Informed Prostate Cancer Support Group Inc.
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Saturday, December 18, 2021

DECEMBER 2021 NEWSLETTER

P.O. Box 420142 San Diego, CA 92142
Phone: 619-890-8447 Web: http://ipcsg.org

STREAMING ONLINE LIVE

Volume 14 Issue 12

- No Meeting in December
- **Next Meeting Saturday, JAN 15, 2021 IPCSG - Live-Stream Event, 10:00am PT**.
- Speaker Dr. Arno J. Mundt, MD—UCSD Radiology.
- February Meeting Speaker Dr. Richard Lam, MD—Prostate Oncology Specialists
- March Meeting—members will share their experiences
- Due to COVID-19, no in-person meetings at the Sanford Burnham Prebys Medical Discovery Institute will take place until further notice. This meeting will be live-streamed and will also be available on DVD.
- **For further Reading: https://ipcsg.blogspot.com/**
- **For Comments, Ideas and Questions,** email to Newsletter@ipcsg.org

November 2021 Informed Prostate Cancer Support Group Meeting

Notes by Bill Lewis

High Intensity Focused Ultrasound (HIFU)

Dr. Robert Pugach is the Medical Director at Western States HIFU. High intensity focused ultrasound is a relatively non-invasive, radiation-free alternative to active surveillance (i.e., no immediate treatment) on the one hand, and invasive surgery (prostatectomy) or radiation on the other hand.

HIFU has been used in over 65,000 treatments worldwide over the past 18 years, and is FDA approved since 2015.

A non-invasive "acoustic scalpel" applies precision focused ultrasonic waves, raising the temperature of the target tissue to 92-100 degrees Celsius in 3 seconds, destroying that tissue. Rapid heat dissipation occurs beyond the focal point.

Treatment can be given to a small area, or to the whole prostate, while avoiding critical structures that affect urinary continence and erectile function.

The procedure takes 1-4 hours, under general anesthesia, and a catheter is used for urine drainage for 2 days to 2 weeks. The patient may return to mild activities and a normal diet later that same day.

For more information, see the video at https://www.youtube.com/watch?v=nwByMTIs-SI

A DVD of the talk will be available for purchase from the IPCSG about one month after the meeting.

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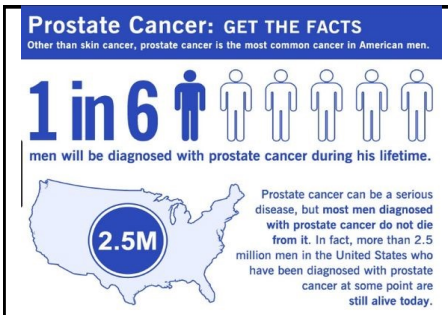

Organization

a 501c3 non-profit organization - all positions are performed gratis

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NEWSLETTER
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PROSTATE CANCER—*2 WORDS, NOT A SENTENCE*

What We Are About

Our Group offers the complete spectrum of information on prevention and treatment. We provide a forum where you can get all your questions answered in one place by men that have lived through the experience. Prostate cancer is very personal. Our goal is to make you more aware of your options before you begin a treatment that has serious side effects that were not properly explained. Impotence, incontinence, and a high rate of recurrence are very common side effects and may be for life. Men who are newly diagnosed with PCa are often overwhelmed by the frightening magnitude of their condition. Networking with our members will help identify what options are best suited for your life style.

Meeting Video DVD's

DVD's of our meetings are available for purchase on our website at https://ipcsg.org/purchase-dvds and are generally available by the next meeting date.

Join the IPCSG TEAM

If you consider the IPCSG to be valuable in your cancer journey, realize that we need people to step up and HELP. Call **President** Bill Lewis @ (619) 591-8670 ; or **Director** Gene Van Vleet @ 619-890-8447.

From the Editor

Due to COVID-19, no in-person meetings will be held until further notice. We will continue to post and distribute the newsletter in the interim. Our speaker this month will be broadcast via the IPCSG website at https://ipcsg.org/live-stream and can be watched by scrolling down and clicking on the "WATCH THE PRESENTATION" button. The broadcast will begin approximately 10 minutes before to the listed start time.

In this issue:

Bill Lewis produced a short summary of the last stream video on HIFU. Then, for those in the early stages of deciding what to do, or doing active surveillance, he and Bill Manning wrote up a summary of our brother group, the ASPI.

Articles of Interest 1

- 2021 Pipeline Updates: Examining Ongoing Clinical Research With Potential in Prostate Cancer
  Over the course of 2021, breakthroughs in clinical research within the prostate cancer space abounded. Clinical trials pushed the needle forward for the treatment of prostate cancer. CancerNetwork® examines the most recent updates on these clinical trials, highlighting what may be looked to going forward to in the coming year and beyond.
- Henry Ford Surgeons Perform World's First Precision Prostatectomy with Unique Approach—*minimal side effects for low risk localized Psa*
- Researchers develop AutoProstate to automatically generate prostate cancer diagnostic reports using deep learning—reduce guesswork in treatment sequencing.
- Prostate cancer risk stratification via non-destructive 3D pathology with deep learning-assisted gland analysis - look at 3D image instead of slice.

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Introducing Active Surveillance Patients International (ASPI; aspatients.org)

ASPI is a non-profit based in East Stroudsburg, PA. ASPI is run by volunteers, created by men with prostate cancer (PCa) for men with prostate cancer. The founders all took a proactive approach to Active Surveillance (AS) in their cancer journeys.

We have witnessed many cases of overtreatment and confusion about monitoring. Men from all walks of life contacted ASPI seeking guidance and felt the organization might be a vehicle to help. Two decades ago men on AS were almost unheard of; now, over 50% of men in the United States who have low-grade prostate cancer practice AS. In Europe, the percentage is even higher. We are sure there are still many newly diagnosed men with low-risk (Gleason 3+3) and favorable intermediate-risk prostate cancer, (Gleason 3+4) who might want to consider AS as their "treatment."

ASPI helps empower men diagnosed with low and intermediate risk prostate cancer, including Gleason 3+3 and favorable intermediate prostate cancer, Gleason 3+4, by providing the latest information to allow for informed decisions with your physician, regarding approaches to active surveillance. Our vision is to develop proactive patients by providing the latest data and fostering the understanding necessary to pursue the best outcomes with the least intervention. If the time comes for intervention patients will be better equipped to make those decisions.

ASPI's message of finding some level of peace and assurance in this journey is unique. We have been fortunate to have respected presenters from all over the world. Together we have learned about safer biopsies, safer monitoring methods and more.

There is an ever-increasing amount of information to sort through and ASPI's goal is to help point you to the most relevant material. On the website there is a page of resources of videos and books which is always expanding. Stories where patients have chosen to empower themselves and might offer hope and guidance for others on their journey.

ASPI supports the concept of the proactive patient who is interested in research, participates in support groups and webinars, attends (if possible) relevant conferences, and most importantly, establishes decision-sharing relationships with their doctors. AS includes monitoring and testing involving PSA, imaging, biopsies when called for and much more.

In following Active Surveillance, our life partners or friends are deeply involved in our care. We discuss everything with our family doctors and our specialists. We may choose to consult with dietitians and naturopaths to inform ourselves of food regimens and dietary supplements to improve our prostate health and overall health.

We engage with science-based professionals in updating our AS protocols. And, finally, we include in the information we disseminate, what choices proactive patients make when AS is no longer possible because, over time, it is found through testing that there is evidence of more aggressive PCa.

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Articles of Interest

cancernetwork.com

2021 Pipeline Updates: Examining Ongoing Clinical Research With Potential in Prostate Cancer

Hayley Virgil

Over the course of 2021, breakthroughs in clinical research within the prostate cancer space abounded. Clinical trials assessing everything from promising novel targets, investigational radiopharmaceuticals, and even innovative diagnostics agents with uptake in prostate-specific membrane antigen (PSMA) account for some of the many measures that have been taken in order to push the needle forward for the treatment of prostate cancer. In the third and final part of our series examining promising innovations coming down the oncology pipeline, CancerNetwork® examines the most recent updates on these clinical trials, highlighting what may be looked to going forward to in the coming year and beyond.

Novel Anti–B7-H3 ADCs Take the Spotlight in Prostate Cancer

B7-H3 protein may prove to be a promising novel target for treatment with immunotherapy in prostate cancer.[1] In fact, data on 2 B7-H3 inhibitors read out at the 2021 European Society for Medical Oncology Congress.

B7-H3 is highly expressed in a number of solid tumor malignancies such as prostate cancer, non–small cell lung cancer, breast cancer, head and neck cancer, melanoma, and squamous cell carcinoma of the head and neck. Investigators believe that it may impact immune suppression, as well as tumor-autonomous roles leading to cancer growth. Additionally, B7-H3 appears to be expressed in the epithelium, tumor-associated vascular endothelium, and stroma. In a multicohort phase 1 expansion cohort trial (NCT03729596), 93% of patients with metastatic castration-resistant prostate cancer (mCRPC) had a B7-H3 H-score of 160 or higher.

Investigators evaluated the safety and antitumor activity of antibody-drug conjugate MGC018 in a population of patients with mCRPC (n = 40).[2] Patients within the mCRPC cohort had a best overall response rate of 25%, including 2 confirmed partial responses (PRs) and 2 unconfirmed PRs. Those within this cohort also had a mean B7-H3 H-score of 236. Ten of 16 patients in the mCRPC cohort experienced a reduction in target lesions from baseline

Thirty-nine patients within the cohort were evaluable for prostate-specific antigen (PSA) response. Among these patients, 53.8% had reductions in PSA from baseline of 50% or greater. Additionally, 61.5% of patients continued to receive treatment.

The second phase 2 trial (NCT02923180) evaluated the anti–B7-H3 antibody enoblituzumab in patients with localized prostate cancer.3 Investigators enrolled 32 patients, 12% of whom experienced grade 3/4 adverse effects (AEs). Thirty-four percent of patients experienced pre-prostatectomy declines of over 10%. One year following surgery, 66% of patients had a PSA of 0. Additionally, the median time to PSA recurrence had not been reached (95% CI, 9.4–not evaluable).

"Virtually every prostate cancer cell expresses some degree of B7-H3, which appears to be associated with rapid recurrence and earlier metastasis," Eugene Shenderov, MD, PhD, an assistant professor of oncology at Johns Hopkins Medicine and lead author of both studies, said in a press release. He continued, "Everything seems to point to the fact that B7-H3 is potentially an important therapeutic target in the prostate cancer setting."

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(Continued from page 4)

Phase 3 Clinical Research Kicking Off for 177Lu-PSMA-I&T

Curium recently received a Study May Proceed letter from the FDA in October 2021 regarding its investigational therapeutic radiopharmaceutical product 177Lu-PSMA-I&T, allowing them to advance with the phase 3 ECLIPSE trial assessing the product in patients with mCRPC.[4] The organization is working hand-in-hand with several sites in the United States in order to initiate the multicenter, open-label randomized trial which will compare the efficacy of 177Lu-PSMA-I&T with hormone therapy in this patient population. The radiopharmaceutical works by binding to the PSMA protein.

"We are excited about advancing Lu 177 PSMA I&T to the clinical trial stage, particularly in light of our recent announcement for our Cu 64 PSMA I&T imaging agent.We believe this represents an exciting opportunity for patients nationwide and their healthcare providers," Mike Patterson, chief executive officer at Curium, North America, said in a press release.

Curium noted that they expect to manufacture 177Lu-PSMA-I&T in a facility in Noblesville, Indiana, which will allow them to leverage centralized production capabilities and logistical expertise.

"We are committed to working closely with the FDA to potentially bring this new therapeutic radiopharmaceutical agent to patients and their healthcare professionals," Ed Porter, vice president of Medical and Compliance at Curium, explained."We look forward to engaging additional clinical trial sites as we finalize our clinical development program."

PROPELLER Trial Examining 64Cu SAR-bisPSMA Hits Recruiting Halfway Mark

A total of 15 of 30 patients have been enrolled on the phase 1 PROPELLER trial (NCT04839367), which seeks to assess the diagnostic value of 64Cu SAR-bisPSMA in those with untreated and confirmed prostate cancer who are scheduled to undergo radical prostatectomy.[5]

"We are excited to have quickly and successfully recruited half of the patients planned for the PROPELLER trial with all 3 sites actively recruiting and imaging prostate cancer patients across Australia. We have been able to not only generate strong preliminary clinical data since the trial commencement in July 2021, but also validate our on-demand distribution model where the 64Cu-SAR-bisPSMA has been shipped to the trial sites across Australia from a central manufacturing facility with minimal delays or interruptions," Alan Taylor, PhD, executive chairperson at Clarity Pharmaceuticals, said in a press release.

The multicenter, blinded review, dose-ranging, non-randomized PET imaging trial will administer 64Cu-SAR-bisPSMA to patients prior to undergoing surgery. The study has 4 particular goals:

- Identify safe and tolerability of 64Cu SAR-bisPSMA
- Assess different dose levels
- Identify ability of 64Cu SAR-bisPSMA to detect primary disease
- Assess ability of 64Cu SAR-bisPSMA to detect primary disease vs 68Ga PSMA-11

The trial will enroll patients who are 18 years or older with a life expectancy of more than 3 months. Patients are also required to have confirmed disease via histopathology with plans to receive radical prostatectomy. Adequate renal function is also required.

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"The preliminary data from the patients imaged in the PROPELLER trial to date look very promising as it supports the evidence of higher uptake of 64Cu SAR-bisPSMA in the tumours that has been shown in the pre-clinical studies. Higher uptake in the tumours means that they are more visible on the PET scans and hence have a higher chance of being detected. These initial results are encouraging for further development of this product as a diagnostic, and the higher uptake and retention also make it an exciting therapeutic target with 67Cu," Louise Emmett, MD, FAANMS, FRACP, a clinical research leader in advanced prostate cancer, assistant professor, and director of theranostics and nuclear medicine at Garvan Institute of Medical Research, concluded.

References

1. Studies find B7-H3 protein a novel, promising target for prostate cancer treatments. News release. John Hopkins Medicine. November 2, 2021. Accessed December 9 ,2021. https://bit.ly/3pLqxD2
2. Shenderov E, Mallesara G, Wysocki P, et al. MGC018, an anti-B7-H3 antibody-drug conjugate (ADC), in patients with advanced solid tumors: preliminary results of phase 1 cohort expansion. *Ann Oncol*. 2021;32(suppl 5):S626-S677. doi:10.1016/annonc/annonc702
3. Shenderov E, Mallesara GHG, Wysocki P, et al. MGC018, an anti-B7-H3 antibody-drug conjugate (ADC), in patients with advanced solid tumors: preliminary results of phase I cohort expansion. *Ann Oncol*. 2021;32(suppl 5): 626-S677. doi:10.1016/annonc/annonc702
4. Curium initiates ECLIPSE, a phase 3 clinical trial for its investigational Lu 177 PSMA I&T. News release. Curium. October 27, 2021. Accessed December 13, 2021. https://bit.ly/31XFjP5

Fifty percent recruitment milestone for PROPELLER prostate cancer trial. News release. Clarity Pharmaceuticals. December 1, 2021. Accessed December 13, 2021. https://prn.to/31Up4lV

henryford.com

Henry Ford Surgeons Perform World's First Precision Prostatectomy with Unique Approach

DETROIT (Dec. 13, 2021) – Surgeons at Henry Ford Health System's Vattikuti Urology Institute (VUI) performed what is believed to be the first precision prostatectomy through the bladder using a single port robotic surgical system. (*no cutting the urethra special DaVinci enters through bladder, gives surgeon tool similar to HIFU ed.)*

Precision prostatectomy is a novel surgical approach that allows removal of the cancer while preserving a portion of the prostate capsule in select men in order to improve functional outcomes, such as erectile function and urinary control, compared to traditional prostatectomy. While previous patients have had surgery with a single port robotic surgical system, surgery through the bladder, or a precision prostatectomy, this marked the first time a patient has received the combination of all three at once.

Precision prostatectomy was developed at Henry Ford by robotic surgery pioneer Mani Menon, M.D., and the VUI team using rigorous clinical trial methodology. The development of the procedure has been published in several journals, including in *European Urology* in December 2021, and was presented at the 2021 Annual Meeting of the American Urological Association in September.

"The concept of precision prostatectomy is similar to that of lumpectomy for breast cancer, in which only the cancerous tumor is removed," said Craig Rogers, M.D., Chair of the VUI who performed the procedure with Wooju Jeong, M.D., Senior Staff Physician in the VUI and one of the lead surgeons in the recently published study. Precision prostatectomy helps protect nerves that run in the capsule of the prostate by preserving a thin rim of prostatic capsule on the uninvolved side of the prostate. The rest of the prostate containing the dominant cancer lesion is removed in the traditional manner with the prostate capsule.

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"The thin rim of noncancerous tissue that remains helps minimize the side effects of whole-gland surgery or other treatments in select men with localized tumors," Dr. Rogers said.

For Peter Piccinato, 72, precision prostatectomy offered exactly what he was seeking – an effective prostate cancer treatment option with minimal impact on his quality of life. This precision prostatectomy procedure was completed through a small incision in the bladder, known as a transvesical approach, using the da Vinci® Single Port Robotic Surgical System, which allowed the surgery to be done while avoiding scar tissue from prior hernia repairs.

"I just completed a 5K on November 13, and I'll be hitting the golf course in Florida again soon, too," said Piccinato. "When Dr. Rogers explained the precision prostatectomy to me, I knew that was the option I wanted to pursue – something that would have minimal impact on my quality of life. Now more than two months post-surgery, I'm very happy with the outcome and grateful to Dr. Rogers and his team."

During his annual physical, it was discovered that Piccinato had an elevated level of Prostate-Specific Antigen, or PSA, which is determined through a blood test used primarily to screen for prostate cancer. The next step was to take a biopsy of his prostate, which confirmed his prostate cancer diagnosis.

Under the care of Dr. Rogers and his team, Piccinato underwent the procedure on Sept. 29 at Henry Ford Hospital and was discharged the next day. Four weeks after the procedure, Piccinato – a grandfather to two grandsons, 8 and 10 years old – was back to the active lifestyle he has enjoyed his entire life.

Today, Piccinato is back to exercising regularly and doing the hobbies he enjoys. Like all patients who undergo Precision Prostatectomy, Piccinato has regular follow up appointments with his clinical team to monitor the long-term success of his procedure.

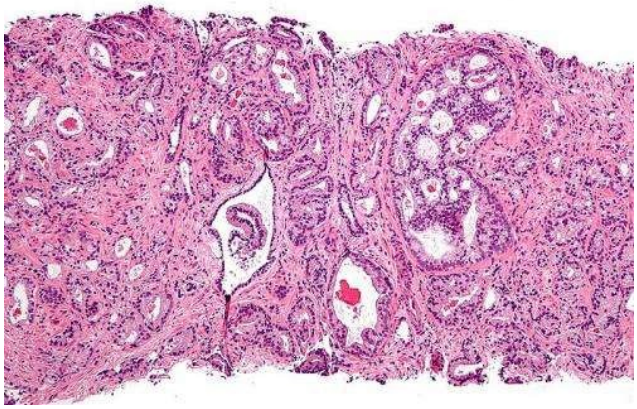
"I'm hyperactive, I feel like I need to be doing something all the time," Piccinato said. "I really enjoy being active and playing ball with my grandsons. I didn't have grandparents growing up, so it's important for me to be the best grandfather I can for them."

To learn more about precision prostatectomy or to request an appointment with a Henry Ford prostate cancer expert, visit henryford.com/prostatecancer.

medicalxpress.com

Researchers develop AutoProstate to automatically generate prostate cancer diagnostic reports using deep learning

Science X staff



Micrograph showing prostatic acinar adenocarcinoma

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(the most common form of prostate cancer) Credit: Wikipedia

Researchers from the School of Biomedical Engineering & Imaging Sciences have developed a computer-aided prostate cancer diagnosis system, AutoProstate, which uses deep learning to generate an automatic report which will aid pathologists in identifying and diagnosing prostate cancers with greater accuracy. Their findings were published in *Cancers*.

The current clinical pathway gives rise to missed cancers, which increases mortality risk, and unnecessary biopsies, with side effects that can include bleeding, infection, and difficulty urinating.

Current pressures on the pathway are set to worsen due to rising case incidence and an increasing shortage of specialist pathologists to read prostate MRI.

The researchers behind AutoProstate say artificial intelligence holds the key to improving the diagnostic accuracy of pathologists, as well as alleviating pressures on the pathway.

AutoProstate is a deep learning-powered framework for automatic prostate cancer assessment and reporting.

On how AutoProstate will fit into the clinical pathway, Mr Mehta explained that following multiparametric MRI, AutoProstate will segment the whole prostate, the prostate's zonal anatomy, and any clinically significant tumors that are present within the prostate, using a patient's scans.

Subsequently, an automatic diagnostic report will be generated, which will be available to the examining pathologist.

"The automatic report generated by AutoProstate will provide pathologists with additional information at the time of diagnosis, helping to improve diagnostic accuracy, save time, and enhance reporting quality," Mr Mehta said.

The automatic report is novel in structure and features four main sections: Patient Details, Prostate Size and PSA Density, Clinically Significant Lesion Candidates, and Findings Summary.

"A key benefit of the report is that it automates the calculation of several prostate and lesion-level biomarkers, replacing the crude estimation methods that are currently used," Mr Mehta said.

"Crucially, all of the biomarkers are easily verifiable as the segmentation outputs of AutoProstate, used to calculate the biomarkers, are displayed in the report in an interactive way."

In an initial trial of their system, the researchers trained the system using a publicly available dataset released by Radboud University Medical Center, and externally validated the system using data from the PICTURE trial that was run at University College London in 2014.

More information: Pritesh Mehta et al, AutoProstate: Towards Automated Reporting of Prostate MRI for Prostate Cancer Assessment Using Deep Learning, *Cancers* (2021). DOI: 10.3390/cancers13236138

Citation: Researchers develop AutoProstate to automatically generate prostate cancer diagnostic reports using deep learning (2021, December 17) retrieved 17 December 2021 from https://medicalxpress.com/news/2021-12-autoprostate-automatically-prostate-cancer-diagnostic.html

cancerres.aacrjournals.org

Prostate cancer risk stratification via non-destructive 3D pathology with deep learning-assisted gland analysis

Weisi Xie, Nicholas P Reder, Can F Koyuncu, Patrick Leo, Sarah Hawley, Hongyi Huang, Chenyi Mao, Nadia Postupna, Soyoung Kang, Robert Serafin, Gan Gao, Qinghua Han, Kevin W Bishop, Lindsey A Barner, Pingfu Fu, Jonathan L Wright, C Dirk Keene, Joshua C Vaughan, Andrew Janowczyk, Adam K Glaser, Anant Madabhushi, Lawrence D True and Jonathan TC Liu

DOI: 10.1158/0008-5472.CAN-21-2843

Abstract

(improving pathology grading by looking at AI 3d model instead of slices, ed.) Prostate cancer treatment planning is largely dependent upon examination of core-needle biopsies. The microscopic architecture of the prostate glands forms the basis for prognostic grading by pathologists. Interpretation of these convoluted 3D glandular structures via visual inspection of a limited number of 2D histology

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sections is often unreliable, which contributes to the under- and over-treatment of patients.

To improve risk assessment and treatment decisions, we have developed a workflow for non-destructive 3D pathology and computational analysis of whole prostate biopsies labeled with a rapid and inexpensive fluorescent analog of standard H&E staining. This analysis is based on interpretable glandular features and is facilitated by the development of image-translation-assisted segmentation in 3D (ITAS3D). ITAS3D is a generalizable deep-learning-based strategy that enables tissue microstructures to be volumetrically segmented in an annotation-free and objective (biomarker-based) manner without requiring immunolabeling.

As a preliminary demonstration of the translational value of a computational 3D vs. a computational 2D pathology approach, we imaged 300 ex vivo biopsies extracted from 50 archived radical prostatectomy specimens, of which 118 biopsies contained cancer.

The 3D glandular features in cancer biopsies were superior to corresponding 2D features for risk stratification of low- to intermediate-risk PCa patients based on their clinical biochemical recurrence (BCR) outcomes.

The results of this study support the use of computational 3D pathology for guiding the clinical management of prostate cancer.

webmd.com

Does Early Prostate Cancer Screening Do More Harm Than Good?

Dec. 14, 2021 -- It's a question that has divided men's health experts for years: Should healthy men, with no symptoms or family history of prostate cancer, get a prostate specific antigen test and treatment right away if a tumor is found?

Men's health experts and cancer specialists say the continuing back-and-forth on PSA testing and active surveillance has deepened widespread confusion for men with questions about what to do.

Proponents of routine PSA testing say it is the best screening tool in oncologists' arsenals for catching prostate cancer early, when it is most treatable.

But opponents argue that it prompts many newly diagnosed men to seek invasive treatments that can cause impotence and incontinence, although up to 80% have low-risk tumors that will never be life-threatening. For them, they say, the best option is "active surveillance," where doctors monitor patients closely for signs their cancer is advancing before treating it.

This fall, the influential National Comprehensive Cancer Network (NCCN) reignited the debate, recommending active surveillance, surgery, or radiation for men newly diagnosed with prostate cancer as a result of PSA testing -- giving equal weight to all three approaches.

After a firestorm of criticism, the NCCN reversed course and now recommends that "most men" with low-risk prostate cancer be managed through active surveillance as the "preferred" first treatment option over surgery and radiation.

The updated guidelines also reiterated the group's stance against routine PSA testing for most men "as a general population screening tool due to its well-documented limitations" and its potential for prompting overtreatment.

Some oncologists even say the debate has eclipsed the most important point about prostate cancer -- that each case requires a personalized, patient-centered approach to testing and care that one-size-fits-all screening guidelines don't take into account.

"These guidelines are always changing back and forth, and I've seen a lot of these changes," says David Samadi, MD, a urologic oncologist and director of men's health at St. Francis Hospital in Roslyn, NY. "But individualized care is the best way to go."

He says men should work with their doctors to determine whether and when to have PSA testing, based on their unique genetic and biological makeup, age, family history, overall health, lifestyle, race, ethnic background, and other factors. Any course of cancer care should be approached in a similar, patient-centered way, he says.

Otis W. Brawley, MD, a professor of oncology and epidemiology at Johns Hopkins University, agrees that PSA testing is an important screening tool, but it should not always lead to treatment. Men need to weigh the risks and benefits of testing and understand that most diagnosed with prostate cancer should not be rushed to surgery, radiation, or other therapies, he says.

"Given the uncertainty that PSA testing results in more benefit than harm, a thoughtful and broad approach to PSA is critical," Brawley says, citing the current position of the American Urological Association.

"Patients need to be informed of the risks and benefits of testing before it's undertaken. The risks of over detection and overtreatment should be included in this discussion."

Brawley says his own position on PSA testing has evolved over the past 3 decades, in part because most men are no longer routinely treated aggressively at the first sign of cancer.

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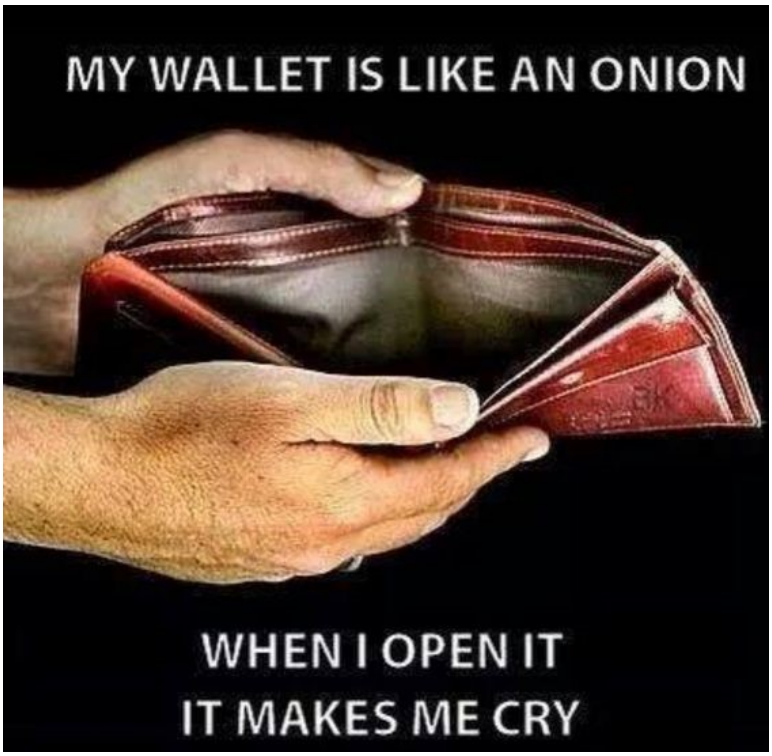
NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Gene Van Vleet is available to speak to organizations of which you might be a member. Contact Gene 619-890-8447 or gene@ipcsg.org to coordinate.

Member John Tassi is the webmaster of our website and welcomes any suggestions to make our website simple and easy to navigate. Check out the Personal Experiences page and send us your story. Go to: https://ipcsg.org/personal-experience

Our brochure provides the group philosophy and explains our goals. Copies may be obtained by mail or email on request. Please pass them along to friends and contacts.

FINANCES



We want to thank those of you who have made special donations to IPCSG. Remember that your gifts are tax deductible because we are a 501(c)(3) non-profit organization.

We again are reminding our members and friends to consider giving a large financial contribution to the IPCSG. This can include estate giving as well as giving in memory of a loved one. You can also have a distribution from your IRA made to our account. We need your support. We will, in turn, make contributions from our group to Prostate Cancer researchers and other groups as appropriate for a non-profit organization. Our group ID number is 54-2141691. Corporate donors are welcome!

While our monthly meetings are suspended, we still have continuing needs, but no monthly collection. If you have the internet you can contribute easily by going to our website, http://ipcsg.org and clicking on "Donate" Follow the instructions on that page. OR just mail a check to: IPCSG, P. O. Box 420142, San Diego CA 92142

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Continued Editors Notes: From Page 2

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- Does Early Prostate Cancer Screening Do More Harm Than Good?
  As time goes on, there will be molecular markers that will be discovered that will help refine this [to] actually predict with a much higher precision those patients who will develop high-grade cancer or metastatic disease much better than PSA or Gleason score. As more men are living longer with prostate cancer as a result of improvements in diagnostics, surgery, radiation, and other advances, treatment decisions should not be based on age, PSA test results, or other single-factor considerations alone. Individualized care is the best way.
- Cancer-specific survival after radical prostatectomy versus external beam radiotherapy in high-risk and very high-risk African American prostate cancer patients cohorts. — *In JHU very high-risk (Gleason 9-10) African American patients, surgery may hold a survival advantage over radiation, but not in JHU high-risk (Gleason 8) African American patients.*
- MRI detects 67% of lymph node metastases in patients with prostate cancer, research shows—"*MRI was capable of detecting LNM and might optimize the preoperative risk assessment and supplement diagnostic (e.g., PSMA-PET) or therapy planning," the authors noted. "CT was inferior to MRI and clearly limited for N-stage determination."*
- Prognostic role of 11C-choline PET/CT scan in patients with metastatic castrate resistant prostate cancer undergoing primary docetaxel chemotherapy- mid-course and posttherapy 11C-choline PET/CT evaluation for mCRPC patients undergoing primary docetaxel chemotherapy can predict full course treatment response and PFS, respectively. 11C-choline PET/CT imaging may provide valuable prognostic information to guide treatment choices for patients with mCRPC
- Prostate Cancer Telomere Length Predicts Metastases, Mortality— *Measuring Telomeres after RP can predict long term results. Compared with men who had less variable telomere length in prostate cancer cells and longer telomere length in stromal cells, men with more variable and shorter telomere lengths after surgery had 3.76-times the risk for death from prostate cancer (P = .01) and 2.23-times the risk of progression to metastasis (P = .05).*

"I was very much against screening for prostate cancer, especially in the 1990s," he says. "Fifteen years ago, every man who was found to have localized prostate cancer in the United States, if he was diagnosed on a Tuesday or Wednesday, he was told it needs to be out of your body by Friday, week after next, literally.

"Now, there are areas of the United States where half of all men with screen-detected prostate cancer are watched and most of those men will never be treated for their prostate cancer."

PSA Testing: Pros, Cons

A PSA test measures blood levels of prostate-specific antigen, which can be high when cancer is present in the prostate, the walnut-sized gland that produces seminal fluid and is key to a man's sexual functioning.

The test was introduced in 1994 to detect the possible presence of prostate cancer, the second-leading cause of cancer deaths in American men. A PSA level of less than 4 nanograms per milliliter of blood is considered normal; when it spikes to 6 or higher in a year's time, doctors are likely to suggest a biopsy to check for a tumor.

If prostate cancer is seen on a biopsy, PSA levels can be used to determine the stage of cancer -- how advanced it is. Cancers are also assigned a grade -- called a Gleason score -- that can show how likely it is to spread. Gleason scores of 6 or less are considered "low grade," 7 is "intermediate," and 8 to 10 is "high grade."

But PSA testing is not foolproof. Cancer isn't the only thing that can raise PSA levels. Inflammation, infection, and an enlarged prostate (common in men over 50) can cause increases in PSA. So it's not as accurate a cancer predictor as, say, genetic tests for the BRCA1 and BRCA2 genes strongly linked to breast cancer (and a very small number of prostate cancers).

Even when testing turns up a tumor, it does not indicate whether it's an aggressive form of cancer that needs treatment right away or is a slow-growing, low-risk tumor unlikely to be life-threatening. In fact, autopsy studies

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have found that undiagnosed prostate cancer is found in about a third of men over 70 who die from some other cause.

But there is no question that PSA testing has helped identify many cancer cases that might otherwise have not been found in early stages. Research shows:

PSA screening can flag cancer about 6 years earlier than a digital rectal exam and 5-10 years before symptoms of the disease emerge.

The death rate from prostate cancer has fallen by more than half since the FDA first approved PSA tests.

Nine in 10 cases in the U.S. are found while the disease is confined to the gland (or nearby), when nearly all men with the disease survive 5 or more years.

About 4 out of 5 men with an elevated PSA who are found on biopsy to have cancer have a low-risk form of the disease that is unlikely to kill them before something else does.

Even so, the doubts about PSA testing have led to widespread debate over who should have it done, at what age, and how doctors and patients should respond to an elevated level.

"Not everyone needs to be screened, not everyone found to have an elevated PSA needs to be biopsied, and Lord knows that not everyone with prostate cancer needs aggressive treatment," said Colorado Springs urologist Henry Rosevear, MD, writing in *Urology Times.*

In the face of the uncertainties, men have to weigh competing and confusing advice on PSA testing and active surveillance.

For instance:

The American Cancer Society recommends that men with at least a 10-year life expectancy "make an informed decision" with their doctor about PSA testing. Discussions should begin at age 50 for men at "average" risk for cancer, 45 for those at "high risk" (African Americans and men with a father, brother, or son diagnosed with the disease before 65), and 40 for "higher risk" people (with more than one close relative diagnosed with prostate cancer at an early age).

The National Comprehensive Cancer Network does not endorse routine screening but advises men 45 to 75 years old to discuss screening risks and benefits with their doctor.

The American Urological Association recommends that men 55 to 69 years old weigh the risks and benefits of PSA screening and advises against testing for men under 40, those between 40 and 54 at "average risk," and men over age 70 or with "a life expectancy less than 10-15 years."

In 2018, the U.S. Preventive Services Task Force (USPSTF) revised its controversial 2012 recommendation against prostate cancer screening and now advises that for men ages 55 to 69, "the decision of whether or not to undergo screening should be individualized." For men 70 and older, the USPSTF recommends against PSA testing.

Samadi says tracking PSA levels and trends over a period of years or decades is far more valuable than a single isolated test result, when it comes to assessing a man's cancer risk and how best to handle it.

"I'm a big proponent of PSA screening and … I always tell the patients to get a baseline PSA at the age of 40," he says. "And if that's absolutely normal, then you can repeat it every 2 or 3 years."

But from the get-go, Samadi says, it's important to understand that an elevated PSA test, on its own, does not necessarily mean any man needs surgery, radiation, or other treatment right away that can affect his quality of life.

Brawley agrees, noting that studies show a prostatectomy (surgery to remove all or part of the prostate) carries a 40% risk for impotence and/or urinary incontinence and a 0.5% chance of dying from the operation, while pelvic radiation can lead to bladder and bowel irritation and bleeding.

"A large number of men who are screened and who are diagnosed with prostate cancer today are going to be told you have one of the more *benign-ish* prostate cancers -- yes, it's malignant, but it's less aggressive," he says. "Therefore, instead of giving you a radical prostatectomy [or] radiation … we're going to watch you."

Advances in Biomarkers, Genetics

In recent years, researchers have been working to develop more refined and sophisticated techniques than PSA testing to help identify more aggressive tumors early, reports James Eastham, MD, of Memorial Sloan Kettering Cancer Center in New York City.

One is the so-called 4Kscore test that assesses the levels of four prostate-specific antigens to gauge a man's risk of having an aggressive cancer.

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Another, called the prostate health index, combines three PSA measurements to identify cancer and help some men avoid a biopsy.

A third test, ExoDx Prostate IntelliScore, examines biomarkers in urine to help predict a man's likelihood of having prostate cancer that will spread and become deadly without treatment right away.

Researchers are also studying an advanced form of MRI that can detect higher-risk prostate cancers.

In addition, other newly developed tests and methods -- some based on molecular and genetic tests -- are showing promise.

Samadi says these personalized, next-wave tests are more precise tools that go beyond PSA testing to help guide oncologists' decisions on care, management, and treatment of their patients.

Maurie Markman, MD, a medical oncologist, believes this new breed of genetic tests and molecular biomarkers will revolutionize cancer therapy.

"As time goes on, there will be molecular markers that will be discovered that will help refine this [to] actually predict with a much higher precision those patients who will develop high-grade cancer or metastatic disease much better than PSA or Gleason score," says Markman, president of medicine and science at the Cancer Treatment Centers of America. "That's the future."

Improvements in Treatment

Samadi says some of these advances have already improved prostate cancer detection and will continue to do so.

But at the same time, vast improvements have been in made in how doctors perform biopsies and treat cancer with surgery, radiation, chemo, or hormone therapy (known as androgen deprivation therapy), he says.

Major strides have been made in surgical techniques (using less invasive laparoscopic and robotic-assisted techniques), digital medicine (using MRI and other scans), and more targeted radiation therapy. Meanwhile, clinical trials are underway for new drugs designed to treat genetic factors that drive cancers of all types.

Samadi says he's also seen major progress in treating prostate cancer as a result of changes in American medicine since the 1990s.

"When I was in training in residency, 25-30 years ago, we would see people coming in with hard-rock prostates, and we were doing a lot of surgery, chemo, hormonal treatment, and radiation," he notes. "But over the course of the last 3 decades, a lot has changed, and [it] all happens to be good."

For one thing, an elevated PSA no longer triggers the "knee-jerk reaction" that a biopsy must be done, and immediate treatment be sought if a tumor is uncovered.

And advances in MRI technology now allow doctors to use imaging -- instead of surgical biopsies -- to assess prostate tumors.

Twenty years ago, urologists would randomly biopsy six or more areas of the prostate in a hit-or-miss hunt for tumor cells that often required patients to have multiple procedures.

"But today, we're using more of a targeted biopsy, we're finding out where the lesion is, we go straight into the lesion, and we're able to find out exactly what the cancer is," Samadi says. "So it's less invasive, less headache, more targeted, and more intelligent."

Radiation techniques have also improved over the past 2 decades.

In the 1900s and early 2000s, full-pelvis radiation was common, often causing serious complications. But more precise radiation techniques -- involving "CyberKnife" therapy and proton therapy -- can now be used to deliver tiny, precisely aimed beams of radiation into tumor cells, sparing healthy surrounding tissues and reducing complication risks.

Cancer specialists are also optimistic about the promise of other therapeutics now in the pipeline.

Early research has found, for instance, that cutting-edge prostate-specific membrane antigen (PSMA) scans can identify high-risk cancers. *These scans* use radioactive tracers that attach to PSMA, a substance often found in large amounts on prostate cancer cells, and are now being used in some medical centers.

Another technique -- called **"**radioligand therapy," already approved overseas -- combines a targeting compound that binds to cancer biomarkers to enable precisely targeted delivery of radiation to the tumor, leaving healthy surrounding tissue unharmed**.**

In addition to these advances in treatment options, Samadi says the approach to treating prostate cancer -- particularly in older men -- has undergone a sea change. Twenty years ago, men older than 70 were not considered good candidates for surgery or other treatment, he says.

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"But that concept doesn't make sense anymore today, and the reason is medicine has improved … and we see a lot of people in their 80s and 90s," he says.

For instance, Samadi says some of his patients are 70 and older who are healthy, physically fit, and great candidates for surgery because they are likely to live many more years. On the other hand, he treats patients in their 50s who are obese, diabetic, and/or have heart disease who aren't likely to benefit as much from prostate surgery.

"I look at my patients individually," he says. "If they are healthy and they are in good physical shape and I think they would be an excellent candidate in the operating room under my care, then I know this guy can be cancer-free with our robotic surgeries and with good continence rate and good sexual function, etc."

The upshot: As more men are living longer with prostate cancer as a result of improvements in diagnostics, surgery, radiation, and other advances, treatment decisions should not be based on age, PSA test results, or other single-factor considerations alone.

"A one-size-fits-all approach is not a good treatment plan," Samadi says. "Individualized care is the best way."

Cancer-specific survival after radical prostatectomy versus external beam radiotherapy in high-risk and very high-risk African American prostate cancer patients

Benedikt Hoeh MD, Christoph Würnschimmel MD, Rocco S. Flammia MD, Benedikt Horlemann MD, Gabriele Sorce MD, Francesco Chierigo MD, Zhe Tian MSc, Fred Saad MD … See all authors

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Abstract

Background

To test for differences in cancer-specific mortality (CSM) rates between radical prostatectomy (RP) vs external beam radiotherapy (EBRT) in National Comprehensive Cancer Network (NCCN) high-risk African American patients, as well as Johns Hopkins University (JHU) high-risk and very high-risk patients.

Materials and methods

Within the Surveillance, Epidemiology, and End Results database (2010–2016), we identified 4165 NCCN high-risk patients, of whom 1944 (46.7%) and 2221 (53.3%) patients qualified for JHU high-risk or very high-risk definitions. Of all 4165 patients, 1390 (33.5%) were treated with RP versus 2775 (66.6%) with EBRT. Cumulative incidence plots and competing risks regression models addressed CSM before and after 1:1 propensity score matching between RP and EBRT NCCN high-risk patients. Subsequently, analyses were repeated separately in JHU high-risk and very high-risk subgroups. Finally, all analyses were repeated after landmark analyses were applied.

Results

In the NCCN high-risk cohort, 5-year CSM rates for RP versus EBRT were 2.4 versus 5.2%, yielding a multivariable hazard ratio of 0.50 (95% confidence interval [CI] 0.30–0.84, $p = 0.009$) favoring RP. In JHU very high-risk patients 5-year CSM rates for RP versus EBRT were 3.7 versus 8.4%, respectively, yielding a multivariable hazard ratio of 0.51 (95% CI: 0.28–0.95, $p = 0.03$) favoring RP. Conversely, in JHU high-risk patients, no significant CSM difference was recorded between RP vs EBRT (5-year CSM rates: 1.3 vs 1.3%; multivariable hazard ratio: 0.55, 95% CI: 0.16–1.90, $p = 0.3$). Observations were confirmed in propensity score-matched and landmark analyses adjusted cohorts.

Conclusions

In JHU very high-risk African American patients, RP may hold a CSM advantage over EBRT, but not in JHU high-risk African American patients.

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MRI detects 67% of lymph node metastases in patients with prostate cancer, research shows

Hannah Murphy | December 17, 2021 | Diagnostic & Screening

A preoperative MRI scan could help guide appropriate treatment plans for patients diagnosed with prostate cancer, according to research published this week analyzing the modality's ability to detect lymph node metastases.

Cancers that have spread outside of their origin are more aggressive and more difficult to treat. Lymph node metastasis (LNM) signals that a tumor is advanced. And

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LNM can be a significant indication of overall prognosis in patients with prostate cancer.

Surgical lymphadenectomy is most often used to detect LNM, but this is invasive and carries risks. And even with surgery, metastases can still occasionally be missed. For this reason, research into alternative methods of LNM identification has gravitated towards the use of CT and MRI. *The European Journal of Radiology* published a study this week that compares the accuracy of the two modalities when used preoperatively for patients with prostate cancer.

"Pathological conditions of abdominal LN include enlarged LN in MRI and CT ... a lack of fat hilus, necrosis, round shape and a low T2WI signal," B. Valentin, with the Department of Diagnostic and Interventional Radiology at the University Dusseldorf, and co-authors explained.

Their research focused on 228 patients that had undergone a preoperative CT, MRI or both prior to prostatectomy and lymphadenectomy. The researchers assessed LNM by size, location and time of detection (before or after surgery).

Overall, MRI identified 67% of patients with LNM. Compared to CT, which detected metastases with a diameter down to 8 millimeters, MRI was able to observe findings as small as 4 millimeters. Sensitivity and specificity were also superior in MRI, at 81% and 99%, respectively, versus 33% and 99% for CT.

"MRI was capable of detecting LNM and might optimize the preoperative risk assessment and supplement diagnostic (e.g., PSMA-PET) or therapy planning," the authors noted. "CT was inferior to MRI and clearly limited for N-stage determination."

The authors caution that patients who have an especially high risk for LNM may benefit from undergoing PSMA-PET in addition to MRI to ensure accuracy.

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Prognostic role of 11C-choline PET/CT scan in patients with metastatic castrate resistant prostate cancer undergoing primary docetaxel chemotherapy

Masaya Jimbo MD, PhD

Abstract

Background

We sought to assess the prognostic utility of 11C-choline positron emission tomography/computed tomography (PET/CT) in patients with metastatic castrate resistant prostate cancer (mCRPC) undergoing primary docetaxel chemotherapy.

Methods

We performed a single institution retrospective analysis of 77 mCRPC patients who were treated with 6 cycles of docetaxel chemotherapy, and who also underwent 11C-choline PET/CT scans at baseline (before chemotherapy), mid-course (after 3 cycles), and posttherapy (after 6 cycles). We evaluated treatment response based on percent change in blood pool-corrected maximum standardized uptake value (SUVmax) of the target lesion on PET/CT, as well as percent change in serum prostate specific antigen (PSA). Logistic regression analysis was used to identify factors associated with complete treatment response. Progression free survival (PFS) analysis was performed using log-rank test and shown on Kaplan–Meier plot.

Results

Percent change in blood pool-corrected SUVmax on mid-course scan was a significant predictor of complete response (odds ratio [OR]: 0.98, 95% confidence interval [CI]: 0.96–0.99, $p = .0003$), whereas percent change in PSA was not (OR: 0.99, 95% CI: 0.99–1.01, $p = .6025$). 57 of 77 patients (74%) achieved ≥20% reduction in blood pool-corrected SUVmax on mid-course; these patients were 3.6 times more likely to achieve complete response after full 6 cycles of docetaxel chemotherapy, compared to patients with <20% reduction in blood pool-corrected SUVmax (OR: 3.56, 95% CI: 1.04–16.52, $p = .0420$). Median PFS in the complete response group was 35.1 months (95% CI: 26.0–52.7 months), compared to 9.4 months (95% CI: 6.9–13.0 months) in the incomplete response group ($p = .0005$).

Conclusions

Our study showed that mid-course and posttherapy 11C-choline PET/CT evaluation for mCRPC patients undergoing primary docetaxel chemotherapy can predict full course treatment response and PFS, respectively. 11C-choline PET/CT imaging may provide valuable prognostic information to guide treatment choices for patients with mCRPC.

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Prostate Cancer Telomere Length Predicts Metastases, Mortality

M. Alexander Otto, MMS, PA

Key Takeaway

A combination of telomere measurements in prostatectomy tissue samples — more variable telomere length in cancer cells plus shorter telomere length in associated stromal cells — predicts the subsequent risk of metastasis and death.

Why This Matters

Current biomarkers — prostate-specific antigen level, grade group, and clinical stage — don't work well to predict how men will fare after prostatectomy.

There is an urgent need for better biomarkers to distinguish men who need additional treatment from those who don't.

Telomere length variability and shortening indicate chromosomal instability, a hallmark of aggressive prostate cancer.

Determining if telomere aberrations predict how men will fare after prostatectomy could improve treatment and surveillance decisions.

Study Design

The team assessed telomere length in tissue microarrays from prostatectomies in 2255 men across five cohorts.

Relative telomere length was determined through a semiautomated process involving immunofluorescence, fluorescent microscopy, and image analysis of individual cells.

The findings were correlated with disease outcomes.

Key Results

Compared with men who had less variable telomere length in prostate cancer cells and longer telomere length in stromal cells, men with more variable and shorter telomere lengths after surgery had 3.76-times the risk for death from prostate cancer (P = .01) and 2.23-times the risk of progression to metastasis (P = .05).

The findings held in men with intermediate-risk disease and with *PTEN*-intact tumors.

Only more variable telomere length in cancer cells — not shorter length in stromal cells — was associated with recurrence.

Limitations

It's unknown if the telomere biomarker is associated with poor outcomes in men undergoing radiation or hormone treatment.

Recurrence, progression to metastasis, and prostate cancer death couldn't be assessed for every cohort because of study designs and/or study population issues.

This is a summary of a preprint research report led by Christopher Heaphy, PhD, at Johns Hopkins University, Baltimore, Maryland, provided to you by Medscape. This study has not yet been peer-reviewed. The full text can be found at medRxiv.org.

M. Alexander Otto is a physician assistant with a master's degree in medical science, and an award-winning medical journalist who has worked for several major news outlets before joining Medscape. He is an MIT Knight Science Journalism fellow. Email: aotto@mdedge.com

Credits:

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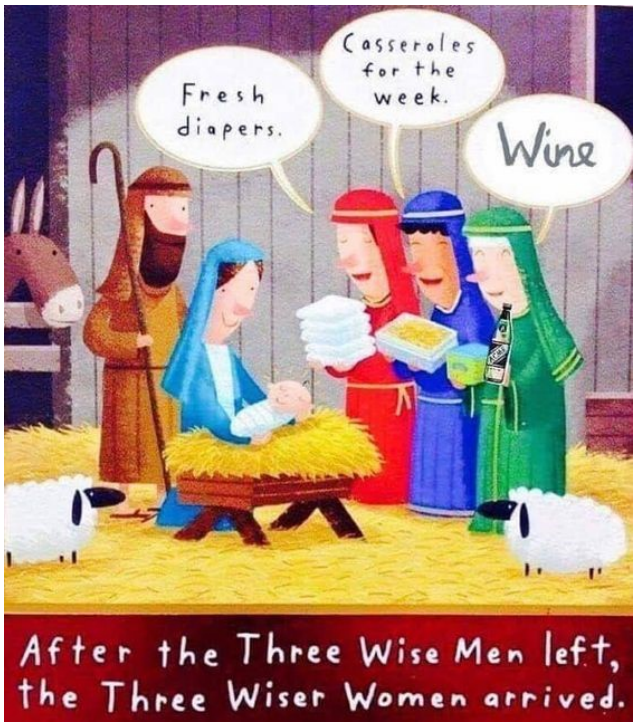

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