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.

Be your own health manager!!
and **Southwest PET/CT Institute in Yuma, AZ**, Dr. Almeida oversees clinics in Phoenix, Yuma, and Tucson, providing his extensive clinical expertise in PET/CT imaging. He continues his research, focused on applied medical informatics with emphasis on imaging and networking systems, optimization of fusion technology, and volumetric tumor assessment for radiation therapy planning. He actively participates in several oncology and neurologic clinical trials and is the principal investigator for a novel Carbon-11 PET agent for prostate cancer imaging.

Dr. Almeida was Imaging Director at the University of Arizona, but left due to politics and difficulties in getting things done quickly, and started his own center. Cardinal Health provides the imaging agents. Recently he merged with Insight Imaging, for better national exposure, to get information out to physicians -who are slow to adopt new technologies and are often actually learning about imaging developments from their patients.

Kinds of imaging discussed in this talk are mpMRI, and PET/CT with one of the following agents -- Sodium Fluoride (NaF), Fluciclovine (Axumin), C-11 Acetate, C-11 Choline, or various PSMA agents.

mp-MRI is the best imaging technique of all, for imaging the prostate tissues, with great anatomic detail, and with the new parameters used, gives functional information. Its advantage over Color Doppler Ultrasound imaging is that the results are much less dependent on having an expert technician. It’s very useful as a precursor to biopsy when there is a rising PSA (as this author can attest). It’s also very useful during active surveillance, to monitor if the disease is stable or progressing (along with PSA data), and to assess recurrences following radical prostatectomy or radiation therapy.

Urologists typically oppose the early use of MRI. They want to see a traditional biopsy first. (Not the best idea!)

Bone scans with Technetium-99 – Dr. Almeida has done thousands of them, but it is limited in value, especially for middle-aged and older adults where other bone damage has typically occurred. Need the lesion to be 1-1.5 cm in diameter to be visible with Technetium.

NaF-18 PET/CT bone scans provide a 3-D image with much better detail. Resolution is down to 2 mm. It has good “negative predictive value” – that is, a clean scan really does mean there is no disease present.

CT scans are done with various radioactive agents, discussed here in turn.

Fluorinated glucose is used in many other cancers, but is not effective for prostate cancer. Something is different about glucose uptake/metabolism vs. other cancers, but the difference is not yet well understood.

Axumin (Fluciclovine) is FDA and Medicare-approved. However, in a recent multi-site study, the detection rate was only 68% for 595 men scanned, although all “should” have shown lesions since they had rising PSA’s. Among those 68% with detected lesions, the overall positive predictive value was only 62%; that is, biopsy or other follow-up confirmed the lesions found were cancerous in only 62% of the cases. (albeit 92% for cases of extraprostatic involvement). Overall, these numbers are disappointing, though still a big improvement over Technetium bone scans. Another issue is that the patient needs to avoid any physical exertion for 2-3 days before the scan, to minimize uptake of the agent by the muscles, which would obscure the desired image. Dr. Almeida expects this technique to be superseded by some better technique within two years.

Carbon-11 acetate studies at Dr. Almeida’s lab on men with prior negative Technetium or NaF bone scans or CT imaging, but with rising PSA: of 721 patients, 88% had detectable lesions, and the positive predictive value when it could be determined (that is, on about half of the patients) was 91%. Since this report was published, his total patients are 1800, with about the same percentages. Much better than Ax-
umin! Scan results were best when the PSA was above 1.1, or when the PSA doubling time was short. Like with the Axumin scans, the patient needs to avoid physical exertion before the test.

An example was shown of a C-11 scan that allowed focusing radiation on one spot in the prostate bed (instead of blindly irradiating the whole area) where cancer recurred after radical prostatectomy, boosting the likelihood of success from 40 or 50%, to where the patient has now had an undetectable PSA for over 5 years. Three similar examples were shown, including detections of lymph node and bone metastases, and head-to-head comparisons with Axumin scans. Dr. Almeida now only does Axumin scans in conjunction with NaF bone scans, to avoid the danger of missing a tumor in the bones, because Axumin performs poorly in the bones.

PSMA (which is called glycoprotein #3 by oncologists who don’t work with prostate cancer) is found not only in the prostate, but also in the brain, in kidney proximal tubules, in intestinal brush border membranes, in lachrymatory glands, and in salivary glands. But expression of the protein is massively increased in aggressive prostate cancer and tumor neovasculature. The function of PSMA in the prostate cancer is unclear, but it is believed to play a role in tumor invasiveness. The detection rate for prostate cancer tumors is 83-93% using various PSMA-targeted agents, which are now commonly used across Europe and in Asia and Australia. Nineteen agents currently in clinical studies were listed by Dr. Almeida, including agents based on gallium, copper, technetium, iodine and fluorine. None are FDA approved. The agent 68GA-PSMA-11 is the most commonly used in this country, and is made available by a consortium of universities (including UCSF), but it’s not likely to ever get FDA approval because it is not a proprietary or patentable molecule, and there is no pharmaceutical company funding studies that would lead to approval.

In contrast with carbon-11, which has a 20-minute half-life, so has 68Ga, so has to be used very close to the cyclotron in which it is generated (and is only used by Dr. Almeida as C-11 acetate and by the Mayo Clinic as C-11 choline), fluorine-18 has a half life of 110 minutes, and is made daily in many sites around the country because it is also used for F-18 glucose and for F-18 sodium fluoride. It can be used anywhere within 2 hours of the many cyclotron sites.

Gallium is done in a reactor, not in a cyclotron, so is much less expensive. A reactor only yields about 3 doses per day, so multiple reactors may be needed. And the world supply of gallium is limited, which may lead to price increases as its use increases. Gallium has a half-life of 68 minutes, which coincidentally is the same as its atomic number.

Dr. Almeida predicts that the most likely to succeed in getting FDA approval are 68GA-PSMA-617 (available at UCLA), 68GA-PSMA-R2 (he plans to start trials with it next year) and 18F-PSMA-1007, because each of these is proprietary and being funded by a pharmaceutical company.

In contrast to Prostascint, which was a “large” antibody molecule labeled with Indium, and with its binding site on PSMA being inside the cell, and therefore requiring 2-5 days of delay between administering the drug and doing the scan, all the current agents are small protein molecules that travel quickly through the bloodstream and bind to PSMA on the outside of the cell. So imaging can be done immediately after administration.

Note that 10% of prostate cancers do not express any PSMA, even aggressive cancers. And the agents are excreted through the urine, making it hard to visualize the prostate area or even nearby lymph nodes. 11C-acetate and 11C-choline are not eliminated through the bladder. Axumin is partially, about 10%. Among the nineteen PSMA agents listed, 18F-DCFBC may be a near-ideal agent, so Dr. Almeida will be watching closely for study results.
Treatment with higher-radioactive-energy PSMA agents: Lu-177 labeled PSMA peptides may be useful for treatment of prostate cancer. There is about 1000X more PSMA on prostate cancer cells compared to normal cells, and clinical studies are showing promising results in efficacy (30-70% drop in the PSA and/or reduction in tumor size or number, and some pain relief) and safety. A Ga-68 PSMA scan can be used to identify good candidates — showing those who have a high expression of PSMA receptors. About 20% of prostate cancer patients don’t express enough PSMA for the therapy to be worthwhile (of which about half have no PSMA at all). The studies are so recent that the survival benefit is not yet known, but it is expected to be appreciable. Universities in Houston & L.A. have a Lu-177 PSMA-617 type agent they are studying. Dr. Almeida will be studying a Lu-177 PSMA-R2 treatment beginning in January. Other studies around the country are opening up.

Q & A:

1.5 vs 3T resolution? Dr. Almeida uses as low as 1.2T for large body parts, but higher field strength is necessary for finer anatomic detail, such as in the prostate. He feels the 3T allows imaging the prostate adequately without an endorectal coil, but feels the coil is necessary if using 1.5T. (Note: see Dr. Cooper’s recent talk at the IPCSG for a different perspective on this issue.) There’s a new “diaper coil” that is shaped like Bermuda shorts, that is being studied for improved imaging without the discomfort and anatomical distortion of an endorectal coil.

Was the PSMA imaging shown in the talk done with ADT? Typically patients are not on ADT, because they are still figuring out what to do next. But if the PSA is rising, C-11 acetate almost always gives a positive finding in the scan (98% on 200 patients).

Would imaging be appropriate after prior therapy with a PSA of 30? The purpose of the imaging is to guide therapy decisions — if current therapy is working, there’s not much need. But if not, then scans may help in deciding what to do next.

ADT and Alzheimers? Wait to discuss with Dr. Lam next month.

Medicare payments? C-11 choline is covered at the Mayo clinic — but they tend to add other scans that can be significant as to potential co-pay expenses. Axumin is covered, at least in this area. Private insurance rarely covers Axumin or the other agents — extremely hit or miss. Out-of-pocket costs for Axumin would be $5-7,000. C-11 acetate costs $3000 at Dr. Almeida’s group, and is not FDA approved. It’s not proprietary, and it’s unlikely anyone will pay the $1.8 million filing fee, or the $1 million annual fee for ongoing FDA approval.

When can we expect Lutetium treatments in the US? Only available now in trials, and FDA approval takes at least two years. One member has been to Germany and Australia for these treatments, with the latter being a lot less expensive. There are issues with controlling the radiation the patient emits (Germany requires 3 days in the hospital), and even urine disposal. Not difficult, but it has to be dealt with.
Is the drug approval process broken? It’s incredibly slow and expensive, but there’s a benefit in being rigorous for safety, especially with radioactive agents. Australia and Germany have fewer regulations. There is a sodium fluoride issue that may warrant a writing campaign, because Medicare may stop paying for those scans after December. The dose only costs $150, and sometimes Dr. Almeida provides the scan at no charge, if an insurance company won’t pay for the scan.

Repeat C-11 acetate scans? Done if there is a resurgence in the PSA. Also done on some patients from Dr. Snuffy Myers, who strives for “no evidence of disease,” and wants the essentially-zero

Radiation from the CT/PET scans? There is some, more from the CT than from the imaging agent. The dose is typically about 20-30 millisieverts (like getting a diagnostic chest CT, or 200 chest X-rays), but his group is able to use “low-dose CT” techniques, and get by with about 10-15 millisieverts in their scans.

What therapies seem to be best, after the imaging? Being an independent group, he has patients that have undergone every type of treatment back at the referring organization – whether a university or urologist or oncologist, or whatever. He prefers radiation over surgery for local disease (including nearby lymph nodes). He noted that when Keytruda is working, he really sees tumor shrinkage, though the PSA may not go down dramatically.

What about sugar metabolism in prostate cancer? Dr. Almeida is actually an internist, though doing imaging, and is very involved with integrative medicine. In most cancers, the Warburg effect is that glucose receptors are upregulated, and sugar is aggressively taken in and metabolized in the growth of the cancer. Prostate cancer is different, and fatty acids and other nutrients may have more of an impact on prostate cancer than limiting sugar – although there continue to be good reasons to limit sugar for overall health. He supports Dr. Mark Moyad’s phrase: “If it’s good for your heart, it’s good for your prostate,” and favors an Asian-Mediterranean diet “that tastes good.”

Differences in effectiveness of agents/scans? There are differences among individuals, where PSMA, Axumin, and C-11 acetate may be of different efficacy in imaging a particular tumor.

IMRT vs. Proton therapy? Very similar, for the prostate. Proton therapy is superior for very specific targets, such as tumors immediately next to the rectum, the spine or major organs.

FUTURE MEETINGS

- November 18, 2017—ADVANCES IN IMMUNE THERAPY Richard Lam M.D.
  A board-certified internist and oncologist, Richard Lam, MD, has been specializing full time at Prostate Oncology Specialists in the treatment of prostate cancer since 2001. He is the director of clinical research. Dr. Lam has written numerous articles based on his research. He is an active member of the American Society of Clinical Oncology and the American Society of Hematology. Dr. Lam continues to promote prostate cancer awareness and education by giving lectures at various medical conferences and prostate support groups throughout the country. He is particularly interested in utilizing state-of-the-art therapeutics for advanced prostate cancer.
- December—no meeting, next meeting in January.
ON THE LIGHTER SIDE

...AND FARMER BROWN GETS NOTHING IF I DIE UNDER SOSPICIOUS CIRCUMSTANCES...

That must suck, having your birthday on the same day as Christmas

We don't know what is wrong with you yet the doctor said he will look into it after his holidays

We're still eating.
INTERESTING ARTICLE

To Biopsy or Not To Biopsy?
June 21, 2017 by Prostatepedia

Why did you become a doctor?
Dr. E. David Crawford: I got my interest in medicine from my family. They had a nursing home. I worked there when I was in high school and college, so I was around patients and doctors. I saw the compassion the doctors had and really liked it. I got to know a few of them.

Even though that was only a snapshot, I thought medicine would be a good thing to do. Then I got a job during college doing evaluations of people before surgery. That was how I got interested in urology.

My interest in prostate cancer began when I was at the University of California, Los Angeles, as a Fellow. I was dumbfounded that most of the patients we saw with prostate cancer were advanced and incurable.

I had an opportunity to work with Schering Corp. I did a study and got one of their drugs called Eulexin (flutamide) approved.

A man named Perry Lieber from Las Vegas came to see me. The only way he could get Eulexin (flutamide) was on my Phase III trial. He was a spokesman for Howard Hughes. He wanted to get the word out about early detection for prostate cancer. We started some of the early screening back in the 1980s in Las Vegas and in Colorado. Unfortunately, he died of prostate cancer.

This was in 1988. We didn’t know what we were doing. We had PSA; we were testing and biopsying a lot of people. At first, that was good because we found a lot of aggressive prostate cancers.

Once we filtered through those, though, we were biopsying people at lower and lower PSAs and finding prostate cancers that didn’t need to be found. There was a lot of over-diagnosis and overtreatment.

That went on for a while. Then the US Preventive Services Task Force said they think screening does work, but that it does more harm than good, so they couldn’t recommend it. (They have more recently changed their recommendations.)

That put the brakes on things, but I think it was needed. When we do too many biopsies and rebiopsies and overtreat people, we have no way to re-stratify them.

I think the way forward is pretty simple. It involves prostate cancer markers: blood, urine, and tissue-based markers.

But first consider who orders PSA tests in the United States: family practice doctors order 92% of PSA tests. We have to educate these family practice doctors.

I did a study a few years ago that looked at the PSA cutoff of 1.5 ng/ml. What if you find prostate cancer in that zone of 1.5 to 4? We found that 70% of men who had their PSA analyzed had a level of less than 1.5 ng/ml and, therefore, could come back in 5 years for another one.

That’s an easy message: a PSA above 1.5 to 4 ng/ml is a danger zone. Prostate cancer marker tests come into play in men with PSAs in that gray zone of 1.5 to 4 ng/ml.

Everyone is talking about informed decision-making with these tests before a PSA is performed, but this is not going to happen. Family practice doctors do not made significant things to talk about with their patients: obesity, hypertension, or diabetes. They don’t get informed decision to check your cholesterol, your blood pressure, or your weight. They get informed decision after the fact.

I think you should do the same thing with PSA. Doctors should order the PSA tests in the right group of people. If the PSA is less than 1.5, no discussion is needed. Tell the man to come back in five years.

If his PSA is greater than 1.5, we need the next layer of testing and discussion. The goal right now is simple.

PSA is a frontline test to help identify people at risk for having prostate cancer. PSA doesn’t tell us what kind of risk. It doesn’t tell us if the man has low-grade or high-grade prostate cancer. That is where some of these new tests come in. PSA screening by itself, without any further testing, is gone. PSA is just the first test.

If a doctor were considering doing a biopsy and worried about prostate cancer, the next step would be genomic testing.

What sorts of genomic testing would be appropriate in this setting? Dr. Crawford: The tests fall into three buckets: blood-based, urine-based, and tissue-based.

The ones I’m working on now are either blood- or urine-based tests. The prostate health index (PHI) is a formula that looks at several forms of PSA to come up with the relative risk of having prostate cancer. PHI is FDA-approved in the US for use in men with a PSA above 4: it gives their relative risk of having prostate cancer.

There are two issues with PHI. First, in Europe, the PSA cutoff is 2. In the United States, the PSA cutoff is 4. But we still have a lot of prostate cancer in men with a PSA between 1.5 and 4. We published a paper that showed a 10-13% higher risk in men with a PSA between 1.5 and 4.

Second, we need more data on PHI levels and high-grade cancers. We’ve done some studies that show that there seems to be a good corre-
There are approximately 1.4 million prostate biopsies done in the United States every year, but we only diagnose a couple hundred thousand people with prostate cancer. Many get biopsied and rebiopsied and rebiopsied.

If your biopsy is positive and you've picked up a low-grade cancer, you might then choose a molecular marker to determine your cancer's aggressiveness. These are the tissue-based genomic tests, such as Oncotype DX, Prolaris, and Decipher.

Another is called ConfirmMDx. This is a tissue-based test that looks for genetic changes called methylation genes around the cancer. (These are areas of cancerization.)

If the biopsy is negative and we order ConfirmMDx on the tissue and that test comes back as positive, it means we've widened the target area: we may have missed something and need to go back and look again with another biopsy.

Are prostate cancer markers covered by insurance?

Dr. Crawford: Only PHI and PCA3 have been approved. (PCA3 has pretty much gone by the wayside, though, after the introduction of SelectMDx.)

It happens this way: the company does some clinical trials, they bill insurance, and then they submit to Medicare. They get local coverage determination in which the test will be covered for a period of time while they continue to investigate.

The companies who make these markers are not big companies with deep pockets. They have a limited budget.

If we wait for an endpoint of death on some of these studies, none of us will be around to see the results. We need to think about other endpoints. We are looking at these other endpoints.

I'm excited about all this. I think we've got a way forward now. Most family practitioners believe that screening does do some good, but they know that it also does some harm. Now that we've got the tools to deal with screening, let's deal with it. Patients believe in screening. We don't want to go back to where we were with metastatic disease being the norm.

Do you think the former recommendation against screening ended up having a positive impact? That it forced the prostate cancer community to reevaluate the issue of overtreatment?

Dr. Crawford: A lot of people don't think that, but I do. There was a lot of overdiagnosis and overtreatment.

Sometimes when you tell a man he has cancer, he wants it taken care of yesterday. Many don’t understand that some prostate cancers are like skin cancers. You don’t cut off your arm because you have a small basal cell cancer on your wrist. It's the same way with prostate cancer.

There are low-grade, nonthreatening Gleason 6 cancers.

Are these prostate cancer markers now widely accepted among family practitioners?

Dr. Crawford: No. Family practice doctors don’t know much about these markers at all. Urologists don’t either. This is the beginning of a long educational process. It'll take patients asking about the tests. Often, patients drive change: that's just the way things happen.

Many of our readers are influential in their communities. What would you say to those men about getting the word out about prostate cancer markers?

Dr. Crawford: There are a lot of hereditary and germine mutations being put forth in prostate cancer: as many as 5% up to 20% of prostate
(Continued from page 8)

cancer patients will have some of these mutations.

One of my recommendations is that if you have germline mutations of prostate cancer like BRCA2 (and others) your family members should get tested.

The PSA cutoff of 1.5 falls in very nicely with this. If your PSA is 1.5 or above, get the tests we discussed—like the SelectMDx or the 4K.

What about repeating these tests? If a man consistently has a high PSA, would it make sense to keep repeating these tests?

Dr. Crawford: He should be referred to a urologist.

Are these tests at all useful in men on active surveillance or with low-grade cancers?

Dr. Crawford: Thirty percent of patients fail active surveillance. When these men eventually have surgery, sometimes they have adverse pathology. Why did that happen? It happened because when we did the biopsy, we missed the bad cancer—the Gleason 7s, 8s, 9s, and 10s. Some of these tissue markers, like Prolaris and Oncotype DX, can help in that scenario.

Part of the follow-up for men on active surveillance is a repeat biopsy. I haven’t met a lot of men who like to have biopsies every year, but they do it.

After a while, doing repeat biopsies and monitoring gets to be more expensive than treatment. A urine test like SelectMDx or 4K can help you determine who needs to be re-biopsied.

What I’m looking at now is whether or not doing the SelectMDx every other year can eliminate the need for biopsies. And I’m finding the answer is yes.

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**NETWORKING**

The original and most valuable activity of the INFORMED PROSTATE CANCER SUPPORT GROUP is “networking”. We share our experiences and information about prevention and treatment. We offer our support to men recently diagnosed as well as survivors at any stage. Networking with others for the good of all. Many aspects of prostate cancer are complex and confusing. But by sharing our knowledge and experiences we learn the best means of prevention as well as the latest treatments for survival of this disease. So bring your concerns and join us.

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@ipcsg.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: [http://ipcsg.org](http://ipcsg.org)

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.

Ads about our Group are in the Union Tribune 2-3 times prior to a meeting. Watch for them.

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**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://ipcsg.org](http://ipcsg.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.