EF preservation rates and long-term tumor control outcomes in 144 men treated with vessel-sparing RT from 2001-2009. Sixty-one percent received a combination of intensity-modulated RT (IMRT) with brachytherapy (BT), and 33% also received androgen deprivation therapy (ADT).

At five years, 35% of men could be sexually active without the use of aids, and 53% reported that they were sexually active but required

(Continued on page 5)
Discord Among Radiation Oncologists and Urologists in the Postoperative Management of High-Risk Prostate Cancer


Am J Clin Oncol 15 March 2017; Epub

To query specialty-specific differences regarding postoperative radiotherapy (RT) for high-risk prostate cancer, an electronic mail survey of radiation oncologists (ROs) and urologists was sent. We sought to maximize the absolute response number to capture contemporary practice ethos. The outcome of interest was association between response and specialty. Training level/expertise, practice setting, percentage of consultation caseload consisting of high-risk prostate cancer, and nationality were set as effect modifiers for multivariate logistic regression.

In total, 846 ROs and 407 urologists responded. ROs were more likely to prefer adjuvant RT (ART), ART or early salvage RT (SRT), defined as RT delivered at PSA <0.2 ng/mL, whereas urologists were more likely to prefer early or delayed SRT (P <0.0001). ROs were more likely to prefer lower PSA thresholds for initiating SRT (P <0.0001), and more likely to recommend ART in the setting of adverse pathologic features or node-positive disease (P <0.0001). Significantly more ROs would recommend concurrent androgen deprivation therapy (ADT) or pelvic nodal RT in the setting of node-positive or Gleason score 8 to 10 disease (P <0.0001). Specialty-specific differences were readily elucidated with respect to timing and indications for ART and SRT, as well as for indications for ADT and (Continued on page 6)
Doc Moyad’s What Works & What is Worthless Column, Also Known As “No Bogus Science” Column

“Vitamin D = Bad Start to 2017, but VITAL Results will be Available Soon?”

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.

Vitamin D supplements cure everything right? Wrong! Vitamin D is overrated, but that does not mean that it still cannot help some folks. Regardless, in women, the supplements just failed to prevent cancer and just also failed a major study to prevent cardiovascular disease, but all is not lost! The results of one of the best clinical trials is expected in 2017. So stay tuned you vitamin D lovers and read this column for the true untold story of all of these clinical trials (cue the dramatic music)!

Why does Moyad write about vitamin D so much? Why do people back their cars into a parking spot while others are waiting to park? Why do people talk on their cell phone while in an elevator? I have no idea, but the reason we need to keep up with the vitamin D research is due to the fact that it gets so much biased positive attention and, when big studies show no benefit, it gets minimal attention, so let’s change that now. A total of over 2,300 postmenopausal women taking 2,000 IU of vitamin D$_3$ and 1,500 mg of calcium per day vs. placebo for four years had no reduction in cancer compared to a placebo. Still, the average person in these studies is obese or almost obese and over half have been diagnosed with hypertension and are taking medication for it in the U.S. VITAL study! These studies are just reflections of the current state of health in the U.S. and around the world of so-called “healthy people.” I just wish someone would design a study whereby reducing weight or blood pressure for example through diet/lifestyle would go against vitamin D or other highly-touted pills. Dreamers have to dream!

References:

Intermediate-Term Outcomes of Men with Very Low/Low- and Intermediate/High-Risk Prostate Cancer Managed by Active Surveillance


J Urol 24 March 2017; Article in Press

Purpose: To compare intermediate-term clinical outcomes among men with favorable-risk and intermediate/high-risk prostate cancer (PCa) managed with active surveillance (AS).

Materials and Methods: Since 2002, 635 men with localized PCa have been managed with AS at a high-volume U.S. academic hospital with a median follow-up of 50.5 months (interquartile range [IQR] 31.1-80.3). Time to event analysis was performed for our clinical endpoints.

Results: 117 men (18.4% of the cohort) had intermediate/high-risk disease. The overall five- and 10-year all-cause survival was 98% and 94%, respectively. The cumulative metastasis-free survival at five- and 10-years was 99% and 98%. To date, no cancer-specific deaths have been observed. The overall freedom from intervention was 61% and 49%, at five- and 10-years respectively. Overall, the cumulative freedom from failure of AS — defined as the development of metastasis or biochemical failure after local therapy with curative intent — was 97% and 91% at five- and 10-years, respectively. Twenty-one (9.9%) men experienced biochemical failure after deferred treatment and the five-year progression-free probability was 92%. Compared to men with favorable-risk disease, men with intermediate/high-risk cancer experienced no difference in metastases, surveillance failure, or curative intervention. However, higher-risk patients experienced significantly higher risk of all-cause mortality, likely reflecting patient selection factors. These conclusions may be limited by the small number of events and duration of our study period.

(Continued on page 6)
USPSTF 2017 Update (Continued from page 1)

“The other thing we have now is evidence that three men who would have developed metastatic PCAs won’t have metastatic disease with screening,” he added. Specifically, the new evidence showed that PSA screening would prevent three cases of metastatic PCAs, and one or two deaths due to PCAs.

ACS and AUA both welcomed the USPSTF support for individualized decision making about PSA-based PCa screening.

“The draft recommendations are thoughtful and reasonable and are in direct alignment with the AUA’s clinical practice guidelines and guidelines from most other major physician groups,” AUA president Richard K. Babayan, MD, of Boston University, said in a statement. He stated, “The USPSTF clearly utilized a more inclusive and transparent process to develop these draft recommendations.” Babayan alluded to criticisms of the lack of medical specialty representation on the task force. “This process demonstrates how the task force, specialists, patients, and the medical community as a whole can work together to develop recommendations that better reflect the clinical and research landscapes.”

In their latest review, the USPSTF compared potential harms and benefits of PSA-based screening for men, ages 55 to 69, followed for 10 to 15 years. The panel found that for every 1,000 men screened (or offered screening), 240 would have a positive result. Positive results would lead to positive biopsies in 100, and 80 of the 100 men would opt for surgery or radiotherapy (RT) – 65 immediately and 15 after a period of active surveillance (AS).

They observed that “Many men will learn they have a false-positive [test] result after getting a biopsy. The potential side effects of biopsy include pain, bleeding, and infection.”

“We have data now showing that AS can save the same number of men from dying of PCa; that there isn’t an increased number of deaths due to PCa with AS compared with radiation (RT) or surgery,” said Krist. “AS can reduce the potential harms in this whole screening-and-treatment pathway.”

ACS Chief Medical Officer Otis Brawley, MD, said he’s “thrilled” that the USPSTF, AUA, ACS, and other organizations are becoming more like-minded about PCa screening. The only real difference is that the task force and AUA suggest that the discussions begin at age 45, whereas the ACS recommends starting the discussion at age 50.

However, Brawley emphasized an issue often lost in the controversy about when and how to begin PSA-based screening for PCa. “I hope the lay public and the medical community understand that the harms of PCa screening are better proven than the benefits,” Brawley said. “It’s never been that there’s no benefit to PCa screening. The problem has always been these harms.”

The USPSTF recommendation reflected a response to the “sea change” in American medicine; the “knee jerk” reaction of the need for immediate treatment; and the adoption of the option of AS for many men with early-stage PCa. Krist agreed that emerging data on AS played a role in the updated recommendation.

Updated Guideline on Brachytherapy (Continued from page 1)

The new recommendations update the systematic review and clinical practice guideline on low-dose rate (LDR) BT for men with low- or intermediate-risk prostate cancer that Cancer Care Ontario published in 2013. It incorporates evidence from five randomized clinical trials reported since 2013.

The guidelines sought to answer the following clinical questions:

- In men with newly diagnosed prostate cancer, what is the efficacy of BT alone for clinical outcomes compared with EBRT alone or radical prostatectomy (RP) alone?
- In men with newly diagnosed prostate cancer, what is the efficacy of BT combined with EBRT for clinical outcomes compared with BT alone, EBRT alone, or RP alone?
- Among the isotopes used for LDR BT (e.g., iodine-125 [125I], palladium-103 [103Pd], and cesium-131 [131Cs]), which isotope maximizes clinical outcomes when used in men with newly-diagnosed prostate cancer?

Key Recommendations

Among all eligible patients with low-risk disease who require or who select to undergo active treatment, low-dose BT alone, EBRT alone, or RP should be offered. All patients should be counseled about all their treatment options in a balanced, objective manner, preferably from a multidisciplinary team. This recommendation is unchanged from the previous guidelines, because no new data had a bearing on this clinical question.

In the population with intermediate-risk prostate cancer, men who select EBRT, with or without androgen-deprivation therapy (ADT), BT boost (either low- or high-dose) should be offered to all eligible patients. In the low-intermediate risk group (Gleason 7, PSA <10 ng/mL or Gleason 6, PSA 10 to 20 ng/mL), low-dose BT can be offered as monotherapy. For eligible patients with high-risk disease who are being treated with EBRT and ADT, BT boost (LDR or high-dose rate) should be offered.

For men receiving low-dose BT, 125I and 103Pd are each reasonable isotope options, but no recommendation could be made for or against using 131Cs or high-dose BT. Patients who opt for BT should only be treated at centers that follow strict quality-assurance standards, the document emphasizes. It also notes that there may be increased genitourinary toxicity after BT vs. EBRT alone. Also, the authors note that it “cannot be determined whether there is an overall or cause-specific survival advantage for BT vs. EBRT alone, because none of the trials were designed or powered to detect a meaningful difference in survival outcomes.”

Men should be encouraged to participate in clinical trials evaluating novel or targeted therapies, the authors add.

Medscape Oncology
30 March 2017
Vessel-Sparing Radiotherapy
(Continued from page 1)

ads. Most of the sexual aids used were phosphodiesterase-type 5 inhibitors (e.g., Viagra, Cialis, and others).

Two-thirds of men at five years reported moderate to very high confidence in the ability to achieve and keep an erection. Overall, 13 of 135 men developed biochemical failure (BCF), which translated into biochemical relapse-free survival rates of 99.3% at five years and 89.9% at 10 years.

Based on previously validated models, this cohort would have an expected potency rate (able to achieve an erection firm enough for intercourse) of 42% at two years after standard external beam RT (EBRT) and 24% at two years after nerve-sparing radical prostatectomy (RP), in contrast to the actual observed rate of 78% here.

Among men with erections firm enough for intercourse at baseline, two-year preservation of EF was 87% for vesSEL-sparing RT, 69% for conventional EBRT, and 42% for nerve-sparing RP.

Results were similar in men receiving EBRT vs. EBRT plus BT, but men receiving ADT generally had worse EF outcomes at two years and modestly recovered by five years.

“This proves that dose can be intensified to the prostate without affecting sexual outcomes,” Dr. McLaughlin said.

“It validates what we term the functional anatomy approach—by defining critical adjacent functioning tissues visible on MRI and poorly visualized on CT we can include these structures in the treatment plan and drastically limit dose compared to CT based plans.”

“In any man diagnosed with prostate cancer with good baseline sexual function, vessel-sparing RT will have a role,” he said.

“Although this study emphasized defining and sparing critical adjacent structures related to sexual function, other critical functional domains, such as bladder and sphincter function and rectal and anal function, can all be mapped and spared through MRI-based planning,” Dr. McLaughlin said. “We will be reporting improved outcomes in these critical domains similar to improvements in sexual function outcomes.”

Reuters Health
9 March 2017

Prognostic Significance of a Negative Prostate Biopsy: An Analysis of Subjects Enrolled in a Prostate Cancer Screening Trial

J Urol 2017; 197: 1014-1019

Purpose: To our knowledge the optimal treatment of patients following a negative prostate biopsy is unknown. Consequently, resources are increasingly being directed toward risk stratification in this cohort. However, the risk of prostate cancer mortality in this group before the introduction of supplemental biomarkers and imaging techniques is unclear.

Materials and Methods: The PLCO (Prostate, Lung, Colorectal and Ovarian Cancer) Screening Trial provides survival data prior to the implementation of new diagnostic interventions. We divided men with an initial positive screen and a subsequent prostate biopsy into cohorts based on positive or negative results. Prostate cancer-specific mortality was then compared to that in the trial control arm to estimate the prognostic significance of biopsy results relative to the general population.

Results: A total of 36,525 and 36,560 patients comprised the screening and control arms, respectively. Of 4,064 subjects with a positive first screen, 1,233 underwent a linked biopsy, of which 473 were positive and 760 were negative. At a median follow-up of 12.9 years, 1.1% of men in the negative biopsy cohort had died of prostate cancer. The difference in mortality rates between the negative biopsy and control arms was 0.734 deaths per 1,000 person. The proportional subhazard ratios of prostate cancer-specific mortality for negative biopsy and positive biopsy relative to the control arm were 2.93 (95% CI 1.44–5.99) and 18.77 (95% CI 12.62–27.93), respectively.

Conclusions: After a negative prostate biopsy, men face a relatively low risk of death from prostate cancer when followed with traditional markers and biopsy techniques. This suggests limited potential for new diagnostic interventions to improve survival in this group.

Magnetic Resonance Imaging in the Diagnosis of Prostate Cancer in Patients with a Total Prostate-Specific Antigen Level of 2-10 ng/mL

Scand J Urol 29 March 2017; Epub ahead of print

More accurate diagnostic procedures for prostate cancer are needed to avoid unnecessary biopsy due to the low specificity of prostate-specific antigen (PSA). Recent studies showed that the percentage of serum isoform [2]proPSA (p2PSA) to free PSA (%p2PSA), the Prostate Health Index (PHI) and magnetic resonance imaging (MRI) were more accurate than PSA. The aim of this study was to test the accuracy of %p2PSA, PHI and MRI in discriminating patients with and without prostate cancer.

The subjects were 50 consecutive men with a PSA level of 2.0-10.0 ng/mL, who underwent prostate biopsy from October 2012 to July 2014. These patients underwent multiparametric MRI before biopsy, and their serum samples were measured for PSA, free PSA and %p2PSA. The sensitivity, specificity and accuracy of PHI, %p2PSA and MRI were compared with PSA in the diagnosis of biopsy-confirmed prostate cancer.

In a univariate analysis, %p2PSA [area under the curve (AUC): 0.811] and PHI (AUC 0.795) were more accurate than MRI (AUC: 0.583) and PSA (AUC: 0.554) for prostate cancer detection. At 60% sensitivity, the specificity of PHI (76.5%) was higher than that of MRI (52.9%). For significant cancer detection, %p2PSA (AUC: 0.745), PHI (AUC: 0.791) and MRI (AUC: 0.739) were marginally more accurate than PSA (AUC: 0.696). At 85% sensitivity, the specificity of MRI (62.1%) was higher than that of PHI (34.5%).

PHI and %p2PSA can be used for screening the general population and MRI can be used for detection of significant cancer in patients suspected, from screening tests, of having prostate cancer.

PROSTATE CANCER HELPLINE: 1-800-808-7866 WWW.USTOO.ORG
Men Uncertain About Risks and Benefits of PSA Screening  (Continued from page 2)

in the quality of pre-PSA screening discussions that men are having with healthcare practitioners before blood work is drawn,” they stated. “While some literature has proposed that shorter office visit times related to high patient volumes and increased practice demands may provide sufficient explanation as to why clinicians are not routinely talking to all men about both the advantages and disadvantages of PSA testing, we believe the true explanation is likely much more complex.”

The authors said a 2012 statement from the United States Preventive Services Task Force (USPSTF) may be part of the explanation. The statement recommends against PSA screening for the general population, citing the potential harms associated with complications of screening and overdiagnosis.

“The USPSTF report very clearly dissuades clinicians from recommending routine PSA screening in healthy males, and we believe our findings may be indicative of a shift in practice patterns away from detailed pre-screening discussions among healthcare practitioners who have implemented the USPSTF recommendation into their caregiving,” they wrote.

In an editorial comment, Simon Kim, MD, MPH, of Case Western Reserve University School of Medicine in Cleveland, and colleagues agreed with that assessment.

“To a large degree, this clinical debate is attributable to the marked disagreement ranging from the USPSTF issuing a Grade D recommendation against prostate cancer screening for all men at average risk for prostate cancer contrasted to the American Urological Association, American Cancer Society, and the National Comprehensive Cancer Network endorsing shared decision making about reviewing the merits of screening and eliciting patient preferences into the decision for early detection of prostate cancer,” Kim’s group wrote.

“At this time of uncertainty regarding prostate cancer screening, it is now more important for patients and providers to engage in thoughtful discussions about the risks and benefits of a PSA test and incorporate shared decision making into the clinical encounter,” they advised.

Turini’s group analyzed data from 217,053 men who participated in the 2012 and 2014 Behavioral Risk Factor Surveillance System (BRFSS) surveys. These telephone surveys were administered by state health departments using a standardized questionnaire. Approximately 80% of the men surveyed were white, 9% were black, and 8% Hispanic.

In 2012, before the task force made its recommendation, 30.5% of the men surveyed reported discussing neither the advantages nor disadvantages of screening with their healthcare provider; 30.1% said they discussed both, 38.5% discussed only advantages, and 0.8% discussed only disadvantages. In 2014, after the recommendation, 33.9% reported discussing neither pros nor cons while 29.5% discussed both, 35.7% only talked about advantages, and 0.8% only talked about disadvantages.

In 2012, black men were twice as likely to have discussed both advantages and disadvantages with their healthcare provider compared with white men (relative risk ratio 2.07, 95% CI 1.84-2.34, P<0.01). That figure didn’t change much in 2014 (relative RR 1.95, 95% CI 1.76-2.18, P<0.01), the study found.

“We feel this finding is encouraging on multiple levels,” the investigators said. “First, it suggests that general healthcare providers, represented in the BRFSS, appreciate published literature identifying not only a higher prevalence of prostate cancer among certain populations (in this case, African American men) but also a higher risk of mortality, and consequently a need to provide more educational information about advantages and disadvantages of PSA testing to those men.”

A study limitation was that it didn’t distinguish between first time PSA checks and annual screening tests. “If healthcare practitioners more frequently discuss advantages and disadvantages with a patient prior to his first PSA test than before subsequent routine screening, our finding that men were less likely to receive comprehensive counseling in 2014 relative to 2012 may be more accurately explained by a higher percentage of repeat screening tests than a true shift away from appropriate pre-screening advice,” the authors acknowledged.

Nevertheless, “the trend we’ve identified towards a large number of patients undergoing PSA testing without any counseling about either [sic] advantages or disadvantages should not only be viewed as a serious problem but acted upon swiftly so as to minimize the chances of cultivating a growing cohort of patients ill-prepared to handle the repercussions of prostate cancer screening,” they stated.

USPSTF 2017 Update  (Continued from page 4)

Of the 100 men with a positive biopsy, “20-50% will have cancer that never grows, spreads, or harms them.” Of the 80 men who opt for definitive treatment, “60 or more will experience serious complications [including] urinary incontinence and/or impotence.”

Despite support for discussion-driven decision making, a recent study showed that a third of men did not discuss the pros and cons of PSA tests with clinicians prior to testing. Krist said the findings disappointed but did not surprise him.

“Only by incorporating men’s values and preferences into the decision-making process can we make the right decision,” he said. “It’s extremely important for physicians to discuss this with patients, and patients really shouldn’t be getting a PSA test without understanding the benefits and the harms.”

USPSTF did not change its recommendation against PSA-based screening for PCa in men ages ≥70.

MedPage Today
11 April 2017

Post-RP Management  (Continued from page 2)

nodal RT. These differences are likely to create a sense of dissonance for patients, which may, in turn, explain the underutilization of post-operative RT in general urological practice.

Intermediate-Term  (Continued from page 3)

Conclusions: Patients with localized prostate cancer on AS demonstrated a low rate of AS failure, PCa-specific mortality, metastases, regardless of baseline risk.
**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, “USPSTF Backs...”** Since development of PSA, screening for prostate cancer has been a major controversy. For many years the message was strongly in favor of doing the test with little discussion of its shortcomings. Based on randomized studies, the USPSTF has issued changes in its guidelines. Prior to 2012 and even afterward, Turini et al. has found that less than one-third of men were being given proper counseling. Either only the benefits were discussed or nothing was presented. So, at present, about 70% of men are not being given proper counseling. Surprisingly, African American men were twice as likely to receive proper counseling. Regardless of the reason, clearly the problem is that men are not being informed to make an educated decision about what to do. This issue is likely to be re-addressed because of the new guideline about to be released. They have changed their recommendation from level D (against screening) to Level C (the harms and benefits are about equal). They now advise counseling for all men between ages 55-69 about the risks and benefits so they can make an informed decision. This change is likely to present doctors with a greater challenge and efforts are needed to make this an easy transition. One option would be to develop a standardized informed consent form for screening that EVERY man reviews and signs before deciding what to do. It would make the doctor’s job easier while insuring that all men get the same basic information throughout the U.S.

**The Bottom Line:** Men have not been given proper counseling about the pros and cons of screening for prostate cancer and, with the new recommendation about to be published, something is needed to help this process.

**P1, “Update Guideline on...”** The American Society of Clinical Oncology (ASCO) and Cancer Care Ontario have issued a joint clinical practice guideline update on the use of brachytherapy (BT) for prostate cancer patients. The new guideline was published online in the *Journal of Clinical Oncology* on March 27th. The major change is for men with intermediate-risk disease. Unfortunately, they have made a recommendation that says all men who receive external beam radiotherapy (EBRT) should also be offered a boost with high dose RT or BT. This is based on results from several randomized trials, however, none of them used survival as an end point; they only used biochemical or clinical recurrence. Side effects with combined therapy are higher compared to EBRT alone. One should strongly question whether the absence of survival data justifies this new recommendation. Certainly, men being offered the therapy should be made aware of this limitation. For studies on surgery and even monotherapy studies of EBRT, survival has been the outcome needed to make a strong recommendation, so this is a weakness of the new guideline.

**The Bottom Line:** New recommendations for combining BT with EBRT for intermediate- and high-risk disease are not based on survival as an outcome and would appear to be premature.

**P1, “Vessel-Sparing RT...”** Can RT be modified to spare the vessels responsible for EF? McLaughlin and co-workers addressed this question in a non-randomized study. They spared the corpus cavernosum and internal pudendal artery in 144 men given external beam RT alone, or in combination with brachytherapy (BT). Compared to historical results, they observed a higher rate of sexual function at two years and five years using this approach. Importantly, the PSA failure rate was very low. This is potentially important information but it needs additional validation in a randomized study.

**The Bottom Line:** Vessel sparing RT has the potential to reduce erectile dysfunction, but before widespread adoption the findings need to be validated in a prospective randomized study.

**P2, “Comparison of...”** As active surveillance (AS) becomes increasingly acceptable to patients and doctors, an unanswered question is whether there is a long-term risk to delaying therapy. As yet, no randomized data are available. The new report by Diniz et al. attempts to add new information. They compared men who received immediate radical prostatectomy (RP) to those who had an upgrading after some time on AS. They found no significant difference in biochemical failure for the men given immediate RP for Gleason 3+4 or higher disease compared to those getting delayed treatment. Does this prove the safety of AS? Not really, because the study was not randomized and PSA recurrence is not a good outcome measure. Unfortu-

nately, a proper study will be difficult to design. The means would be to prospectively collect data on those getting immediate vs. delayed RP and then follow those men long enough to measure survival. Until then, it will remain an open question whether AS with delayed therapy poses any added risk to men compared to immediate treatment.

**The Bottom Line:** The long-term safety of AS, followed by RP, compared to immediate therapy remains unknown.

**P2, “Discord Among...”** Past studies have demonstrated a specialty-related bias regarding treatment recommendations for prostate cancer; surgeons have in general preferred radical prostatectomy (RP) and radiation oncologists have preferred RT. Additional bias is demonstrated in the report by Kishan and co-workers who obtained written surveys regarding the use of adjuvant and salvage RT after RP. They found radiation oncologists were more likely to recommend adjuvant RT and earlier salvage RT. Randomized studies do support adjuvant RT in high-risk patients, since the odds of benefiting are around 1 in 10. Similarly, the odds of benefiting from salvage RT are very low. Given the difference in approaches by the different specialists, it is critical that both groups provide a balanced presentation between risks and benefits so that men can share in the decision rather than rely on the individual biases of the treating physician.

**The Bottom Line:** Urologists and radiation oncologists

*Continued on page 8*
have different attitudes about recommending adjuvant and salvage RT after RP, which means both groups need to give patients adequate information so they can make a shared decision.

P3, “Intermediate-Term...”

Another study on AS is being reported by Nyame et al. who followed 635 men over a median follow-up of five years. About 20% had intermediate/high-risk disease. At five and 10 years, 61% and 49% did not have treatment intervention. Freedom from metastatic disease at 10 years, 61% and 49% did not have treatment intervention. Freedom from metastatic disease was very high at five and 10 years. These results add to the body of data confirming that men on AS have a low risk of progression, including repeat biopsies over time. Lewicky and co-workers asked an important question; what is the risk of eventually dying from prostate cancer after having one negative biopsy? They looked at men who had a negative biopsy in the PLCO trial and found that at nearly 13 years, only 1.1% died of prostate cancer if their initial biopsy was negative. What is unclear from the abstract is what fraction of men had multiple biopsies and what fraction ended up with a diagnosis of prostate cancer. This finding has important implications for men who are being screened. Other reports found that men often undergo multiple biopsies during follow-up. This study suggests that little follow-up may be needed if the first prostate biopsy is negative.

P5, “Prognostic...”

One of the problems with screening for prostate cancer is the need for repeat testing, including repeat biopsies over time. Preliminary data suggest that PHI and %p2PSA can be used for detecting prostate cancer while PSA had the lowest accuracy. Their conclusion is that PHI and %p2PSA can be used for screening the general population. Unfortunately, their findings are far too premature to make such a conclusion. They need to provide information about the positive and negative predictive values for the test so estimates of detection in a broad population can be determined. Ultimately, if those look favorable, a recommendation to use any of them for screening would need the same kind of prospective randomized study as was done for PLCO.

P5, “Magnetic...”

Many articles have been written about the shortcomings of the PSA test for prostate cancer screening. Other methods are being evaluated including serum isoform [-2]proPSA (p2PSA) to free PSA (%p2PSA), the Prostate Health Index (PHI) and magnetic resonance imaging (MRI) with some studies suggesting better accuracy than PSA. In a small study by Furuya of only 50 men undergoing biopsy, each of these parameters was used. They found that %p2PSA and PHI were more accurate than MRI for detecting prostate cancer.