



## June 2018 NEWSLETTER

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We Meet Every Third Saturday (except December)

<p><b>Officers</b> Lyle LaRosh President</p>	<p><b>Next Meeting</b> <u>June 16, 2018</u> <u>10:00AM to Noon</u></p>	<p>Tuesday, June 12, 2018      Volume 11 Issue 5</p>
<p><b>Additional Directors</b> Gene Van Vleet George Johnson John Tassi Bill Manning</p>		<p><b>What We Are About</b></p>
<p><b>Honorary Directors</b> Dr. Dick Gilbert Judge Robert Coates</p>	<p>Meeting at Sanford-Burnham- Prebys Auditorium 10905 Road to the Cure, San Diego CA 92121</p>	<p>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.</p>
<p>George Johnson, Facilitator Bill Manning, Videographer John Tassi, Webmaster Bill Bailey, Librarian Jim Kilduff, Greeter Chuck Grim, Meeting Set-up</p>	<p>SEE MAP ON THE LAST PAGE</p>	
<p><b>Table of Contents</b></p> <p>Pg.  #1 What We Are About  #1 Video DVD's  #1-4 Feb. Meeting Recap  #5 On the Lighter Side  #6 Future Meetings  #6-8 Noteworthy Articles  #9 Networking, Finances  #10 Directions and Map to Where We Meet</p> <hr/> <p>Editor: Stephen Pendergast</p>	<p><b>PROSTATE CANCER</b> <b>IT'S ONLY 2 WORDS NOT A SENTENCE</b></p> <p><b>Ross Schwartzberg, MD – Irreversible Electroporation (IRE / Nanoknife) Ablation of Prostate Cancer</b></p> <p>May 2018 IPCSG Meeting Summary by Bill Lewis.</p> <p>Dr. Schwartzberg is a diagnostic radiologist. He's an expert in multiparametric MRI of the prostate, and has</p> <p>(Continued on page 2)</p>	<p><b>Video DVD's</b></p> <p>DVD's of our meetings are available in our library for \$10ea. Refer to the index available in the library. They can also be purchased through our website: <a href="http://ipcs.org">http://ipcs.org</a> Click on the 'Purchase DVDs' tab.</p> <p>The DVD of each meeting is available by the next meeting date.</p>

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recently begun to offer IRE (**Irreversible Electroporation**) treatments, following appropriate imaging of the prostate. As a new treatment modality, IRE has seen some controversy, just as other new treatments have had slow acceptance in the past. It is a form of local (or "focal") treatment of tumors in the prostate, which has a great advantage of lower side effects vs. the traditional whole-gland therapies: prostatectomy or radiation.

A world expert and early user of IRE, Dr. Mark Emberton, at the University College London (he has published 62 articles on focal therapy in 10 years, with 39 in the last three years), says that focal therapy for men with intermediate risk prostate cancer and a solitary lesion should be the standard of care. Dr. Schwartzberg doesn't go that far, but suggests that it is a reasonable choice. A number of urologists still believe it's just crazy to do things differently than in the past. But progression in understanding and treating the prostate is occurring at an increasing pace.

There has been a need for accurate imaging of the tumor within the prostate. The "big four" articles on the value of mpMRI in diagnosing prostate cancer (PCa):

Pokorny, et al. Prospective Study of Diagnostic Accuracy Comparing Prostate Cancer Detection By TRUS Biopsy vs MRI with subsequent MRI-guided biopsy in men without previous prostate biopsies. European Urology. 2014 Volume 66, Issue 1, 22-29.

Siddiqui MM, Turkbey B, et al. Comparison of MR/Ultrasound Fusion-Guided Biopsy With Ultrasound-Guided Biopsy for the Diagnosis of Prostate Cancer. JAMA. 2015;313(4):390-397.

Ahmed, et al. Diagnostic accuracy of mpMRI and TRUS biopsy in Prostate Cancer (Promis): a paired validated confirmatory study. Lancet 2017; 389:815-822.

Kasivisvanthan, et al. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N Engl J Med 2018; 378:1767-1777.

The take-home message from these articles is that men should have an MRI imaging study BEFORE a biopsy, and that the biopsy should be MRI guided (either in-bore as is done by Dr. Schwartzberg's associate Dr. Cooper, or using a fusion of MRI images with ultrasound as is done at Genesis Healthcare locally). MRI provides information on the tumor location, volume, and precise risk stratification.

The Focal Therapy prostate cancer rationale is that it is intended to target a predefined cancerous part of organ, and spare uninvolved tissue. Key patient issues are the PSA, Biopsy results with histopathologic parameters of the cancer foci, patient life expectancy and quality of life, and the PATIENT'S PREFERENCE.

#### Articles on IRE:

Onik G, Mikus P, Rubinsky B. Irreversible electroporation: implications for prostate ablation. Technol Cancer Res Treat. 2007;6:295-300. Apoptosis and necrosis result from the applied voltage and current.

Maor E, Rubinsky B, et al. The Effect of Irreversible Electroporation on Blood Vessels. Technology in Cancer Research and Treatment. August 2007 Vol 6: 4; 307-312. Non-cellular tissue scaffold (collagen, elastin, basal membranes, interstitial matrix) is preserved. Smooth muscle cells are damaged temporarily yet endothelial cells are regenerated and blood vessels are preserved. Nerves are preserved. So erectile function and the external sphincter are only rarely damaged.

Randomized comparative long-term studies of IRE are yet to be done, and need to consider the natural history of PCa disease, cost, and ethics. All patients treated by Dr. Schwarzberg are enrolled in a NCI trial, including following them for 20 years. It is a very safe procedure, with minimal adverse events. Muscles require deep anaes-

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thesia, in a hospital, to prevent contractions. Electrodes are placed through the perineum. Here is the schedule for treatment, following pre-operative mpMRI for 3D planning to define the "Index" (largest) lesion and spatial distribution of any other clinically significant cancer as precisely and accurately as possible. 3D-mapping biopsy with a template having 2.5 mm spacing is considered when MRI is suboptimal, e.g. chronic prostatitis, hip prosthesis, bowel peristalsis, or motion artifact. Dr. Stehling has done a few such mappings (ouch!), but they have not yet been needed here.

Day 1: Arrival and preparation in the morning, followed by approx. 2 hours in the procedure room, with full anaesthesia and a Foley catheter. Ultrasonic (fused with MRI) guided transperineal IRE-electrode placement (Using no grid! Gives 1-2 mm of placement accuracy. More time intensive, but they are the only group that does without the grid). Deep muscle relaxation is administered to suppress IRE-induced muscle contractions. After the procedure, the patient spends approx. 2 hours in the recovery room. Day 2: Follow-up MRI. The Foley catheter remains for 3-7 days.

The target is to preserve gland function and quality of life, while also controlling the cancer.

Johns Hopkins website "Han" tables predict recurrence. PCa is a chronic disease, that tends to come back. Cancer control rate after IRE is tracking the same as other focal therapies, for the 5-6 years of experience thus far.

Comparison:

<u>IRE</u>	<u>Prostatectomy</u>
Minimally invasive	Open surgery
24h (outpatient/overnight in-patient) procedure	7-10d, up to 3 weeks in hospital
5-14d Foley	7-14d Foley, additional suprapubic catheter
No rehabilitation	3-6w rehabilitation
No wound pain (!)	5-6d analgesia via peridural catheter
Zero incontinence rate	20 - 50% incontinence
Low (< 10%) impotence rate	50 - 70% impotence
Low recurrence rate of 5% at 50 m (25% in Gl.>8 group)	Depending on stage/grade 20-40 % at 60 m
Can be repeated as often as needed	Repeat surgery difficult
Suitable for recurrent PCa after surgery, Rx, HIFU, etc.	Repeat surgery difficult
Suitable for T4 PCa (rectal, sphincter, bladder infiltration)	Stage T4 problematic
Secondary (anti-tumoral) immunological effects	none
Patient satisfaction high	Patient satisfaction low

The historical trend is from open surgery to minimally invasive procedures, including IRE. In the future, we can expect no invasion at all: in ten years we will have cellular-level treatments such as immune system augmentation, etc.

Additional notes: mpMRI can find higher grade cancer missed on random biopsy! Misattribution of low grade

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cancer to patients who harbor occult higher grade cancer (as much as 25-30% of patients diagnosed with Gleason 6 by random biopsy). Undergrading! Did not get the most rotten part of the apple core. True biologic grade progression is rare (1-2%/year). Most risk guidelines differentiate between very low risk and low risk based on VOLUME. Why does VOLUME of Gleason 3 matter if Gleason 3 + 3 doesn't metastasize? NOT because higher volume more likely to metastasize, because high VOLUME is a marker for OCCULT higher grade cancer! MRI shows you the volume -- but even it still underestimates volume.

IRE is a suitable technique for the treatment of recurrent PCa, as is radiation or HIFU.

Questions:

IRE for a single metastatic bone lesion? Cryotherapy or other energy is a better choice. IRE requires full anesthesia. In bones, it is not needed to avoid damaging surrounding tissue.

Useful for what stages? Dr. Schwartzberg offers treatment to men at all stages, except not to Gleason 3+3 in a small lesion, which he believes should not be treated. They have done whole-gland treatments, but prefer to keep IRE for focal use.

What treatment is appropriate for recurrence after IRE? The easiest thing is to do another IRE. It's also OK to do surgery, since there would not be much scar tissue from a prior IRE.

Proton therapy or EBRT vs. IRE? Normally either type of radiation is used for whole-gland therapy. Bowel, erectile dysfunction, bladder problems are higher for radiation vs. IRE.

IRE after brachytherapy? Not known if it is feasible.

Recurrent metastatic multiple sites treatable by IRE? If no local treatment previously given, radiation or surgery of the prostate may (now more often) be given under the conclusion that the primary tumor is continuing to "seed" additional metastases. Whether a met begets other mets is currently debatable. But doing IRE of multiple sites is not very practical.

Cost? Not yet covered by any insurance. About \$25,000.

What do extra small lesions signify in biopsies? What do we need to treat, what do we need to discover? The small lesions generally do not have the "hallmarks" of cancer – that is, they aren't "really" cancer if Gleason is 3+3. If they are 3+4, then that becomes of more concern.

Targeting the biopsy with MRI? 107 in-bore biopsies have been done by Dr. Cooper, Dr. Schwartzberg's associate. 3 Tesla for imaging. 1.5 for the biopsy. It's getting to be the gold standard, instead of ultrasound-guided biopsy. Fusion biopsies combine the MRI image with the real-time ultrasound imaging. Fusion gives 1-3 mm of error, but still way better than the old "TRUS" biopsy procedure.

Can the ADC (apparent diffusion coefficient) be used instead of a biopsy to diagnose cancer? Next month we will hear about molecular imaging, which may be better for diagnosis.

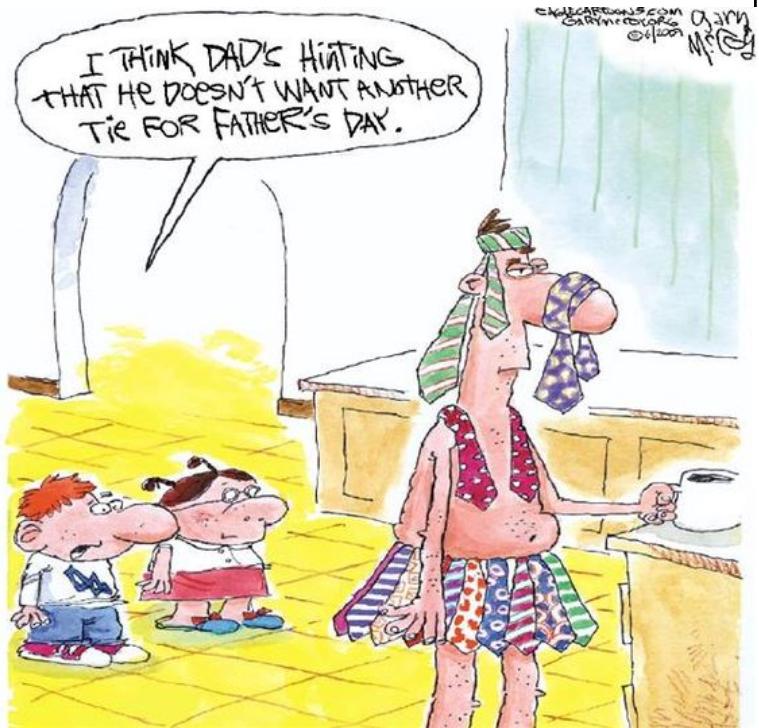
Han table usefulness? It gives the probability of recurrence of PCa after prostatectomy, after X number of years. It works from the parameters of your specific cancer, to predict likely behavior.

Other types of cancer that IRE is used for? – Most common: liver, pancreas, and kidney cancers. Starting to look at breast cancer.

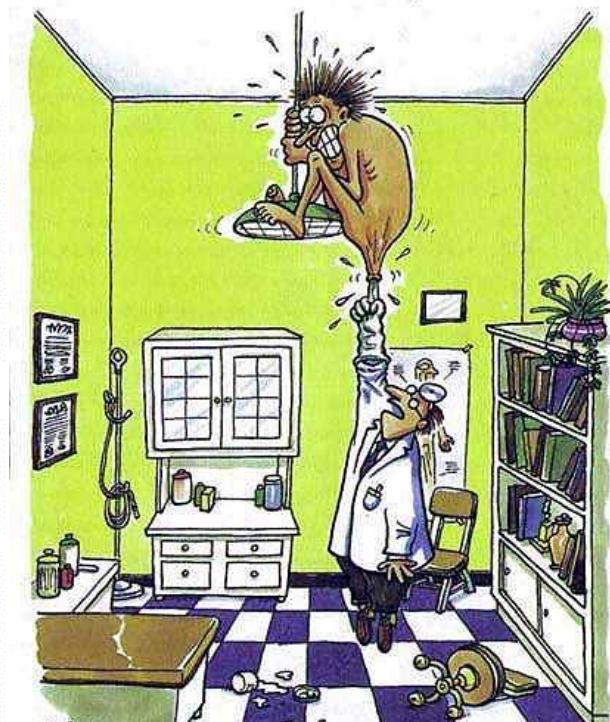
Recurrence rate of IRE: In Dr. Stehling's over-700 cases, he has found almost the same as the Hahn tables – that is, about the same as for a prostatectomy. But the side effects of IRE are much less.

## ON THE LIGHTER SIDE

### THE 7 DWARVES OF FATHERHOOD



*"For Father's Day, I'm giving my dad an hour of free tech support."*



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## FUTURE MEETINGS

- Meeting Date SPEAKERS
  - JUNE 16 - DR. SCHECHTER- DIAGNOSTIC IMAGING



- Dr. Mark Schechter is a board certified diagnostic radiologist who has subspecialty Certified Added Qualifications (CAQ) in angiography and interventional radiology. Over the past 15 years, Dr. Schechter has helped to build one of San Diego's finest interventional radiologic practices with expertise available in needle biopsy and male infertility (varicocoele).

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## INTERESTING ARTICLES

## Special Reports > A Patient's Journey

## **Prostate Surgery and Outright Lies- What happened to one patient with low-grade cancer pressured into the OR**

by Howard Wolinsky, Contributing Writer, MedPage Today

June 10, 2018

Jim Schraadt has been to hell and back.

A third-generation prostate cancer patient, the Chicago attorney was diagnosed with prostate cancer at a major Chicago teaching hospital in March 2010 at age 58. The biopsy revealed extremely low volume (a small part of one biopsy core) mostly Gleason 3, with a tiny amount of Gleason 4, yielding a Gleason score of 7 (3+4).

Schraadt was opposed to immediate treatment and suggested to his urologist that they talk about it again in six months and see if the PSA changes. However, his urologist and separately his surgeon insisted that immediate treatment was absolutely necessary due to his age and the presence of Gleason 4. He was told that immediate radical treatment was necessary to avoid progression of the disease and possibly save his life.

Concerned about the reported sexual consequences of treatment, he read extensively, and asked his urologist and surgeon very specific questions including questions about orgasm and erectile dysfunction. In response, he was told that orgasm could be expected to be normal, even in the absence of erections and that something could almost always be done about erections. His surgeon asserted that because of his age and overall health, he could expect an excellent recovery, and that he would find treatment and recovery to be a mere "speed bump" (presumably on the road of life.)

The name of the hospital and the surgeon don't matter. Schraadt received standard care in 2010.

He trusted his surgeon. He took it as gospel that a prostatectomy was what was needed. He didn't

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seek a second opinion on either the biopsy pathology or the treatment recommendation.

Contrary to the reassurances he received from his urologist and surgeon, Schraadt had a far from easy recovery for which he was totally unprepared. Looking back, he said: " I have struggled with treatment consequences, including, without limitation, apparently permanent ED, anorgasmia, leakage of urine during sexual activity, penile shrinkage and low testosterone. I was not informed, was misinformed or was outright lied to concerning these consequences."

Upset by sexual and psychological side effects from his surgery, Schraadt developed a clinical depression that took him to the brink of suicide -- all because of a supposedly life-saving procedure.

That same year, I was in a similar boat. Like Schraadt, I was diagnosed prostate cancer. Unlike Schraadt, mine was low grade Gleason 6 (3+3). Nonetheless, it was enough for a community urologist to recommend that I have a prostatectomy immediately. Instead, I got a second opinion and opted for active surveillance and have been thriving with it ever since. As it happens, I interviewed Schraadt's surgeon for an article and described what I was doing with AS. He told me I was crazy and ought to have my prostate out.

I didn't. Schraadt did.

My second urologist at the University of Chicago told me I was a poster boy for AS and showed me the research by Laurence Klotz, MD, in Toronto. Scott Eggener, MD, told me he expected I would be the same as far as my prostate cancer was concerned in 10 years as I was then. I am eight years out now and, in fact, my PSA has improved and I have had no signs of any cancer at all in biopsies and mpMRIs.

I wasn't smarter than Schraadt. But I was luckier. There but for fortune...

On the upside, Schraadt's surgery has so far apparently been a success in treating the cancer. But he questions whether it was necessary. His depression required two years of medication and five years of individual psychotherapy along with ongoing participation in support groups. He leads a full life with a mission -- to help prostate cancer patients make informed choices. He facilitates a monthly support group in Chicago and serves as vice chair of Us TOO International, the major support and education organization for patients with prostate cancer and their partners.

But Schraadt remains upset over the way prostate cancer is treated and what most men still undergo without proper advice about the side effects of treatment. "Even after eight years, my anger and frustration with the way prostate cancer is treated and way treatment is promoted by the medical community is white hot," he said.

I met Schraadt by accident. As a result of a blog I posted on MedPage Today about how I was rebuffed as the first patient panelist at an ASCO symposium on genitourinary cancer, I met a group of other men on AS. We are organizing a meeting of world experts on prostate cancer in Iceland in October 2019. The group is Active Surveillance Patients International. I ran across Schraadt because he maintains an email list of his Chicago support group participants, and I wanted to ask him to let his list members know about ASPI, because we're looking for volunteers. As a result, he told me his story.

I didn't anticipate his enthusiasm for ASPI's mission and his willingness to help us out. He has joined the ASPI board.

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Schraadt said: "One of the few things that helps me is working with others to change the treatment paradigm. Active surveillance is an important part of this, and I wish it could have been the path I chose."

He said he is looking out for the future of his 28-year-old son -- as well as all of our sons

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### 'Notable Differences' With 3 Prostate Cancer Genomics Tests Study Author Admits: 'I Need a Lot of Help'

Nick Mulcahy May 20, 2018 [www.medscape.com](http://www.medscape.com)

SAN FRANCISCO — There are "notable differences" in the oncologic outcomes predicted by the three leading prostate cancer genomics tests, according to a small retrospective study of Oncotype Dx, Prolaris, and Decipher clinical usage.

"You can do a Prolaris test on one man and tell him you think he should undergo active surveillance, and then do an Oncotype on the same man and tell him he may need treatment," senior study author Joseph Wagner, MD, from the Hartford Healthcare Medical Group in Connecticut, told an audience here at the American Urological Association 2018 Annual Meeting.

The comparative study also "highlights the difficulty of interpreting genomic tests for prostate cancer," Wagner and his colleagues write in their meeting abstract.

"I need a lot of help figuring out how to use these tests," Wagner acknowledged during a meeting press conference.

Traditionally, clinicians have used Gleason score, prostate-specific antigen (PSA) level, clinical staging, the number of positive needle cores, and related measures to risk-stratify patients with biopsy-confirmed disease and to help with subsequent treatment and management decisions, including active surveillance (AS), he explained.

But it is now becoming increasingly common for clinicians to use genomics tests, also known as molecular tests, to predict outcomes and guide treatment for favorable-risk prostate cancers (including very low, low, and intermediate [GS 3+4] risk).

Genomics tests incorporate both traditional measures and genetic data. However, discrepancies can exist among genomics tests in terms of their recommendations for treatment or for AS, said Wagner.

In their retrospective chart review, the research team identified 22 prostate cancer patients who had undergone at least two of the three genomic tests at Hartford Hospital from 2014 to 2017. "Multiple testing was by patient choice, not physician recommendation," Wagner emphasized.

Most patients undergo only one test, but multiple tests facilitated the aims of the study, he noted.

Study participants were first assessed to determine whether they qualified for AS on the basis of National Comprehensive Cancer Network (NCCN) guidelines (i.e., traditional measures). The results of each of their genomics tests were then compared with the NCCN determination to see if they were in agreement.

Of the 22 participants, 21 met the NCCN criteria for AS.

There was 75% agreement between the 20 Prolaris tests and NCCN recommendations for AS, and the  $k$  score, which indicates whether a measure is above or below chance, was 0.21 ( $P = .117$ ). In other words, Prolaris and NCCN agreed on active surveillance 75% of the time for these patients, which is the highest degree of conformity among the three tests.

For the 15 Decipher tests, there was 60% agreement and the  $k$  score was 0.15 ( $P = .268$ ). And for the 10 Oncotype DX tests, there was 50% agreement but, because there were too few patients, the

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k score could not be calculated.

The results "don't mean Polaris is a better test than Decipher," Wagner cautioned.

Instead, the team concluded that the majority of patients (21 of 22) met the NCCN criteria for AS and that the analysis "suggests Polaris is most apt to confirm this [NCCN] recommendation while Oncotype DX is more likely to go against it."

The findings were not statistically significant, and the k scores indicate that the results might be the result of chance, said Wagner. However, they do show that there are potential differences in the test outcomes, he noted.

He acknowledged that the study was not scientifically rigorous and was conducted to more to provoke questions about the utility of the tests.

**There's no clear evidence of a superior test.** Stacy Loeb, MD, New York University

Because there are no head-to-head studies of these genomics tests, "there has been very little reason necessarily to choose one over another," said Stacy Loeb, MD, from New York University in New York City, who moderated the press conference. "There's no clear evidence of a superior test."

Clinicians tend to use the test that is preferred at their institution, if they use one at all, Loeb explained.

Mark Stovksy, MD, from the Cleveland Clinic, who attended the press conference, said that his institution predominantly uses the Oncotype DX test, which was tested at the Ohio clinic.

The three tests provide reports that have largely converged in their analyses, said Loeb. But they still have some differences.

For Decipher and Polaris, a "favorable" clinical prediction (indicating suitability for AS) is defined as a 3% or less likelihood of 10-year prostate cancer mortality. For Oncotype DX, it is defined as a more than 70% likelihood of organ-confined, grade group 1 or 2 disease at surgery (determined on pathology).

In everyday practice, using more than one test with a patient can become tricky and confusing, Wagner noted.

He described a recent patient with an elevated PSA (7 ng/mL), a favorable intermediate-risk Gleason score (7; i.e., 3+4), and only one positive needle core out of 12. Polaris indicated a projected 10-year prostate cancer mortality rate of 2.4%, which is considered favorable and thus appropriate for AS. However the man pushed for another test, the Oncotype DX, which indicated a 39% risk for unfavorable pathology.

"He sees that Oncotype [score] and goes, 'Holy crap, I've got to get my prostate out,'" said Wagner. "That's what can happen when you give more than one test."

The tests cost \$5000 to \$6000, most of which is covered by Medicare and private insurance. However, when asked by a reporter if these costly tests have ever been shown to actually improve outcomes, such as disease-specific or overall survival, Loeb answered no.

*Dr Wagner reports financial ties to Genomic Health, the maker Oncotype DX. Dr Loeb reports ties to Lilly, MDx Health, GenomeDx, General Electric, Astellas, Sanofi, Minomic, and Boehringer Ingelheim.*

American Urological Association (AUA) 2018 Annual Meeting: [Abstract PD06-09](#). Presented May 18, 2018.

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## NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Lyle LaRosh, Gene Van Vleet and George Johnson are available to speak to organizations of which you might be a member. Contact Gene 619-890-8447 or gene@ipcs.org to coordinate.

Member and Director, 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://ipcs.org/personal-experience>

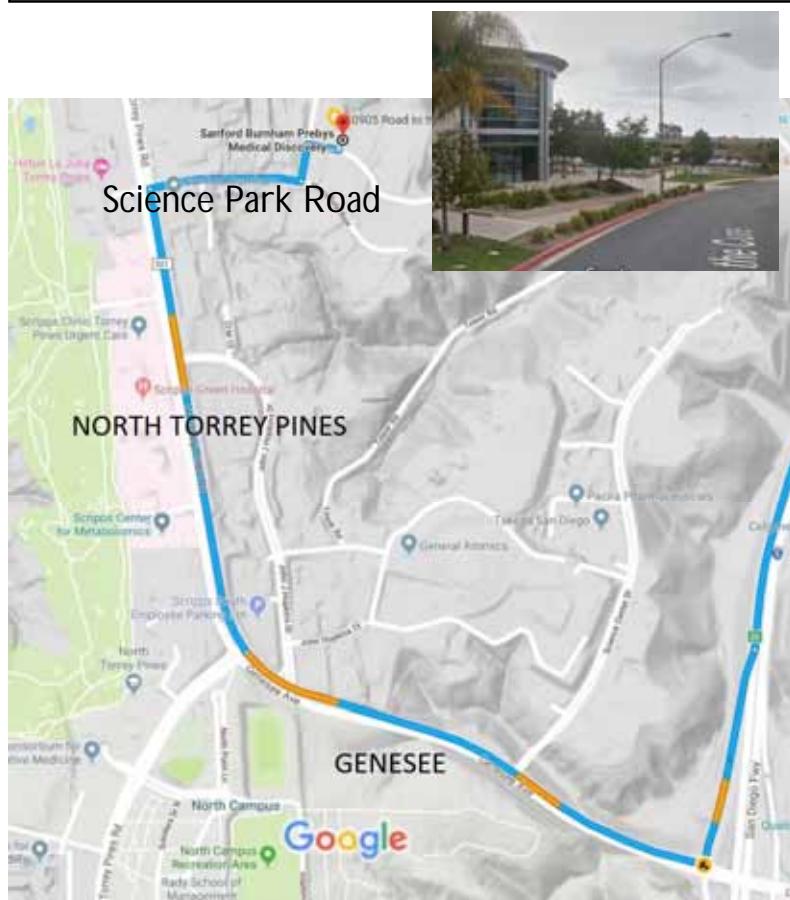
Our brochure provides the group philosophy and explains our goals. Copies may be obtained at our meetings. Please pass them along to friends and contacts.

## 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!

If you have the internet you can contribute easily by going to our website, <http://ipcs.org> and clicking on "Donate". Follow the instructions on that page. OR just mail a check to: IPCSG, P. O. Box 4201042, San Diego CA\_92142



### Directions to Sanford-Burnham-Prebys Auditorium 10905 Road to the Cure, San Diego, CA 92121

Take I-5 (north or south) to the Genesee exit (west).

Follow Genesee up the hill, staying right.

Genesee rounds right onto North Torrey Pines Road.

**Do not turn into the Sanford-Burnham-Prebys Medical Discovery Institute or Fishman Auditorium**

Turn right on Science Park Road.

Watch for our sign here.

Turn Left on Torreyana Road. Watch for our sign here.

Turn Right on Road to the Cure (formerly Altman Row). Watch for our sign here.