longest follow-up to date of active surveillance (AS) in men with favorable or intermediate-risk prostate cancer shows that it is a safe and feasible approach for as long as 20 years after diagnosis. Men in the study cohort had early-stage disease and were managed with AS; they were treated only if there were signs of disease progression. Up to 20 years after diagnosis, 1.5% of the 993 men had died, and 3.1% had developed metastatic disease.

In addition, death was 10 times more likely from other causes than from prostate cancer, reported Laurence Klotz, MD, from the Sunnybrook Research Institute in Toronto, who presented the results at the European Association of Urology (EAU) 29th Annual Congress.

“This is the longest, most mature follow-up with the explicit strategy of conservative management and selective delayed intervention,” he stated. “Even at 15 to 20 years, the prostate cancer mortality rate is really very low, you’ve avoided treatment in the majority of patients, and even the ones treated late still had a long period of normal quality of life before they had treatment.”

At 5, 10, 15, and 20 years after diagnosis, 75.7%, 63.5%, 55.0%, and 55.0% of men, respectively, remain untreated and on active surveillance. During the follow-up period, 15 died from prostate cancer and seven developed metastatic disease.

A quarter of prostate cancer patients participating in a Swiss active surveillance study didn’t bother showing up for their recommended appointments, lead researcher Dr. Lukas Hefermehl reported to the annual meeting of the European Association of Urology, held this month in Stockholm.

“These findings leave us with a practical and ethical dilemma,” said Hefermehl, a urologist at Kantonsspital Baden in Switzerland, in an association news release. “We often recommend that men go onto an active surveillance program, but these results indicate that more than a quarter of men will disappear from the system.”

Active surveillance — also known as “watchful waiting” — is a pragmatic
Methods: We queried the Johns Hopkins radical prostatectomy database to identify 753 men with NCCN high-risk localized prostate cancer (Gleason sum 8–10, PSA >20 ng ml−1, or clinical stage ≥T3). Twenty-eight alternate permutations of adverse grade, stage and cancer volume were compared by their hazard ratios for metastasis and cancer-specific mortality. VHR criteria with top-ranking hazard ratios were further evaluated by multivariable analyses and inclusion of a clinically meaningful proportion of the high-risk cohort.

Results: The VHR cohort was best defined by primary pattern 5 present on biopsy, or ≥5 cores with Gleason sum 8–10, or multiple NCCN high-risk features. These criteria encompassed 15.1% of the NCCN high-risk cohort. Compared with other high-risk men, VHR men were at significantly higher risk for metastasis (hazard ratio 2.75) and cancer-specific mortality (hazard ratio 3.44) (P<0.001 for both). Among high-risk men, VHR men also had significantly worse 10-year metastasis-free survival (37% vs 78%) and cancer-specific survival (62% vs 90%).

Conclusions: Men who meet VHR criteria form a subgroup within the current NCCN high-risk classification who have particularly poor oncological outcomes. Use of these characteristics to distinguish VHR localized prostate cancer may help in counseling and selection of optimal candidates for multimodal treatments or clinical trials.
PSA Doubling Time Calculator
Now you can measure your PSA doubling time using your iPhone.

This application is useful for doctors and patients alike as it quickly and accurately calculates the rate of rise of two or more PSA blood measurements over time. This is called the Prostate Specific Antigen doubling time (PSAdt) or velocity and is a much more important measurement than an isolated single PSA serum level.

This is particularly useful for men with early prostate cancer managed with active surveillance or experiencing a PSA relapse after previous treatments, or those being managed with intermittent hormone therapy.

The PSAdt over any period of time is displayed in an easily readable graph so one can accurately see if it is shortening (bad) or lengthening (good) in response to treatments which can include lifestyle changes or oral supplements such as Pomi-T®. The graph can be updated with each blood test and the results automatically emailed to the patient’s home computer and doctor.

The App also has lots of useful additional features such as information on PSA testing, prostate cancer and the lifestyle factors that help combat the disease. Patients can be linked to weekly news feeds reporting the latest scientific developments in prostate cancer treatments and prevention.

Developer: Simon Blackburn
Rated 4+
Compatibility: Requires iOS 6.1 or later. Compatible with iPhone, iPad, and iPod touch. This app is optimized for iPhone 5.

Long-Term Results with Surveillance Promising (Continued from page 1)

The prospective single-group cohort study enrolled men (median age, 69 years) with histologically confirmed prostate adenocarcinoma who had undergone no previous treatment. Definitive intervention was offered to men if they had a PSA doubling time of less than 3 years, Gleason score progression (to 4+3=7 or greater), or unequivocal evidence (including MRI) of clinical progression. The remaining 993 men were followed with AS.

In an earlier follow-up analysis at a median of 6.8 years after enrollment, only five men had died of prostate cancer—all of them fairly early into their surveillance (J Clin Oncol. 2010;28:126-131). In all five, it looked like their disease “wasn’t preventable with earlier treatment,” said Dr. Klotz.

In the latest analysis, median follow-up is 8.1 years. “But now it’s slightly more sobering. We’re starting to see some deaths in patients who have actually developed their metastases late. Perhaps if they’d been treated a decade before, they might have been cured.”

“The devil is really going to be in the details about these men who progressed,” said session chair Matthew Cooperberg, MD, MPH, associate professor of urology at the University of California, San Francisco.

“The question is how many men died of prostate cancer because they went on AS instead of getting immediate treatment. The answer to that question is always going to be greater than 0,” Dr. Cooperberg explained. “However, we all think that it’s very, very, very low; it’s far lower, most likely, than the number of men who have actually developed their metastases late. Perhaps if they’d been treated a decade before, they might have been cured.”

“At this stage, AS “is a treatment approach in evolution,” said Dr. Klotz. Research continues into how to refine the parameters for triggering intervention. “We’ve shifted to a more MRI-based evaluation of patients, which I think in the long run is going to change the shape of the time-to-treatment curve,” he said. “When something doesn’t seem right – either a patient has a short [PSA] doubling time or some small amount of Gleason pattern 4 – we now go to MRI; before, we treated them.”

Dr. Klotz, Dr. Cooperberg, and Dr. Bangma have disclosed no relevant financial relationships.

Presented at the EAU 29th Annual Congress, Abstract 26, 12 April 2014
Medscape Medical News, 14 April 2014

FDA Fast-Tracks OncoGenex Drug Custirsen for Prostate Cancer

OncoGenex Pharmaceuticals Inc. announced that the U.S. Food and Drug Administration (FDA) has granted fast track designation to the investigation of custirsen when administered in combination with cabazitaxel/prednisone for the treatment of men with metastatic castrate-resistant prostate cancer (CRPC) following prior treatment with a docetaxel-containing regimen.

Fast track is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need.

The purpose is to get important new drugs to the patient earlier.

The international, randomized, open-label Phase 3 AFFINITY trial is designed to evaluate if custirsen, when combined with second-line chemotherapy cabazitaxel and prednisone, has the potential to improve survival outcomes for prostate cancer patients compared to second-line chemotherapy alone. AFFINITY will enroll approximately 630 men and is expected to complete enrollment in the second half of 2014.

Custirsen has also received fast track designation from the FDA for treatment of patients with metastatic non-small cell lung cancer as part of the Phase 3 ENSPIRIT trial and for men with metastatic CRPC as part of the Phase 3 SYN-ERGY trial. Enrollment in the ENSPIRIT trial is ongoing and top-line survival results from SYNERGY are expected by mid-2014.

Drug Discovery and Development
23 April 2014
score of 4+3 or a maximum cancer core length of 6 mm.

Whole gland analysis using mpMRI produced promising results, with an area -under-the-curve of 0.78 for the detection of clinically significant disease, 69% sensitivity, 78% specificity, a positive predictive value of 67%, and a negative predictive value of 79%. In contrast, HistoScanning displayed high sensitivity (84%), but poor specificity (6%) and poor positive and negative predictive values (37% and 36%, respectively).

Session chair Boris Hadaschik, MD, from the University of Heidelberg, Germany, agreed. HistoScanning, which uses raw ultrasound data, is not available in North America, but is used routinely in parts of Europe and at some trial centers in the UK.

Prior positive studies for HistoScanning were based on a different population. “Previous studies looked mainly at radical prostatectomy cohorts, where all men were known to have cancer. In this study, some men have cancer and some don’t, and the burdens of disease are different,” Dr. Simmons noted. “I think that’s what’s reflected in this study.”

“There is a slight learning curve with MRI, which means the MRI may not have performed as well in these first men as it will in the overall cohort, so the final MRI results might be even better,” Simmons explained. “We think that mpMRI might be a useful test at this point in the diagnostic pathway, and it’s encouraging negative predictive value may allow men to safely avoid biopsy,” she added.

“The PICTURE trial is an excellent study, and we’re all looking forward to the final results,” Dr. Hadaschik observed. “The aim in the future would be that if MRI does not show anything, you can avoid the biopsy. But we need studies like PICTURE to be able to evaluate the risk of that approach.”

“Here it’s showing that MRI is excellent but not perfect; there are some tumors that will be overlooked. This is probably not a problem because you can decrease overdiagnosis and then follow-up with the patient a year later. It’s probably safe to treat that tumor a year later.”

Presented at the EAU 29th Annual Congress, Abstract 951, 14 April 2014
Medscape Medical News, 24 April 2014

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Bottom Line:
Contrary to popular belief and hysteria, artificial sweeteners have turned out to be safe overall and can help some folks lose a little weight/waist when used to reduce calories (especially sugar) from your diet. However, if you think that switching to an artificial sweetener by itself will be enough to get you to your ultimate weight loss goal, then I’ve got some swampland in the back of the Us TOO headquarters filled with oil and gold that I want to sell you ASAP.

Overall, artificial sweeteners have a good safety record despite all the controversy and internet buzz suggesting otherwise. Still, what they are lacking are more studies suggesting that they can actually help you lose weight when you try to substitute these substances for sugar. A small, but well-done (like a good steak) study administered supplements consisting of sugar-sweetened beverages and foods or identical beverages and foods containing artificial sweeteners for 10 weeks in overweight men and women (BMI 27–28). Interestingly, body weight increased in the sugar group (about +2.5 pounds on average) and decreased in the artificial sweetener group (about -2.5 pounds on average). Nothing to write home about, as they say. But something is better than nothing! In addition, the sugar group consumed more calories and felt less full compared to the sweetener group at week 10. Also, the metabolic rate in the sugar group increased but this appeared due to the greater intake of calories. Thus, the researchers concluded that the benefit of the sweeteners were simply due to assisting in reducing caloric intake.

What does all this stuff mean? It means that artificial sweeteners are just one very tiny piece in a massive puzzle on how to cut back on calories. Other important tips such as eliminating fruit juices, greater intake of protein and fiber (from unprocessed fruits, veggies, beans…) and healthy fat intake along with more movement time are all just more pieces of this large puzzle. Artificial sweeteners ran into a problem when folks began to believe the sweeteners could help overweight individuals lose a large amount of weight and suppress appetite. But they cannot do either of these things. At the same time, artificial sweeteners have become the target of ridiculousness, where some people want to claim these synthetic substances cause all kinds of problems (probably even global warming) and are useless for solving the obesity epidemic.

Well, this last part is true – artificial sweeteners will NEVER resolve obesity because again, they are just one little tiny hair on a horse’s head with a full large and thick mane. So, I am going to have my Coke Zero on the plane now (not kidding here – I love this stuff almost more than crazy politicians that say they are going to solve all the problems in Washington DC, if elected). However, I promise you that after drinking a maximum of one or two of these beverages a day. I have had enough, and I do not believe for one second that they will help me lose more than 2.5 pounds. Oh, and finally, I do think it is time to pay college football players!

Reference:
ABANDONMENT OF ACTIVE SURVEILLANCE (Continued from page 1)

“The patient must be willing to have regular follow-ups that will consist of regular PSAs [blood tests], physicals and ultrasounds to closely watch if the cancer is progressing, resulting in long-term follow-ups with close surveillance,” Samadi said. “Compliance from the patient throughout the whole process is a must, as watchful waiting can lead to metastasis and spread to other organs.”

Dropout rates are probably even worse in the U.S. than in Switzerland,” said Dr. Otis Brawley, chief medical officer for the American Cancer Society. “Men in the United States face more difficulty finding transportation to the doctor, may not be able to afford the co-pays required for each visit or might lose their insurance during active surveillance.”

“Prostate cancer patients also might put their condition on the back burner because they are facing other, more critical medical issues; or just don’t want to hassle with invasive probes on a regular basis,” he said. “On the other hand, the new study actually is a success story for active surveillance, in that three-fourths of the men who kept their appointments never needed treatment.

“It’s a glass-half-full, glass-half-empty situation,” he said. “I look at the same data and say ‘aha, there were a large proportion of men who stayed in follow-up and never got treated,’ and that’s good.”

Because this study was presented at a medical meeting, the data and conclusions should be viewed as preliminary until results are published in a peer-reviewed journal.

HealthDay News, 17 April 2014

STUDY FINDS NO INCREASED RISK OF MYELODYSPLASTIC SYNDROMES AFTER RADIATION TREATMENT FOR PROSTATE CANcer

A new Cleveland Clinic study has found that men who undergo therapeutic radiation treatment for prostate cancer have no greater risk of developing myelodysplastic syndromes (MDS) than the general population.

Senior study author Mikkael A. Sekeres, MD, MS, of the Department of Hematologic Oncology and Blood Disorders in Cleveland Clinic’s Taussig Cancer Institute says the findings came as a surprise.

“The medical community had long assumed that patients who received radiation therapy to treat prostate cancer were at a higher risk for developing MDS,” he says. “The reason for that is quite simply geography, since the prostate is right in the middle of the pelvis, and the pelvis is a major site of bone marrow production in the body.”

The study, which was published recently in the Journal of the National Cancer Institute, was a joint effort between Taussig Cancer Institute and the Glickman Urological & Kidney Institute. The retrospective cohort analysis was based on data from 10,924 prostate cancer patients who were treated at Cleveland Clinic from 1986–2011 with either surgery, radiotherapy with external beam radiation (EBRT), or radiation therapy with brachytherapy.

A total of 31 cases of therapy-related MDS were observed during the study period. In multivariable analyses, MDS rates were similar in patients who underwent surgery for prostate cancer compared with those who received some type of radiotherapy. The MDS rates observed in the study were found to be comparable to rates in population-based registries, including the Ohio Cancer Incidence Surveillance System (OCISS) and the Surveillance, Epidemiology, and End Results (SEER) database.

Advancing age is an independent risk factor for developing MDS, which the study analyses confirmed.

Approximately 14 percent of MDS cases are considered therapy-related, occurring in cancer patients approximately five to seven years after treatment with cytotoxic chemotherapy, radiation or both. In addition, exposure to ionizing radiation treatment strategy derived from two known facts about prostate cancer. First, prostate cancer grows so slowly in most men that they are likely to die from other causes. Second, the surgery and radiation therapy used to treat prostate cancer often cause impotence, incontinence and other side effects that affect the man’s quality of life.

Prostate cancer is the most common cancer in American men other than skin cancer, according to the American Cancer Society. But the 15-year survival rate for prostate cancer is an impressive 94 percent. As a result, many doctors have concluded it’s better to leave the prostate cancer alone and only act if it accelerates.

This new study followed 157 men during 13 years of active surveillance. After 13 years, researchers found that about 28 percent of all patients required treatment because their prostate cancer flared up. Nearly all the men were cured of their prostate cancer, with an overall group survival rate of 94 percent.

However, another 27 percent of the men in the study didn’t bother coming back for check-ups after being placed on active surveillance, leaving themselves potentially vulnerable to a prostate cancer flare-up. In addition, researchers found that about 19 percent of the men refused to undergo a second biopsy three months after their diagnosis, to confirm the results of their first prostate cancer biopsy.

“We don’t know exactly what the reasons are,” Hefermehl said. “It may be that once the patient was told that this cancer is probably ‘not immediately threatening,’ he might downplay the importance of another test. On the other hand, some men might have real concerns about the risk of there being a more severe cancer,” he said. “Or it may have to do with the risk of incontinence or impotence after treatment, the idea of having cancer, a sense that nothing will really happen to them; or it may be due to another reason which we just don’t know about.”

“The study highlights the need for doctors to impress upon prostate cancer patients the importance of check-ups,” said Dr. David Samadi, chairman of urology at Lenox Hill Hospital, in New York City.

(Continued on page 8)
**Potency After Prostate Brachytherapy Hinges on Many Factors**

Erectile dysfunction (ED) after prostate brachytherapy is largely predicted by pretreatment sexual function and age in addition to smoking status and comorbid conditions, such as diabetes and hypertension, according to new research presented here at the European Society for Radiotherapy and Oncology (ESTRO) 33rd annual conference.

“Of men younger than age 60 years who have full sexual function before treatment, about half will maintain it five years after brachytherapy, whereas among those with satisfactory pretreatment function, about a quarter will maintain it,” said Renée Oismüller, MD, from SMZ-Ost Donau spit at Vienna, Austria.

“I was pretty surprised with these results – they’re pretty good,” she stated in an interview after her presentation.

“The findings compare similarly to previous studies in this area,” said session moderator Ann Henry, MD, a consultant at St James’s Institute of Oncology in Leeds, United Kingdom.

“Brachytherapy is generally one of the better treatment options for maintaining sexual function and is considered to be as effective [for cancer treatment] as any of the other treatments – surgery or external-beam radiotherapy – for prostate cancer,” Dr. Henry told Medscape Medical News. “This study adds to what is already known on this.”

In a written statement, Professor Vincenzo Valentin, a radiation oncologist at the Policlinico Universitario A. Gemelli in Rome, Italy, and president of ESTRO, said, “Modern radiotherapy is increasingly able to provide less demanding treatments that preserve organ function. This study provides the radiotherapy community with a benchmark for erectile dysfunction, and I hope it will encourage more centers to include brachytherapy in their treatment options.”

The study analyzed 542 men who underwent permanent prostate brachytherapy from July 1999 to October 2013. The men completed International Index of Erectile Function (IIEF) questionnaires before treatment, one month after treatment, then every three months for two years, every six months for up to five years, and then yearly.

The simplified 5-item IIEF version was used (questions 2, 4, 5, 7, and 15). The highest score (22 to 25) indicated no ED; lower scores indicated mild (17 to 21), mild/moderate (12 to 16), moderate (8 to 11), and severe (1 to 7) ED.

Only 21% of men had the highest scores before treatment, indicating no ED, and among this group 55.6% of those under age 60 years and 35% of those over age 60 years had maintained their full sexual function at five years after therapy, Dr. Oismüller reported.

When the category was widened to include men who had “satisfactory” sexual function before treatment (scores of 17 to 21), defined as “able to achieve and maintain erection for satisfactory intercourse, even if sometimes suboptimal,” 78% of men under age 60 and 65% of those over age 60 were able to maintain full or satisfactory sexual function five years after treatment, she said.

Using a post-treatment score of 17 as a cutpoint, the study found that age had a significant effect, with 81.1% of men under age 60 and 75.6% of those older than age 60 achieving that score at two years, and 76.5% and 74%, respectively, achieving it at five years (P=0.0109).

Diabetes, hypertension, and smoking also had a significant effect on this cutpoint. For men without diabetes, 79.6% and 77% achieved an IIEF score of at least 17 at two and five years, respectively, regardless of age (P=0.0099), versus none of the men with diabetes. In men without hypertension, 82.2% and 80.2% achieved an IIEF score of at least 17 at 2 and 5 years, respectively, versus 67.3% and 62.5% of men with hypertension (P=0.0022). Similarly, 80.1% and 77.3% of men who did not smoke achieved this score at two and five years, respectively, versus 51.8% of smokers at both time points (P=0.0015).

Neither the addition of androgen deprivation nor external-beam radiotherapy affected sexual function scores.

The study found a high rate of ED among men before treatment, with only 116 of 542 (21.4%) reporting no ED, said Dr. Oismüller. This subgroup of men was younger; their median age was 63.7 years, compared with 67.4 years for the rest of the cohort.

“We need guidelines to assess erectile function pretreatment and in follow-up,” she said. “This would help to simplify comparisons of ED between different treatment modalities.”

Presented at the ESTRO 33rd Annual Conference, abstract OC-0073, 5 April 2014

Medscape Medical News, 7 April 2014

(Continued on page 8)
Imagine being able to do a non-invasive test to tell if a man has prostate cancer. It sounds like Star Trek but indeed progress is being made. A report by Simmons at EAU looked at early results using multi-parametric MRI (mpMRI) and HistoScanning. Their preliminary results show that the mpMRI performed much better than the HistoScanning, however, the positive (PPV) and negative predictive values (NPV) still were not very good. A PPV is a measure of how often the test is correct when it says cancer is present and an NPV is how often it is correct when no cancer is present. For a test to be truly effective for men to avoid a biopsy, the NPV would need to be near 100%, otherwise many cancers may be missed. Even so, more work is warranted to see if things can improve.

**The Bottom Line:** Neither mpMRI nor HistoScanning are accurate enough at this time for replacing a prostate biopsy.

The information available about active surveillance (AS) continues to expand. Dr. Klotz did another update of his large case series with up to 20 years of follow-up in some men and a median 8.1 years. The risk of dying from prostate cancer was 1.3% and the risk of metastatic disease was 3.1%. Importantly, 55% of men remained on AS. As Dr. Klotz acknowledged, AS is still evolving, in part because doctors are not exactly sure what changes warrant treatment. The criteria being used today may not ultimately be the right approach. The good news, however, is that the mortality rate has not changed significantly even with the longer follow-up. The results also have implications for evaluating other treatments for this disease. Given that so many men do well even up to 20 years, looking at results after only five or 10 years is simply not adequate to know if that treatment is effective.

**The Bottom Line:** Long-term results show that AS carries a very low risk even up to 20 years of follow-up. More men should be informed of this option.

Of course, good results with AS require that men adhere to the recommendation for follow-up but that may not always occur as was reported by from a small Swiss study. They found that over a 13-year period, about 25% of men failed to keep their appointments. However, many questions need to be answered. First, did those men go elsewhere for their care? Second, how many died over that period and were lost to follow-up? Third, the study is very small and perhaps different results would have occurred in a larger study? These results are very different from the Canadian results reported above.

**The Bottom Line:** Men choosing AS have a greater responsibility to make sure they do appropriate follow-up if they want to avoid long-term harm from their disease.

Miano and co-workers compared transrectal and transperineal biopsies to determine which cancers were located on only one side of the prostate. Their purpose was to find a way to determine which men might be suitable for focal therapy by treating one-half of the gland. Their findings provide another reason why focal therapy has a long way to go to be a useful treatment. The problem is that few men have their cancer on only one side of the prostate. Miano found that neither method was very accurate and so some other method will be needed before men could be identified for focal treatment. This is just one of many reasons why focal therapy is not an appropriate treatment at this time.

**The Bottom Line:** Neither transrectal nor transperineal biopsy are accurate for identifying which patients have unilateral prostate cancer.

Another new drug under investigation for advanced prostate cancer is custirsen. It works by blocking a protein called clusterin, which plays a role in cancer cell survival and resistance to other drugs. The company has announced a new study combining this drug with cabazitaxel, the second line chemotherapy agent. Unfortunately, a recent report revealed that the study of custirsen in combination with docetaxel and prednisone did not improve survival. Whether it will work better in this new study is unclear.

**The Bottom Line:** Custirsen is under investigation in combination with second line chemotherapy and hopefully the results will be better than they were when the drug was combined with docetaxel.

For years, doctors have been concerned that radiation therapy (RT) for prostate cancer could result in secondary problems such as bladder cancer, rectal cancer or cause damage to the bone marrow resulting in myelodysplastic syndrome (MDS). Now a retrospective study of a large number of men found that the incidence of MDS was similar in men having RT or undergoing radical prostatectomy. The study included patients treated up to 2011. Although these results are encouraging, one limitation is that the dose for external radiation has been increasing and longer follow-up may be needed in men receiving these higher doses to know if the risk for MDS does increase.

**The Bottom Line:** The risk for MDS does not appear to be higher following external RT although longer follow-up is needed in those men receiving higher doses than were used in the 1990’s.

Another side effect of RT was analyzed by Oismüller and co-workers. They reported on the incidence of erectile dysfunction (ED) over time following brachytherapy. Overall, the results were better when compared with other types of treatment. This study was well done because they started measuring sexual function before treatment and then at multiple points in time after the therapy was completed. An important finding was the negative impact of diabetes, hypertension, smoking and age. In each case, men with one of those problems had significantly worse function when compared to healthier men. This study demonstrates one of the difficulties in comparing results of different treatments; given the negative impact of each of these factors. Comparison studies need to separate their results according to men with and without these problems. Although the authors did not report the effect in men with more than one of them, we can expect even worse function for those men. Given both the high percent of men retaining sexual function and the ease of treatment, we must ask why the use of brachytherapy is on the decline and external RT is on the rise? Could doctor compensation have anything to do with this trend?

**The Bottom Line:** Long-term results show that healthy men with good erectile dysfunction (ED) over time following brachytherapy. Overall, the results were better when compared with other types of treatment. This study was well done because they started measuring sexual function before treatment and then at multiple points in time after the therapy was completed. An important finding was the negative impact of diabetes, hypertension, smoking and age. In each case, men with one of those problems had significantly worse function when compared to healthier men. This study demonstrates one of the difficulties in comparing results of different treatments; given the negative impact of each of these factors. Comparison studies need to separate their results according to men with and without these problems. Although the authors did not report the effect in men with more than one of them, we can expect even worse function for those men. Given both the high percent of men retaining sexual function and the ease of treatment, we must ask why the use of brachytherapy is on the decline and external RT is on the rise? Could doctor compensation have anything to do with this trend?
had been linked to subsequent development of MDS in several cancer cohorts. Until this study, the risk of MDS in prostate cancer patients treated with therapeutic radiation had remained unclear.

“What’s been problematic is that when an older man who has a history of receiving radiation for prostate cancer develops MDS, the radiation has been viewed as the cause for MDS – when it most likely was unrelated,” Dr. Sekeres explains. “Based on the results of our study, patients receiving radiation for prostate cancer can rest assured that they do not have excess risk for developing MDS within their lifetime.”

As patients were collected over a 25-year period, follow-up was limited. However, given the median patient age of 64 and average life expectancies, Dr. Sekeres says any influence that therapeutic radiation for prostate cancer develops MDS, the radiation has been viewed as the cause for MDS – when it most likely was unrelated. Alternatively, the investigators report.

“The authors should be applauded for conducting a single-institution randomized trial,” said Rahul Tendulkar, MD, a radiation oncologist from the Cleveland Clinic, who was not involved in the study. “It is generally understood that higher RT doses to the rectum are associated with more adverse effects,” he explained. “But this specific information for hypofractionated therapy is very valuable.”

**Medscape Medical News, 24 April 2014**

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**Hypofractionated RT**

(Continued from page 6)

treated with hypofractionation, the development of grade 2 or higher GI toxicity was associated with the proportion of the rectum receiving 36.9 Gy, 46.2 Gy, 64.6 Gy, and 73.9 Gy (P < 0.05). Risk escalated considerably with 64.6 Gy.

For grade 2 or higher GI toxicity, the five-year rate was higher in men who received 64.6 Gy to at least 20% of the rectum than to less than 20% of the rectum (27.3% vs 6.0%; P = 0.016).

This study started in 2001, during the “early era” of IMRT. Technical improvements since that time should result in even less RT being delivered to normal tissue, and therefore even less toxicity, the investigators report.

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**The Bottom Line:**

The incidence of GI side effects following hypofractionated RT were evaluated by Hoffman and co-workers, who conducted a randomized trial comparing it to conventional IMRT. The hope is that the advantages of decreasing the time to complete external RT will outweigh any disadvantages. The first question is how this treatment will affect side effects. The authors found that the greater the dose delivered to the rectum, the greater the incidence of GI side effects. This was not the case for bladder side effects. Limiting the amount of RT to the rectum will therefore be important. The next question is what is the cancer control using the higher fractionation doses. The answer is critical to know whether the results are similar to the standard approach.

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