

#### INSIDE THIS ISSUE

- PCAM Activities
- Study Finds Acceptable Levels of Anxiety in Men Living with Early, Untreated Prostate Cancer
- Heavy Drinking Boosts Prostate Cancer Risk
- Prostatectomy May Not Always Be Necessary
- Awareness of Prostate Cancer in the General Public
- Some Cancer Rates Higher in the Military
- HIFU in the Treatment of Primary Prostate Cancer
- Doc Moyad's "What Works and What Is Worthless Column" — Acupuncture: Real vs. Simulated
- Newly Discovered Gene Fusion Protein
- NCCN Stresses Importance of PSA Testing in High-Risk Men
- 2009 PCRI Prostate Cancer Conference
- What's Your Type (of Prostate Cancer) — That's the Most Important Question
- The Doctor's Note — Gerald Chodak, MD
- Sneakers @ Work Day: Friday 18 September 2009
- Prostate Drug Appears Safer Than Thought



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EDUCATION & SUPPORT

# HOTSHEET

September 2009

## SEPTEMBER IS PROSTATE CANCER AWARENESS MONTH!

### JOIN IN SEPTEMBER AWARENESS & EDUCATION ACTIVITIES

Sat-Sun, Sept 12-13 — PCRI Prostate Cancer Conference, <<http://prostatecancer.org>>

Sun, Sept 13 — SEA Blue Prostate Cancer 3K Walk in Chicago, <[www.SEABlueProstateWalk.org](http://www.SEABlueProstateWalk.org)>

Fri, Sept 18 — Sneakers@Work Day, <[www.ustoo.org/sneakers@work](http://www.ustoo.org/sneakers@work)>

Week of Sept 20-26 — various no-cost PSA screenings across the country, <<http://www.prostateconditions.org/screening-site-finder>>

Wed, Sept 23 — Us TOO University Presents: "Estrogen Deficiency Side Effects Due to Androgen Deprivation Therapy", Webinar/Teleconference w/ Samir Teneja MD, 8:00 pm ET / 7:00 pm CT, 5:00 pm PT, <[www.ustoo.org](http://www.ustoo.org)>

Sun, Sept 27 — 13th Annual Quad Cities Marathon Walk for Prostate Cancer, <[www.ustooevents.org/QCMarathon](http://www.ustooevents.org/QCMarathon)>

And many more! Check out your local support group and Us TOO for details.

### STUDY FINDS ACCEPTABLE LEVELS OF ANXIETY AMONG MEN LIVING WITH EARLY, UNTREATED PROSTATE CANCER

Men with early stages of prostate cancer who delay radical treatment in favor of an approach of "expectant management" do not have high levels of anxiety and distress. That is the conclusion of a new study scheduled for publication 1 September 2009 in the peer-reviewed journal of the American Cancer Society *Cancer*, which was published online ahead of print on 27 July 2009. The study's results suggest that living with untreated cancer is not upsetting for many patients with early prostate cancer.

The rapid increase in the use of screening using prostate specific antigen (PSA) testing has led to a large number of men diagnosed with prostate cancer, many of who do not require treatment. In these cases, close clinical monitoring – or active surveillance – is often recommended. If progression of the cancer occurs during active surveillance, patients may undergo radical therapy. While active surveillance may

### HEAVY DRINKING BOOSTS PROSTATE CANCER RISK

Regular, heavy consumption of alcohol increased the risk of high-grade prostate cancer and blunted the chemopreventive effect of finasteride, data from the Prostate Cancer Prevention Trial (PCPT) showed. Men who consumed at least 50 grams of alcohol (at least four drinks) daily doubled their risk of high-grade prostate cancer, Zhihong Gong, PhD, of the University of California San Francisco, and colleagues reported online in the journal *Cancer*. The risk was similar in the placebo and finasteride arms of the trial.

Heavy drinking did not influence the risk of low-grade cancer in the placebo arm, but significantly increased the risk in men taking finasteride. The overall risk increase in the finasteride group came about from a significant risk reduction in men who drank less than 50 grams of alcohol, combined with finasteride's lack of effect among heavier drinkers.

Before this analysis, most individual studies showed no association, although at least two meta-analyses

(Continued on page 3)

(Continued on page 7)

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**PROSTATECTOMY MAY NOT  
BE NECESSARY FOR SOME  
PATIENTS**

In a study published online in the *Journal of Clinical Oncology*, researchers found that in a group of 12,677 men who had radical prostatectomies (RP) between 1987 and 2005, the 15-year mortality rate that could be directly linked to prostate cancer was only 12%, even though many of the men's cancers had aggressive features.

Comparatively, the rate of non-cancer-related death in this group was 38%. A small fraction, 4%, of patients treated surgically within the past 10 years had a 5% or greater risk of dying of prostate cancer within 15 years. It is not clear at this time whether the outcomes may be related to the effectiveness of surgery and any secondary therapy or to the low lethality of certain types of prostate cancers to begin with.

"The importance of this paper is that it shows a remarkably low risk of dying of prostate cancer within 15 years for treated men, supporting the concept that men with slow-growing cancers may not need immediate treatment," said senior author Peter Scardino, Dept. of Surgery, Memorial Sloan-Kettering Cancer Center in NY.

As part of the study, 12,677 patients treated with RP between 1987 and 2005 were tracked. Of these patients, 6,398 underwent RP for localized prostate cancer, with 809 (13%) receiving neoadjuvant androgen-deprivation therapy for an average of 3.2 months. External validation of the nomogram was performed on 4,103 patients treated at Cleveland Clinic and 2,176 treated at University of Michigan in Detroit during the same period.

Prostate biopsy specimens were reviewed by pathologists at each institution before RP. In general, patients were followed for disease recurrence post operatively with regular PSA tests and clinical exams at 3 to 6 month intervals for the first 5 years, and then annually. The year of RP was also a consideration, as methods and effectiveness have changed over the years.

"The good news is that surgery was very effective in preventing death in men with aggressive cancers – defined

*(Continued on page 5)*

**AWARENESS OF PROSTATE  
CANCER AMONG PATIENTS  
AND THE GENERAL PUBLIC:  
RESULTS OF AN  
INTERNATIONAL SURVEY**

The objective of this study was to assess the level of awareness of prostate cancer among the general public and PCa patients in Europe and North America. A survey was undertaken across four European countries (UK, Germany, Italy and Spain), and across the US and Canada in late 2007.

In total, 1,008 men with prostate cancer and their partners (the 'prostate sample'), and 911 men without prostate cancer and their partners (the 'well sample') participated in the survey, all aged ≥50 years. Interviews were conducted through telephone, pen and paper, and online.

Many people surveyed (53%) thought that breast cancer is more common than prostate cancer. Moreover, 1 in 10 people from the well sample (10%) thought that prostate cancer affects both men and women. When the prostate sample was asked about their perceived level of risk of cancer before diagnosis, 50% believed that they/their husband or partner were at low or very low risk, before they were diagnosed. Awareness of the major risk factors for prostate cancer (age and family history) was generally good, but respondents were less clear about the role of other potential factors, such as smoking and drinking alcohol.

This international survey, thought to be largest of its type, shows that although patient and public awareness of prostate cancer is generally satisfactory, there is still a considerable lack of clarity about prostate cancer risk factors, and a danger for people to underestimate their own/their partner's perceived risk for prostate cancer.

Programs to responsibly educate and inform men and their partners about risk factors, prevalence and screening tools for PCa are required.

**Written by:** Fitzpatrick JM, Kirby RS, Brough CL, Saggerson AL

**Citation:** Prostate Cancer and Prostatic Diseases, E-pub ahead of print, 21 July 2009

## SOME CANCER RATES HIGHER IN MILITARY

A new study shows that while active-duty service members have lower rates of cancer overall than civilians, they have higher rates of breast cancer and double the rates of prostate cancer. And though that could be attributed in part to early screening efforts, the authors suggested prostate cancer rates have gone up as a result of troop exposure to depleted uranium, while breast cancer rates may have risen because military women are more inclined to use birth control pills and be exposed to industrial chemicals at levels most civilian women avoid.

In the June 2009 edition of *Cancer Epidemiology Biomarkers & Prevention*, lead writer Kangmin Zhu, of the Uniformed Services University of the Health Sciences, and colleagues stated that they wanted to find out if regular exercise and good health care, combined with a population that had been screened for major health issues, would yield lower rates of cancer.

They also wondered if service members, who smoke at higher rates than civilians do, would have a higher rate of lung cancer. And the researchers also wanted to see whether sun exposure, as well as other deployment exposures such as immunizations and depleted uranium, would influence results.

But looking at the years 1990 to 2004, they found that colorectal cancer rates were “significantly lower” in the military population for white men; lung cancer rates were lower for white and black men, as well as white women; and cervical cancer rates were lower in black women. However, breast and prostate cancers for military personnel were “significantly higher” among whites and blacks. Prostate cancer increased over that time for both the civilian and military populations, but the civilian rate doubled, while the rates for white male troops tripled.

Researchers again reasoned that this may be because of early screening – the cancer is being identified early. But there may be other reasons: A recent study shows 34 percent of female service members use oral birth control pills, compared to 29 percent of the general population. The pills have been linked to breast cancer.

“Military women are also more likely to be engaged in industrial jobs than females in the general population and hence potentially more likely to be exposed to chemicals that may be related to breast cancer,” Zhu wrote. A study of military women 34 and younger find higher breast cancer rates than civilians, and the rate was even higher for those military women exposed to volatile organic chemicals as part of their work.

Zhu also linked prostate cancer to exposure. “Although the results have been inconsistent, depleted uranium has been suggested to increase the risk of prostate cancer,” Zhu wrote.

“Because military personnel are more likely to be exposed to depleted uranium, these factors may have contributed to the increased risk for prostate cancer in military members, although most of the elevated rates and more dramatic increase over time in rates in military personnel may be attributed to screening in the population.”

Zhu reasoned that some cancer rates might be lower because service members are more likely to go in for cancer screening because they have free health care. Precancerous lesions and polyps might be treated early. Colorectal cancer rates may be lower for troops because they are less likely to be overweight and are more physically active.

Researchers were surprised to find that lung cancer rates were lower in the military in all groups except black women. Troops smoke more than civilians do, but the researchers said service members are more likely to begin smoking as adults – rather than in their teens, as civilians tend to do.

“Cigarette smoking is the single most important risk factor for lung cancer,” Zhu wrote. “Therefore, the lower rate of lung cancer in military personnel is an unanticipated finding.”

The researchers used data from the military’s Automated Central Tumor Registry, as well as the civilian Surveillance, Epidemiology and End Results program for the National Cancer Institute. They adjusted the civilian data to include only those age groups one might expect to find in the military.

<[www.armytimes.com](http://www.armytimes.com)>, 22 July 2009

## ALCOHOL CONSUMPTION

(Continued from page 1)

showed an increased risk of about 20% among heavy drinkers.

Dr. Gong and colleagues decided to clarify the association by analyzing the PCPT database. Additionally, they wanted to determine whether alcohol consumption affected finasteride’s ability to prevent prostate cancer.

The authors’ analysis encompassed 10,920 of the 19,000 participants in the PCPT. The study group consisted of 2,129 men who developed prostate cancer during the trial and 8,791 who had negative end-of-study biopsies.

Overall, heavy alcohol consumption and regular heavy drinking five or more days a week doubled the risk of high-grade prostate cancer (RR 2.01 and RR 2.05, respectively). The impact was similar in the placebo and finasteride arms. Lower levels of consumption did not influence the risk of high-grade prostate cancer. The risk of low-grade cancer in the placebo group was unaffected by alcohol consumption. However, consumption of  $\geq 50$  g of alcohol daily doubled the risk of low-grade prostate cancer in the finasteride group (RR 2.01, P=0.02 for trend).

“For low-grade cancer, finasteride decreased the risk by 43% among men who drank <50 g of alcohol per day and increased the risk by 12% among heavy drinkers,” the authors noted. The authors acknowledged several limitations of the study. Heavy drinkers accounted for fewer than 3% of the study population, while data on alcohol consumption were limited to the year before enrollment in PCPT.

Because almost all of the cases of prostate cancer were screen detected, investigators could not examine associations between alcohol consumption and regional or distant disease.

The impact of heavy drinking “is somewhat unique in the literature and requires replication,” the authors said. “However, it would be prudent for physicians who are recommending finasteride for prostate cancer prevention to assess their patients’ alcohol intake and recommend limiting it to 3 or fewer drinks per day,” they added.

*MedPage Today*, 13 July 2009

**HIGH-INTENSITY-FOCUSED  
ULTRASOUND IN THE  
TREATMENT OF PRIMARY  
PROSTATE CANCER:  
THE FIRST UK SERIES**

*Br J Cancer* 101: 19-26, 2009

The use of minimally invasive ablative therapies in localized prostate cancer offer potential for a middle ground between active surveillance and radical therapy. An analysis of men with organ-confined prostate cancer treated with transrectal whole-gland HIFU (Sonablate® 500) between 1 February 2005 and 15 May 2007 was carried out in two centers. Side-effects using validated patient questionnaires, biochemical and histology were evaluated. A total of 172 men were treated under general anesthetic as day-case procedures with 78% discharged a mean 5 hours after treatment. Mean follow-up was 346 days (range 135-759 days). Urethral stricture was significantly lower in those with suprapubic catheter compared with urethral catheters (19.4 vs. 40.4%, P=0.005). Antibiotics were given to 23.8% of patients for presumed urinary tract infection and the rate of epididymitis was 7.6%. Potency was maintained in 70% by 12 months, whereas mild stress urinary incontinence (no pads) was reported in 7.0% (12 out of 172) with a further 0.6% (1 out of 172) requiring pads. There was no rectal toxicity and no recto-urethral fistulae. In all, 78.3% achieved a PSA nadir  $\leq 0.5$  ng/mL at 12 months, with 57.8% achieving  $\leq 0.2$  ng/mL. Then, 8 out of 13 were re-treated with HIFU, one had salvage external beam radiotherapy and four chose active surveillance for small-volume low-risk disease. Overall, there was no evidence of disease (PSA  $\leq 0.5$  ng/mL or negative biopsy if PSA nadir was not achieved) after one HIFU session in 92.4% (159 out of 172) of patients. HIFU is a minimally invasive, day-case ablative technique that can achieve good biochemical outcomes in the short term with minimal urinary incontinence and acceptable levels of erectile dysfunction. Long-term outcome needs further evaluation and the inception of an international registry for cases treated using HIFU will significantly aid this health technology assessment.

**DOC MOYAD'S WHAT WORKS & WHAT IS WORTHLESS  
COLUMN, ALSO KNOWN AS "NO BOGUS SCIENCE" COLUMN**

**"Life is too short to have a bad doctor!! Or, simulated acupuncture may be just as effective as traditional acupuncture for some health conditions."**

Mark A. Moyad, MD, MPH

University of Michigan Medical Center, Department of Urology

**Bottom Line:** Toothpicks may work as well as acupuncture or even conventional medicine for some conditions?!

Acupuncture has been touted by some alternative medicine "experts" as being able to treat everything from allergies to cancer to heart disease to solving the mystery of why some people like to talk on their cell phones in a public elevator! Anyhow, the vast majority of the objective research suggests that the greatest potential impact of acupuncture may be in reducing nausea from chemotherapy and in reducing chronic pain, such as chronic low back pain.

Recently, a total of 638 adults with chronic low back pain were randomized to one of four groups: individualized (personalized), standardized (regular/traditional), or simulated (placebo) acupuncture, or to a usual care group.<sup>1</sup> Simulated acupuncture consisted generally of a toothpick making contact with skin, but not piercing the skin. A total of 10 treatments were provided over 7 weeks by licensed and experienced acupuncturists. Back-related dysfunction and symptom improvement were evaluated at baseline, 8, 26, and 52 weeks.

The side effect rate was 4% with the needle insertion acupuncture groups and 0% with the simulated group (p=0.04) – heck toothpicks are safer than I thought. At 8 and 26 weeks, mean dysfunction and symptom scores were significantly better in all 3 acupuncture groups compared to usual care. After 1 year, results were similar, and all 3 acupuncture groups displayed similar benefits without one being more beneficial versus the other.

Acupuncture was effective for chronic low back pain, but specified anatomical tailoring of the needle sites and needle penetration of the skin was NOT related with the actual benefit. Whether a placebo or another unidentified response was responsible for the results needs further study.

Let me get straight to the point (pun intended) and insert (pun intended again) some more of my opinion here without needling (pun intended again) you to death on this point (did not intend a pun there-damn I am good at this)! Toothpicks touching the skin were basically equally effective compared to traditional needle insertion acupuncture for lower back pain, and more effective compared to conventional medicine?! Also, it is important to mention that a 10 week treatment with real acupuncture costs approximately \$600-\$1200 total dollars, which does not necessarily relate to any medical cost savings!

Does this mean we should start recommending toothpick skin touching for patients in pain? Not necessarily, but what this means to me is that like any medical intervention, acupuncture has its positives and negatives, but what this also means is that the traditional health care professional and patient relationship tends to get underestimated in general in the health care debate. Acupuncturists tend to give at least 30 minutes to 1 hour with each patient and they talk about lifestyle changes with each program. If physicians' were allowed to give regular lifestyle advice and spend 30 minutes to 1 hour with patients I wonder what their overall outcomes research would demonstrate for each specific medical condition including chronic pain!

The next time you think that not having a good doctor is important please remember the toothpick study, because a good doctor (skilled, good personality, treats you with respect, listens, does not think he or she is Moses/Charlton Heston/God, does what is in your best interest and not their best interest, encourages a second opinion...) can have profound effects on you that you never could have imagined. I love my doctor, trust my doctor, he listens, he is the smartest

*(Continued on page 8)*

**NEWLY DISCOVERED GENE FUSION MAY LEAD TO IMPROVED PROSTATE CANCER DIAGNOSIS**

Researchers from New York-Presbyterian Hospital/Weill Cornell Medical Center have discovered a new gene fusion that is highly expressed in a subset of prostate cancers. The results may lead to more accurate prostate cancer testing and new targets for potential treatments.

The new findings, published in the August 2009 issue of the journal *Neoplasia*, are exciting, because unlike two previous gene fusions that were co-discovered by the same Weill Cornell Medical College laboratory group, this fusion, called NDRG1-ERG, produces a protein that may be a potential target for drug therapies.

“The prostate cancer gene fusions, and proteins they produce, are important because they serve as a cancer-specific marker,” says Dr. Mark A. Rubin, the Homer T. Hirst Professor of Oncology in Pathology, professor of pathology and laboratory medicine, and vice chair for experimental pathology at Weill Cornell Medical College.

Dr. Rubin, working in collaboration with Dr. Chinnaiyan’s group at the University of Michigan, previously described the TMPRSS2-ERG fusion found in 45 percent of prostate cancers. The new gene fusion is seen in 5 percent of prostate cancers.

*PRNewswire, 27 July 2009*

**NCCN STRESSES IMPORTANCE OF PSA TESTING IN HIGH-RISK MEN**

PSA testing performs optimally when conducted intelligently and combined with prompt, effective, high-quality treatment according to the updated NCCN Clinical Practice Guidelines in Oncology™ for Prostate Cancer Early Detection. In the wake of the recent confusion that ensued after the publication of two PSA screening trials, the ERSPC trial conducted in Europe and PLCO trial conducted in the US, the Guidelines’ Panel Members stress that PSA testing is effective and needs to be more rigorous in high-risk populations.

“PSA testing has saved thousands of lives and continues to be an important tool in the fight against prostate cancer,” says Mark Kawachi, MD, Chair of the NCCN Guidelines for Prostate Cancer Early Detection and Associate Professor of Surgery, Urology and Urologic Oncology at City of Hope Comprehensive Cancer Center in Duarte, CA. “We are most likely to produce further declines in prostate cancer mortality if we focus on younger men who are more likely to die of prostate cancer than other causes and the diagnosing of aggressive prostate cancer in all men.”

Information about the ERSPC trial is incorporated into the updated NCCN Guidelines in the section entitled ‘Suggested Talking Points for Discussion with a Potential Screenee about the Pros and Cons of PSA Testing.’ The information summarizes the trial and reiterates the researchers’ conclusions that PSA screening reduced the rate of death from prostate cancer in men who were screened, although it resulted in a high risk of overdiagnosis. This led to several reports suggesting that screening for prostate cancer saves few lives.

NCCN Guideline Panel Members note the importance of the ERSPC trial, but caution that it needs to be considered in view of its flaws.

“Past research indicates that African-American men as well as men with a family history of prostate cancer have a significantly increased risk of developing the disease,” says Kawachi. “The ERSPC study did not include any information about family history or specify the racial composition of its patients.” The US PLCO trial, which

reported that PSA screening did not reduce the risk of prostate cancer death, also lacked in heterogeneity and included a very small number of patients with a family history of prostate cancer or African-American men.

This suggests that the majority of men who participated in the two trials were not at a high-risk of developing advanced prostate cancer, so it is not surprising that PSA screening would have little impact on their risk of death from the disease.

It is important to note that the NCCN Guidelines for Prostate Cancer Early Detection are for the purpose of detecting cancer early in high-risk men, not the screening of mass populations. The updated NCCN Guidelines emphasize this point with a note in the introduction stating that they are specifically for men opting to participate in an early detection program after receiving appropriate counsel.

An additional update recommends high-risk men be offered a baseline PSA and DRE at age 40, and if the PSA is  $\geq 1.0$  ng/mL that they receive annual follow-ups. If their PSA is  $< 1.0$ , the Guidelines recommend that these men be screened again at age 45.

The NCCN Guideline Panel Members acknowledge that there is no “right” answer about PSA testing for everyone, but that each man needs to make an informed decision with his physician.

*<www.nccn.org>, 11 August 2009*

**PROSTATECTOMY**

*(Continued from page 2)*

as those with a high PSA, poorly differentiated with a Gleason grade of 8 to 10, or locally extensive. Currently, there are a number of tools physicians have to help determine the probable course of prostate cancer, but more accurate ones are needed,” he added.

“In the future, what we’d like is to be able to do a molecular or genetic analysis of prostate tumor cells to see if they have the capacity to spread, so that we can ask, does your tumor have that capacity? If not, it would be safe to watch,” said Dr. Scardino.

*Doctor’s Guide News, 28 July 2009*

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**WHAT'S YOUR TYPE – THAT'S THE MOST IMPORTANT QUESTION**

Mark C. Scholz, MD

**Prostate cancer is very different from other cancers**

Not all forms of prostate cancer are life-threatening. As a result, not all prostate cancer requires treatment. The need for treatment is determined by a man's "Risk Type." Men with the Low-Risk type of prostate cancer can safely be monitored without treatment. Men with the Intermediate-Risk or High-Risk type usually require treatment.

**Good news: Even with high-risk prostate cancer, survival is excellent**

Compared to other cancers, prostate cancer has an excellent 10-year survival rate. With High-Risk prostate cancer, only 5% of men die of the disease within 10 years.<sup>1</sup> Remarkably, men with the Low or Intermediate-Risk type are not at any increased risk for dying of prostate cancer within the first 10 years after diagnosis.<sup>2</sup>

**Go slow in making your choice – Don't panic**

Many men wrongly believe that they need to get treatment fast when they hear they have prostate cancer. Fear makes them leap to conclusions without learning about all their options. They don't realize that that prostate cancer is usually found early and grows much more slowly than other cancers.

**Sexual performance is almost always affected by treatment**

Treatments for prostate cancer can cause serious problems such as difficulty holding urine or trouble getting an erection. A study of over 1200 men showed that 2 years after surgery 78% of men were impotent and 10% were permanently incontinent.<sup>3</sup> These problems have a huge impact on daily life.

**Monitoring is the best option for low-risk prostate cancers**

Studies now show that men with the low-risk type can safely be monitored with regular checkups instead of having immediate surgery or radiation. More than half the men on monitoring continue successfully with ongoing monitoring five years later without requiring treatment.<sup>4</sup> In another study, men on monitoring who eventually required

Cancer risk or "type"	Gleason score	% biopsy cores with cancer	PSA (ng/mL)	PSAV*	PSAD*	DRE*
Low	<7	<34%	<10	<2	<0.15	Neg.
Intermediate	7	34-50%	10-20	<2	<0.15	Small nodule
High	>7	>50%	>20	>2		Large nodule

**PSAV** = PSA velocity (ng/mL/year); **PSAD** = PSA density (ng/mL of PSA in blood divided by prostate volume in cm<sup>3</sup>); **DRE** = digital rectal examination findings

treatment were compared with men who had immediate treatment. The outcome was the same in both groups.<sup>5</sup> Waiting is not right for every man with prostate cancer, but it's a good option for men with the low-risk type.

**Many forms of treatment**

Treatment falls into two broad categories – systemic and local. Systemic therapy affects the whole body including the prostate. Testosterone inactivating pharmaceuticals (TIP), also known as androgen blockade, is the most frequently used systemic therapy. These pharmaceuticals work by keeping the male hormone testosterone from stimulating prostate cancer growth. Local therapies are directed at the prostate and its immediate surroundings. Intensity Modulated Radiation Therapy (IMRT), brachytherapy, also called seed implants and surgery are common forms of local therapy.

**You must know your type**

The most important step toward selecting correct treatment is determining your risk-type (see chart). Low-risk means that all your results meet the criteria of the top row in the table. Even one result outside of the top row means you are either intermediate-risk or high-risk. Most experts say that having two or more scores in the intermediate-risk row increases the risk to high-risk.

**Type determines treatment selection**

Men who have the low-risk type can forgo immediate treatment and monitor their situation in an active surveillance program utilizing PSA testing, prostate exams and periodic repeat

biopsies. Imaging with color-Doppler ultrasound or spectrographic MRI is becoming more popular to reduce the number of biopsies. The PCA-3 urine test may also be helpful.<sup>6</sup> Men with the intermediate-risk type should have only one kind of treatment—local or systemic. Men with the high-risk type of prostate cancer usually need a combination of two or more kinds of treatment: TIP and IMRT, for example.

**Side effects matter the most**

While considering the treatment options—and remembering the low mortality—focusing on the potential side effects is paramount. All treatments have side effects. Some of these effects never go away, even after treatment is stopped. There is no convincing evidence that any one treatment leads to better survival compared to the others. Therefore, selecting the best treatment depends on avoiding the side effects you judge most distasteful. The "best" treatment is the last option left after the other, less desirable treatment choices have been ruled out. Combination therapy is always reserved only for the high-risk type because two treatments cause greater side effects.

**Where to learn more**

Unfortunately, there are no good treatments. The goal is to choose the therapy that causes the least harm. Education is essential. Talk to your doctors. Visit a support group. Men in support groups will gladly share their experiences and knowledge. Or contact the

*(Continued on page 8)*

## SURVEILLANCE ANXIETY

(Continued from page 1)

delay or even avoid the possible adverse side effects of radical treatment, it could also cause psychological harm in patients because they must live with untreated cancer. Data on the levels of such potentially negative emotions among men on active surveillance are lacking, however.

Roderick van den Bergh, (MD), of the Erasmus Medical Center, in Rotterdam, the Netherlands, and colleagues assessed levels of anxiety and distress in a group of recently diagnosed prostate cancer patients on active surveillance. They sent 150 men questionnaires to gauge uncertainty about their treatment decision, as well as levels of depression and anxiety among these men. A total of 129 questionnaires were completed and returned an average of 2.7 months after diagnosis. More than 80 percent of the 129 respondents scored favorably low on the parameters measured. Patients' scores were comparable or favorable to scores of men (reported in other studies) who underwent treatment for early prostate cancer.

Certain men in the study – such as men with neurotic personalities and those who were in poor physical health – exhibited more anxiety and distress than others. These findings indicate that mental and physical patient-specific factors are important aspects to take into account when selecting men for active surveillance. The results also suggest that psychological support may be indicated in certain patients undergoing active surveillance.

While this study's findings are useful, Dr. van den Bergh noted that longer-term analyses are needed on the psychological effects of active surveillance in men with early prostate cancer. His research team is currently conducting such a study.

American Cancer Society, 27 July 2009

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## THE DOCTORS NOTE – GERALD CHODAK, MD

One of the more interesting reports in this month's *HotSheet* is the work on androgen receptors and the growth of prostate cancer in the absence of testosterone. Normally, testosterone binds to the androgen receptor and that stimulates prostate cell growth. Eventually, however, some tumors are able to grow in the absence of hormones.

The researchers found that alterations in the androgen receptor enable it to stimulate growth without the presence of testosterone. This finding supports the hypothesis that has been proposed for why intermittent hormone therapy may be advantageous; continual hormone suppression may lead to turning on the genes that permit cell growth without testosterone. This work has broad implications for the use of hormone therapy and for potentially developing new ways to treat patients who become hormone independent.

On the clinical side, evidence is growing in support of more active surveillance for newly diagnosed prostate cancer. A report from New York found a low probability of dying from prostate cancer after radical prostatectomy and suggested that many of those men may have done well because the tumor was not dangerous rather than because of the surgery.

As greater numbers of men are being diagnosed with seemingly low risk cancers, it becomes increasingly important to determine which men can safely be managed without immediate local therapy. Considerable research is being aimed at identifying markers within a cancer that will enable physicians to pick and treat the aggressive cancers and spare the remainder from treatment that is not likely to help them live longer or better.

As we get better at identifying those men who are appropriate candidates for active surveillance, there is a need to help men cope with this option. Presently, many of the men who initially chose active surveillance abandon it because there is simply too much anxiety for them and their family. An interesting survey from Europe involving men on active surveillance

found that most of the men were able to cope but 20% did report very significant difficulty.

Perhaps formal interventional and support programs using psychologists and other professionals are needed to help men who are good candidates for active surveillance live with this choice. This is also important because of the ongoing debate about screening. The concerns about screening will decrease if men who are found to have low risk cancers do not all get treated. In that way the potential harms of screening and treatment can be reduced while the benefits are maintained.

In part because so many men have trouble with not actively treating their cancer, less invasive treatments are being studied, such as focal cryotherapy and High Intensity Focused Ultrasound (HIFU). Although HIFU has been used for many years, there are very little well documented data available on cure rates or complications.

A report from the United Kingdom is attempting to collect that information. The study is too immature to discuss cure rates, but the early data does raise concerns about complications with 30% reporting impotence, between 20-40% developing a urethral stricture, more than 20% developing a urinary infection and 7% developing epididymitis. This type of evaluation is critical so that future patients can be adequately counseled about the risks from this treatment which in the past has been presented as causing far fewer complications than recorded in this study.

Lastly, yet another article about alcohol intake is included, this one suggesting that men consuming ~50 grams of alcohol (4 drinks) per day were twice as likely to be diagnosed with an aggressive cancer. Even though this study design does not prove cause and effect for prostate cancer, there are certainly much stronger health reasons why consuming that much alcohol should be avoided.

**PROSTATE DRUG APPEARS SAFER THAN THOUGHT**

Doctors don't have to be so cautious in prescribing the drug finasteride to men at risk for prostate cancer, a new study suggests.

Physicians face a dilemma when trying to decide whether to use the drug, which has been shown to prevent prostate cancer in about one in five men who take it. However, findings from the Prostate Cancer Prevention Trial (PCPT) published in 2003 concluded that men who developed prostate cancer while taking finasteride were 25 percent more likely to develop an aggressive form of the disease.

But a new study from the Stanford University School of Medicine suggests that the drug does not increase the risk for aggressive prostate cancer but simply makes it easier to diagnose. The study appeared in the 7 July 2009 issue of *Clinical Cancer Research*.

Suspecting a flaw in the analysis of the PCPT, they analyzed data on 1,304 men who'd had an abnormal digital rectal exam or high PSA test results and had been referred to Stanford.

None took finasteride. Prostate cancer was eventually diagnosed in nearly 500 of the men, including 247 who had aggressive, high-grade cancer.

Finasteride shrinks the prostate, making malignancies easier to detect, the researchers said. And the smaller the prostate, the more likely a biopsy would yield a diagnosis of high-grade cancer, they said, and the more likely a high PSA level would predict the disease. For example, the diagnostic rate for one level of high-grade cancer was 29.7 percent in men with prostates between 20 to 29.9 cm<sup>3</sup>, compared with 6.5 percent for men with prostates larger than 80 cm<sup>3</sup>.

"We're showing that this is all related to size" of the prostate, Dr. Joseph Presti Jr., a research professor in urology and director of the urologic oncology program at Stanford, said in a news release from the university.

The authors of the 2003 study reached similar conclusions after they analyzed their own results, according to Catherine Tangen, statistical principal investigator for the first study. The findings of the new study "are consistent with everything we found," Tangen said in the news release.

Men should be given the opportunity to take finasteride if they and their doctors feel it's necessary, she added.

*HealthDay News, 8 July 2009*

**WHAT'S YOUR TYPE**

*(Continued from page 6)*

PCRI helpline at <help@pcri.org> or call +1 800 641-PCRI.

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**DOC MOYAD**

*(Continued from page 4)*

person I know, he is willing to admit he does not know something and I always feel like he has my best interest in mind, but I am lucky cause he is my father. Regardless, I think you get the point (pun intended again), and I will not needle you (last pun of the column) with any more details of this study or my opinion.

Reference

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**US TOO INTERNATIONAL:  
OUR MISSION**

Communicate timely, personalized and reliable information enabling informed choices regarding detection and treatment of prostate cancer.



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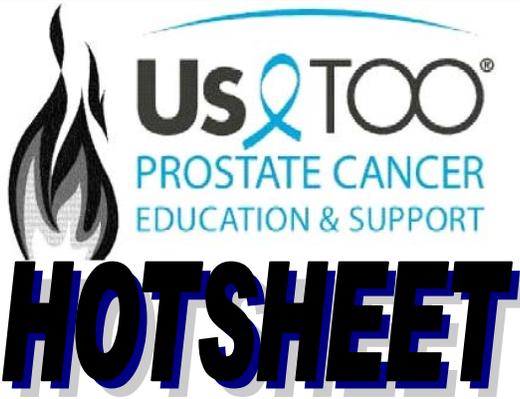
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# SPECIAL BURNING ISSUES SUPPLEMENT SEPTEMBER 2009

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THIS SUPPLEMENT TO THE *US TOO PROSTATE CANCER HOT SHEET*  
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## IDENTIFYING CLINICALLY SIGNIFICANT PROSTATE CANCERS

### INTRODUCTION

Welcome to this Us TOO *HotSheet* Burning Issues Supplement. Us TOO's Editorial Team periodically produces these Supplements to communicate timely, personalized and reliable information on specific issues relevant to prostate cancer that are of current interest or are subjects of controversy.

This month's Burning Issue surrounds the controversy engendered by the two recently published prostate cancer screening trials – showing a reduction in prostate cancer death in men who were screened – but also a significant risk of overdiagnosis. This again raised the most important unanswered question – how to predict whether a newly diagnosed, early-stage prostate cancer will behave like a “pussycat” or like a “tiger” in terms coined by Dr. Donald Coffey. The research community ardently seeks to discover new cancer biomarkers to solve this dilemma.

The main issue of this month's *HotSheet* also contains relevant articles as well, such as the article “Know Your Type” emphasizes the concept of risk assessment (low, intermediate or high for prostate cancer death) for newly diagnosed men considering treatment vs. active surveillance for their disease.

Another article reports the results of a European survey exploring anxiety in men undergoing active surveillance. Anxiety during active surveillance is the primary reason men abandon this effective treatment option. In this survey, 20% of men experienced significant anxiety and difficulty coping with their treatment choice.

(Continued on page 3)

### THE PROSTATE CANCER SCREENING CONTROVERSY

Charles “Snuffy” Myers, MD

Recent science notwithstanding, prostate cancer screening remains controversial. One major question that fuels this controversy is whether screening saves lives. This year European scientists from the EORTC published the first randomized clinical trial that adequately addresses this question. This trial had enough patients enrolled, and extended just beyond 12 years. The results showed that screening for prostate cancer does save lives and that it's comparable to other widely used cancer-screening tests. I quote:

“The number needed to screen (to save a life) in our study is similar to that in studies of mammographic screening for breast cancer and fecal occult-blood testing for colorectal cancer.”<sup>[1]</sup>

As the authors concluded, this study probably underestimates the value of prostate cancer screening. First, with only 12 years of follow up, it is too early to see the full benefit. In fact, the difference between the screened and the control group is still widening. Second, patients were screened every 4 years, which is too infrequent for more aggressive forms of prostate cancer. For those interested, we have published a detailed analysis of this screening study and its implications. You can go to <www.prostateforum.com> or call +1 434 974-1303 to receive it.

As with most good clinical trials, this study generates more questions than answers. One common problem is that a significant number of prostate cancer patients have small, slowly growing

cancers that probably won't be problematic in the next 10-15 years. Aggressive treatment with radical prostatectomy (RP) or radiation therapy (RT) has no proven benefit for these men. So, for every patient saved by prostate cancer screening, other men will be harmed by treatment they do not need. The best solution to this is to only treat men with cancers that pose a significant risk to their health.

We now have access to a rather extensive literature to aid us in identifying “clinically significant” cancer. I would recommend all newly diagnosed patients visit the AUA website and review the “AUA Guidelines for Clinically Localized Prostate Cancer” at <www.auanet.org/content/homepage/homepage.cfm>. This document clearly defines men with low-risk disease characteristics who can safely forego aggressive treatment and follow a “watchful waiting” or “active surveillance” approach (See Table 1).

(Continued on page 3)

**Table 1. Some Characteristics of Candidates for Active Surveillance**

Serum PSA level that is less than or equal to 10 ng/mL
Gleason score that is 6 or below
Cancer less than 1 cm in diameter that is confined to 1 side of the gland
Cancer does not threaten to invade the capsule surrounding the prostate gland

## INSIGHT INTO THE NEED FOR BETTER RISK ASSESSMENT FOR MEN NEWLY DIAGNOSED WITH PROSTATE CANCER

*Recently we had a chance to speak with Robert Shovlin, President and Chief Executive Officer of Aureon Laboratories, the developer of Prostate Px  $\oplus$ , a commercially available prognostic test for prostate cancer.*

### **Why did Aureon choose prostate cancer for their first test?**

Prostate cancer was an obvious choice for us for two reasons. First, so many men and their families are affected by prostate cancer, and the incidence of the disease is expected to increase as the population ages. Second, newly diagnosed men face a bewildering array of choices and many, sometimes conflicting opinions. This is an area where patients need as much information as possible to make informed treatment decisions. We believe that our information provides a unique, useful perspective to these patients.

### **How does the test work?**

Each patient's biopsy sample (from the original biopsy) is sent to our central laboratory. Once at Aureon, the tissue is examined by our patented Systems Pathology approach. Cellular features as well as proteins involved in the disease process are integrated by mathematical tools to provide estimates for personalized patient outcomes. (See Case Studies on page 4).

### **How does your test fit into the debate over the benefits of PSA screening?**

Annual PSA screening has allowed the detection of prostate cancer much earlier in the disease process. The problem is how to differentiate between the less aggressive and highly aggressive cancer cases. Our test is a risk stratification tool and is the first commercial test to address this question. Advanced molecular and computer analysis provides personalized outcome predictions that are a natural addendum to the screening discussion.

### **Why do you believe a molecular prognostic test is beneficial?**

Many believe that PSA screening has resulted in an over diagnosis of prostate cancer that would otherwise be clinically insignificant had they not been detected. Risk assessments using standard clinical/pathological features



*Aureon Laboratories CEO Robert Shovlin*

such as PSA and Gleason score cannot reliably determine which cancers are truly low-risk versus those that are at a high-risk for progression. Today, the overwhelming majority of patients have Gleason scores of 6 or 7 and have PSA values below 20 ng/mL. The question really becomes, if all of the clinical and pathological features are trending within this more narrow range of lower risk, how do you identify the potentially high risk cases? We believe that this is exactly where our test has the most utility today.

### **Is this a genetic test?**

No. This test does not look at a genetic signature. However, the test does examine proteins which are produced by the prostate cancer to support its growth. We believe this is vitally important because proteins represent the final product of the gene and impact upon many tumor promoting properties that are responsible for tumor cells traveling outside the prostate.

### **What information does the Prostate Px $\oplus$ test provide?**

The test provides two endpoints. The first endpoint is 'Disease Progression' which predicts patients with the most serious disease outcomes, including metastasis, death from the cancer or PSA progression through androgen deprivation therapy post surgery. These predictions are provided in the form of a score on a scale from 1 to 100; the higher the number, the more at risk the patient is for this outcome.

The second endpoint is 'Favorable Pathology' which predicts from biopsy tissue what a patient's disease is like in the prostate if it were removed. This is important because the biopsy Gleason

score is often upgraded (increased) after the prostate is removed and examined. Tools that provide improved confidence in the pathology at biopsy are important during treatment considerations. Think of the Favorable Pathology endpoint as if the surgeon could reach in and take out the prostate then examine it before actually doing surgery.

### **Why is this test better than current risk assessment methods?**

Current risk assessment methods such as AUA risk categories or online calculators rely on clinical and pathologic information which has become less informative. Our approach uses the patient's own clinical data but also looks at the cellular organization of the biopsy tissue and various biomarkers associated with prostate cancer. It is this additional set of features that enables the test to provide a deeper layer of information for the individual patient.

### **What would I and my physician do with the information?**

There is no one answer to this question. It depends on many variables about a patient's condition, treatment goals, existing health and how the treating physician wishes to proceed. What the test does do is provide objective information, not available from any other source, which allows one to make a more-informed decision about the path forward. Patients no longer have to fit into broad risk categories nor rely solely on existing information; more informed decisions can be made with a better understanding of each patient's unique situation.

### **Can I use this test to decide to have active surveillance?**

At this time, we don't make a claim about active surveillance. This is because everyone in our study had surgery. We do say that the test can be used as a supportive tool to individually assess active surveillance candidates for prostate cancer progression. Also, we have physicians that use the test to further evaluate patients they already consider active surveillance candidates based on their clinical and pathological features.

*(Continued on page 4)*

## UNDERSTANDING CANCER STAGE AND GLEASON SCORE

### Cancer stage

Knowing the stage of your cancer provides important information for you and your care team as you explore your treatment options. There are treatment options that are specific to the various stages of the disease, whether it is caught early, at the advanced stages of cancer, or somewhere in between.

Stage I (T1) and stage II (T2) cancers are found only in the prostate. T1 cancers are small enough that your doctor is unable to feel it during your DRE. T2 cancers are larger and can be felt as firmness or a lump on a DRE.

Stage III (T3) and stage IV (T4) cancers are no longer confined to the prostate gland. T3 cancers have spread to nearby tissues but still remain inside the pelvic area. T4 tumors deeply invade surrounding tissues and may have metastasized to lymph nodes or bone.

### Gleason Score

Your Gleason score helps your physician determine the best type of treatment for your particular cancer. The Gleason score describes different types of prostate cells and classifies tumors according to their microscopic appearance. The score helps to estimate of the rate your cancer might grow and your life expectancy. The lower your Gleason score is, the better your prognosis is likely to be.

The Gleason score is made up of two numbers (grades) that are determined by a pathologist and then added together. The first number indicates the grade of cancer cells that are most numerous in the biopsy sample. The second number indicates the grade of the cancer cells that are second most numerous. The Gleason score (sum) is determined by adding the primary and secondary grade patterns for each cancerous lesion found. e.g., 3 + 4 = 7.

Cancers having Gleason score of 2, 3 or 4 are considered non-aggressive whereas cancers that are 5 or 6 are considered mildly aggressive. Gleason 7 cancers are considered moderately aggressive while Gleason 8, 9 or 10 cancer are considered very aggressive.

For more useful information, refer to Us TOO's Signposts and Pathways brochures at <[www.ustoo.org](http://www.ustoo.org)>.

## THE PROSTATE CANCER SCREENING CONTROVERSY

(Continued from page 1)

These factors are associated with cancers that grow slowly, if at all. However, your general health is also an important consideration. If you have heart disease, diabetes, or other diseases likely to kill you within ten years, it is very unlikely that a low-risk cancer will effect your survival or quality of life. In contrast, if you are under 60 years of age and in excellent health, you may well have an excellent chance of being alive and well at age 80. In that case, even a low-risk cancer will have enough time to cause problems. For this reason, it is important to meet with your family physician for a frank assessment of your lifespan.

If your prostate cancer fits these low-risk criteria, you have several options. The watchful waiting approach involves no treatment. The patient is only periodically monitored for evidence of aggression. This involves a PSA determination every 3 months. Additionally, most investigators monitor the size and location of the cancer every 6-18 months. (See Table 2 for monitoring tools). In our clinic, we have found saturation biopsies the most accurate assessment tool for determining the extent and location of the cancer at diagnosis. However, it is too traumatic to be used for consistent monitoring. Color Doppler ultrasound is nearly as useful but much less traumatic for monitoring the cancer over time.

<b>Table 2. Methods for determining cancer size and location</b>
Transrectal ultrasound
Color Doppler ultrasound
Saturation biopsy
Endorectal MRI

During watchful waiting, two processes can cause the cancer to become more dangerous. First, the existing cancer can change over time to become more aggressive. Second, a new and more dangerous cancer can arise. Over the past few years, research has uncovered a range of agents to address this:

- Both Proscar® (finasteride) and Avodart® (dutasteride) have been shown to decrease prostate cancer

risk in large, well-designed clinical trials

- There is strong epidemiologic evidence that vitamin D deficiency also increases the risk of prostate cancer (so increasing vitamin D consumption just makes common sense)
- Pomegranate had a dramatic impact on prostate cancer progression in a well-designed Phase II trial. A randomized controlled trial is underway

The Mediterranean diet has been shown to reduce the risk of heart disease, diabetes, and many cancers. In population studies, it is associated with a lower incidence of prostate cancer. Various investigators are looking at the addition of these and other agents to advance the watchful waiting process. This combined approach is now called active surveillance – and offers the chance to improve patients' general health while lowering cancer risk.

While clinical studies might create questions, I am happy to provide any answers you might have on this or any other subject. I invite all who read this to submit their questions to me either through Us TOO or through the FCRE website <[www.prostateforum.com](http://www.prostateforum.com)> and I'll be happy to answer them.

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## INTRODUCTION

(Continued from page 1)

Us TOO International Prostate Cancer Education and Support Network works to support, educate and advocate for men with prostate cancer and their families.

“Our mission and program goal is to educate and empower men and their family members so men and their loved ones can take an active role in their healthcare,” said Thomas Kirk, President and CEO of Us TOO International, Inc., which is based in Downers Grove, IL.

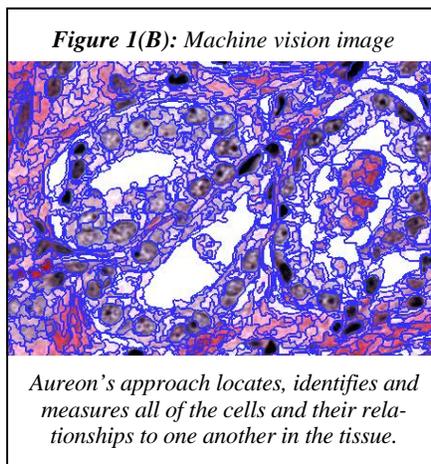
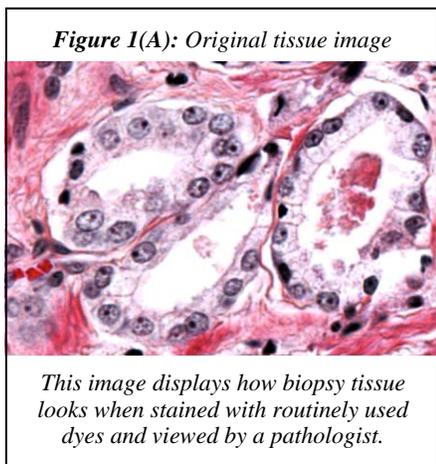
We sincerely hope that the information provided by this Burning Issues Supplement meets our goals and your needs.

## AUREON'S "SYSTEMS PATHOLOGY" APPROACH

Systems Pathology is an approach to combining different types of information to provide personalized cancer-focused, risk assessments for patients and their physicians. Each person's cancer is different and changes on the molecular level are not evident through existing, light-based microscopy. Systems Pathology assesses each individual's cancer by examining the tumor in the biopsy tissue. Using advanced mathematics, the approach objectively analyzes the information unique to the cells and specific molecules in each case. Systems Pathology combines clinical information with:

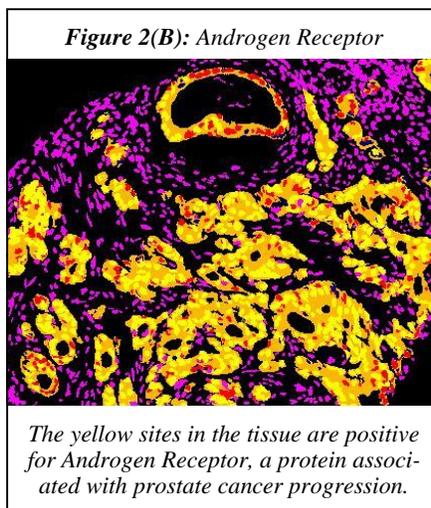
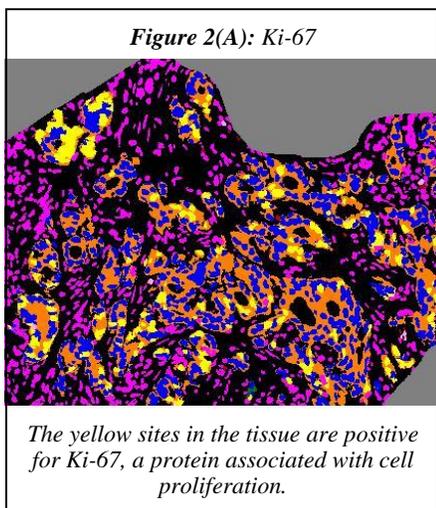
### Image Analysis

A digital image of each patient's biopsy tissue is analyzed by a special image system (Machine Vision) that uses technology to identify and measure hundreds of properties of the tumor.



### Molecule Detection

Eight proteins involved in tissue structure and function are located, measured and analyzed by an advanced fluorescence detection system. The two examples below demonstrate co-localization of multiple protein markers in the same tissue section.



### Advanced Mathematics

Similar to artificial intelligence, advanced mathematics enables computers to learn, recognize patterns and make decisions. It is being applied in many fields such as bioinformatics, Internet search engines and stock market analysis. Aureon's approach can model prostate cancer data and improve upon the existing ability to provide an accurate prediction for patients.

## PROSTATE Px⊕

*(Continued from page 2)*

### How many patients were in the study that supports this test?

We had a very large, multi-institutional cohort. There were 1,487 patients and associated data from multiple physicians practicing at The Mayo Clinic, Duke University Medical Center/Durham Veterans Administration, The University of Graz in Austria, University Hospital at Uppsala in Sweden and The University of Connecticut. After review, there were 1,027 evaluable cases in the cohort.

### Is this test FDA approved?

Prostate Px⊕ does not require FDA approval. The test is considered a Laboratory Developed Test (LDT) and is performed in Aureon's state-of-the-art, CLIA-certified, CAP-accredited, New York State-regulated laboratory.

### How long has the test been available?

The Prostate Px⊕ test was launched in June 2008.

### CASE STUDIES

**Case #1** was a 73 year old male with a negative DRE, and a high PSA of 16.3 ng/mL. He had clinical stage T1c disease and a biopsy Gleason score of 6.

AUA categorized him as intermediate risk. Calculators or nomograms available on the Internet considered him low risk but the Systems Pathology approach considered him at high risk because of his score of 39.

### Actual Result

The patient experienced disease progression in 60 months.

**Case #2** was a 59 year old man with a suspicious DRE, a PSA of 5.0 ng/mL and clinical stage T3 disease according to imaging studies. His biopsy Gleason score was 6.

AUA categorized him as a high risk patient. Calculators or nomograms available on the Internet considered him at a low risk and the Systems Pathology approach also considered him at low risk because of his score of 12.

### Actual Result

The patient had no disease progression after fourteen years of follow-up.