On October 15, Fabio Almeida, M.D. (Medical Director at Phoenix Molecular Imaging - Southwest PET/CT Institute, Yuma AZ) presented an update on various PET/CT Imaging methods and new clinical trials. Detailed statistics about the effectiveness in detecting and locating PCa metastases (Mets) in cases of PSA recurrence after first line treatment such as surgery and radiation were presented and discussed, showing that different techniques yielded best results for different PSA levels, Met types and sites. Dr. Almeida then stayed for an extensive (Continued on page 2)
The importance of PET/CT imaging for prostate cancer stems from the fact that after surgery or radiotherapy, up to 40% of patients experience a rising PSA within 10 years. Standard imaging (CT, MRI, Technetium Bone Scan) often fails to localize the recurrences of the disease, which limits treatment confidence. Over- or under-treating may occur, with negative effects on quality of life.

Newer techniques (e.g., PET/CT) which are able to find the disease sites provide opportunities for more personalized treatment (additional surgery, focal radiation, cryotherapy, HIFU, better selection of medications, etc.). About a third of the time, the new growths are found in pelvic lymph nodes, about a quarter in the prostate (or the residual bed after prostatectomy), and the rest in distant lymph nodes, bones, lungs, etc.

PET/CT can look at the whole body in three dimensions, using one of many available radioactive agents. Most of them are experimental and not FDA-approved. Dr. Almeida’s preferred agent is $^{11}$C-acetate (not yet FDA-approved).

He compared the effectiveness, advantages and limitations of the most popular agents.

FDG ($^{18}$F Fluorodeoxyglucose) works very well for other cancers, but is only 10-20% effective in finding prostate cancer, apparently due to poor uptake by the cells.

FACBC was approved by the FDA early this year, but that’s surprising to Dr. Almeida because of its limited clinical trial data, and only 40-50% effectiveness in finding recurrences.

$^{11}$C-Choline is reasonably effective, but his detailed analysis of available data indicates it may not be quite as good as $^{11}$C-acetate.

In research on new radioactive agents, PSMA (“prostate specific membrane antigen”) has a lot of momentum. Data shown by last month’s speaker seemed to indicate it performs best, but Dr. Almeida’s more in-depth analysis of the same data showed it is actually very similar in overall effectiveness to $^{11}$C-acetate.

For patients with PSA’s that are still below 1, $^{11}$C-acetate seems to provide better success in detecting new growths than the other agents, but for PSA’s over 2, especially if the rise has been rapid, the $^{11}$C-acetate, $^{11}$C-choline, and PSMA agents all give excellent detection. In all cases, a rapid PSA rise will allow easier detection. Hormone therapy can affect the detection rate using $^{11}$C-acetate, if the PSA rise is suppressed or reversed.

PSMA agents becoming available now are improvements over Prostacint (which was FDA approved some 20 years ago), a relatively large protein that had to get inside the prostate cancer cell, and took 2 days after the injection to do so. New, smaller proteins circulate more readily, and only need to attach to the outside of the cell. But these agents are NOT really specific to prostate cancer cells. They bind to many benign tumors of the thyroid, lungs, spleen and vascular system, and to cancerous tumors of the breast, colon, kidneys, liver, thyroid and probably bladder. Two particular problems are the binding of the PSMA agents to celiac lymph nodes, which can obscure the extent of prostate cancer in other nearby lymph nodes, and the excretion of these agents through the bladder. The resulting radioactivity in the bladder can prevent seeing tumors in the adjacent areas of the prostate or its bed, through a halo effect caused by the mathematical algorithms used by the scanning equipment. Also, the radioactivity level of these agents is low, making the scans have longer exposure times, and reducing the clarity of the images.

Despite these limitations, the PSMA based scans can be useful (the site the agent attaches to is upregulated by 100X in prostate cancer cells, compared to normal cells), and these agents are of strong interest because they have longer half-lives and are easier to produce than either $^{11}$C agent, which both require immediate access to a cyclotron because of the short half-life of the $^{11}$C isotope. The currently favored
PSMA agent is based on a Gallium isotope, available from a “generator” that almost any hospital can obtain. The economics of using a generator mean that the Gallium agents are suitable only for use in large hospitals, to bring the cost per dose down. Still, these agents are expected to gain widespread use in this country over the next few years, after current clinical trials are completed. They are already available in about 50 countries, with Germany and Australia in the lead in developments and use.

Quickly afterward, other new agents based on a Fluorine isotope are expected to displace the Gallium agents, because the cost per dose is not so dependent on the number of patients to be treated, and smaller hospitals can then afford the agent.

\(^{11}\text{C}\)-Acetate has an advantage over PSMA agents in being extremely specific to prostate cancer. There are a few potential interferences from uptake by certain groin, chest and armpit lymph nodes, but based on a “physiological pattern” it is possible to “read around” these spots because we know that prostate cancer does not go to these areas in early recurrences.

**Audience comments and responses to questions:**
Medicare does not currently pay for \(^{11}\text{C}\)-acetate scans, but discussions are in progress with the director of the region that Dr. Almeida is in. It may be possible to get approval for payments before FDA approval.

PSMA imaging is available in Australia for 1,100 Australian dollars. \(^{11}\text{C}\)-Acetate scans cost $3,000 but half the cost is covered by a foundation. The patient stays overnight in Phoenix, then the scan is done in about 15 minutes, and the results are discussed the same day. Additional financial assistance may be available.

The PSMA binding site is upregulated by hormone therapy.

PET/CT scans are more easily understood by oncologists than MP-MRI’s for treatment decisions. However, the latter is best for initial diagnosis and targeted biopsies of prostate cancer.

It is curious that FDG (Fluorodeoxyglucose) is not well taken up by prostate cancer, and may have implications about limiting dietary intake of sugars in prostate cancer patients. On the other hand, in one Japanese study, fats vastly promoted growth of human prostate cancer cells transplanted onto mice skin. Dr. Mark Moyad may have further information on this, as he has written about diet in relation to prostate cancer.

Sodium fluoride (\(^{18}\text{F}\) NaF) scans are nearly 100% effective in detecting bone metastases, and are covered by Medicare. These scans provide a 3D image, which is much more informative than the 2D image of \(^{99}\text{Technecium}\). Dr. Almeida uses the \(^{18}\text{F}\) NaF scan before running a \(^{11}\text{C}\)-acetate study, since if bone metastases are present, that may comprise the needed information for selecting the appropriate treatment.

Copies of the DVD of the meeting will be available at the next meeting on November 19th or from our website: [http://ipcsog.org/shop/](http://ipcsog.org/shop/) For those of you that don't use the internet, Call: Gene 619-890-8447 or Bill Manning 619-980-0769 to arrange for a copy. The DVD includes the PowerPoint File.
ON THE LIGHTER SIDE

“Biopsies are no joke, but a physician claimed that the following are actual comments made by his male patients while he was performing their biopsies. I must say I was excited to see this, because there is a lot of potential humor in biopsies.” [Also, DRE’s: seems like everyone has a pet name for these.]

“Take it easy, Doc. You’re boldly going where no man has gone before!”
“Find Amelia Earhart yet?”
“Are we there yet? Are we there yet? Are we there yet?”
“You know, in Arkansas, we’re now legally married.”
“Any sign of the trapped miners, Chief?”
“You put your left hand in, you take your left hand out…”
“Hey! Now I know how a Muppet feels!”
“If your hand doesn’t fit, you must quit!”
“Hey Doc, let me know if you find my dignity.”
“You used to be an executive at Enron, didn’t you?”
And the best one of all..

“Could you write a note for my wife saying that my head is not up there?
These are from Curtis Palmer, originally posted in alt.support.cancer.prostate. Enjoy, and send me your own. When I saw these, I remarked to dear hubby, “You know PC is a ‘gold mine’ for jokes.” A “gold mine” indeed. Not when you’re the one being mined.
New study opens window for OncBioMune cancer vaccine in early and advanced prostate cancer patients.

**Study: OncBioMune Cancer Vaccine in Early & Advanced Prostate Cancer**


Treatment for newly diagnosed prostate cancer remains controversial, largely due to the fact that the disease typically progresses very slowly, so selecting which therapy and when is a topic of debate. Today, early-stage prostate cancer patients have minimal options, mainly comprised to choosing between radiation, a prostatectomy (surgical removal of the prostate) or "active surveillance." Surgery and radiation are known to have side effects that can include incontinence and impotence, sometimes for prolonged periods of time. Designed to monitor for disease progression, active surveillance involves routine doctor visits for physical prostate exams, periodic biopsies, and blood tests to measure the level of prostate specific antigens (PSA).

A new study, published in the *New England Journal of Medicine* last week, followed 1,643 localized-prostate cancer (meaning the cancer was confined to the prostate) patients in Britain (median age of 62) for a decade to evaluate outcomes of the different treatment regimens to provide some clarity on benefits. Patients in the study were randomized equally into groups for radiation, surgery or active surveillance. If disease progression was observed in patients in the active surveillance group, those patients had the option of surgery or radiation treatment.

In line with survival data from the American Cancer Society, study results showed that the 10-year survival rate was almost 99 percent, regardless of treatment plan. The patients are still being followed to analyze mortality rates beyond 10 years. 204 men experienced disease progression, with 112 of those patients in the monitoring group, versus 46 in each of the surgery and radiotherapy groups. 54 percent (291 out of 545) of the patients in surveillance group ended up having radical treatment (surgery, radiotherapy, brachytherapy or high-intensity focused ultrasound therapy), including 56 patients within nine months of starting the trial.

"This first-of-its-kind study is particularly important to our efforts, as it provided comparable information on outcomes and the value of the different treatment options," commented Dr. Jonathan Head, CEO at Baton Rouge-based OncBioMune Pharmaceuticals, who was not involved with the study, in a phone conversation. OncBioMune is developing an immunotherapy cancer vaccine called ProscaVax that combines PSA with adjuvants interleukin-2 (IL-2) and granulocyte-macrophage colony-stimulating factor (GM-CSF) to treat prostate cancer at various stages.

"Our goal is to provide a safe, effective therapeutic option for prostate cancer patients at any stage of disease, whether as a first-line therapy or in advanced disease," said Dr. Head. "In addition to over half of the active surveillance patients requiring radical treatment, the U.K. study data showed that about 6 percent of patients in the surgery and radiotherapy groups still required additional therapies and 14 percent of radiotherapy patients had rising PSA levels following therapy. Start extrapolating that data into the 1.1 million prostate cancer cases recorded globally in 2012 and you begin to realize the necessity and potential for new therapies to help these patients."

ProscaVax is designed to keep PSA levels in check.

Looking to the market opportunity in early-stage prostate cancer goes without mentioning patients with advanced, relapsed or refractory disease for which ProscaVax could be utilized as well. Like other cancers, as the disease progresses, chemotherapy often is the recommended course of treatment. Johnson & Johnson's oral drug Zytiga, which is approved for treating metastatic, castration-resistant prostate cancer in combination with prednisone for pancreatic cancer patients that have failed chemotherapy using docetaxel, was the seventh best selling cancer drug in the world in 2015, with sales of **$2.23 billion**.

(Continued on page 6)
billion.

Funded in part through a grant from the U.S. Department of Defense, ProscaVax is currently being evaluated in hormone-independent and hormone-naive prostate cancer patients with rising PSA levels in a Phase 1 clinical trial at the University of California-San Diego's Moores Cancer Center and Veterans Hospital in La Jolla, California. A Phase 2 trial for prostate cancer patients in the active surveillance category is being prepared for commencement in the Beth Israel Deaconess Medical Center network of hospitals. South of the U.S. border, OncBioMune has partnered with Vitel Laboratorios, S.A. de C.V. for a Phase 2/3 study in Mexico in the same patient population as the UCSD study.

With the potential for the Mexican trial to serve as a registration study, OncBioMune is considering a merger with Vitel, disclosing this month that it is in discussions to acquire Vitel and its portfolio of drugs, some of which are approved or near commercialization in the Mexican market.

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Can A Low Carb Diet Affect the Side Effects of Hormone Therapy (ADT)?

http://advancedprostatecancer.net/can-a-low-carb-diet-affect-the-side-effects-of-hormone-therapy-adt/

Dr. Steve Freedland, from Cedar Sinai conducted a controlled, randomized clinical study that evaluated the efficacy of an extremely low carbohydrate diet on the side effects of hormone therapy (ADT). The study showed that an extreme diet has a positive impact on many of the side negative effects as well as causing significant weight loss that probably has many other additional positive health effects.

An interview with Dr. Freedland is available at:

Briefly, summing up some of his findings he reported that:

“In the control group in our study, we saw that at 6 months they (in the control group who ate a normal diet) gained 1.3 kg, their insulin resistance went up 36%, and they added 11% new fat mass. They experienced the effects that hormones generally have….. Compared to the control group, rather than going up 36%, insulin resistance went down 4% in the diet group. So we completely prevented insulin resistance from happening.”

As my colleague Patrick on our HealthUnlocked online support group has written, “It’s an extreme diet – but ADT is an extreme therapy.”

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What we have learned from radiolabeled choline PET/CT scanning to date


Specifically, the paper by Sobol et al., reports on data from the use of $^{11}$Ccholine PET/CT scanning and multiparametric MRI (mpMRI) scanning at the Mayo Clinic — from 2008 to 2015 — in 202 men who had recurrent prostate cancer after surgery alone (i.e., no additional adjuvant or salvage radiation therapy, no hormone therapy, etc.). A media release from the Mayo Clinic also discusses this paper. These 202 men are just a subset of the nearly 2,500 men who have had an $^{11}$Ccholine PET/CT scan for suspicion of prostate cancer recurrence during the same time frame.

Among these 202 men

118/202 (58.4 percent) had their positive lesion(s) identified by both mpMRI and $^{11}$Ccholine PET/CT.
15/202 (7.4 percent) had their positive lesion(s) identified only by mpMRI.

(Continued on page 7)
69/202 (34.2 percent) had their positive lesion(s) identified only by \[^{11}C\]choline PET/CT. When broken down by category of recurrence:
68/202 men (33 percent) showed local-only recurrence.
45/202 men (22 percent) showed local and metastatic recurrence.
89/202 men (45 percent) showed metastatic-only recurrence.

Pelvic node node-only relapse was observed in 39/202 men (19 percent).
The patients’ average (median) PSA levels at the time of a positive scan were:
- 2.3 ng/ml for all 202 patients combined
- 2.3 ng/ml for the 68 patients with local-only recurrence
- 2.2 ng/ml for the 45 patients with local and metastatic recurrence
- 2.7 ng/ml for the 89 patients with metastatic-only recurrence
The median times from PSA relapse to visualization the recurrent tumor were:
- 15 months for all 202 patients combined
- 33.5 months for the 68 patients with local-only recurrence
- 15.0 months for the 45 patients with local and metastatic recurrence
- 7.0 months for the 89 patients with metastatic-only recurrence
On multivariable analysis, the time from biochemical recurrence to positive imaging was independently associated exclusively with local-only recurrence (odds ratio = 1.10 for every 6-month increase, \(p = 0.012\)).

In their conclusion, the authors state that: Combined choline positron emission tomography and multi-parametric magnetic resonance imaging evaluation of biochemical recurrence after prostatectomy reveals an anatomically diverse pattern of recurrence. These findings have implications for optimizing the salvage treatment of patients with prostate cancer with relapse following surgery.

Now that is a fair conclusion, but what those implications may be for any particular patient are harder to discern. \[^{11}C\]choline PET/CT scanning is available at only one site in America. Thus, a key question is going to be whether other forms of sophisticated scanning technique (e.g., the new Axumin-based PET/CT scan and others currently in development), when combined with mpMRI, can be more accessible for more patients and produce even better results.

Having said that, it is fair to point out that this study does clearly confirm some other conclusions:
Recurrence of what was originally thought to be a localized prostate cancer does not necessarily proceed in some type of stepwise fashion (i.e., in the prostate bed, and then the lymph nodes, and then to true metastatic disease) — but we already had many good reasons to understand that.
Recurrence of localized prostate cancer can be fast — and a great deal faster than the average of 8
years proposed many years ago by Pound et al. (in 1999), based on a subset of the highly selected patients treated by Walsh at Johns Hopkins, many of whom would probably be considered as good candidates for active surveillance today.

We are getting better at knowing how best to treat men with recurrent disease after their first-line treatment for presumed localized prostate cancer. The $[^{11}C]$choline PET/CT scan has helped to contribute to that knowledge, but it is not going to be the answer that helps the majority of patients because access to this test is so restricted. We are going to need much better ways to identify, with accuracy, the location of early recurrent prostate cancer lesions so that we can treat them with a high degree of accuracy. And we may need to be able to use some of those tests in the work-up of higher-risk patients prior to any form of first-line treatment, because there is not much point in just removing someone’s prostate as first-line treatment if they already have a tiny metastatic lesion that is not visible on a bone scan or an mpMRI in somewhere like their bone marrow.

Links to additional stories for the past month can be found at:


If you have comments or additional news to share please email the editor, including reference or URL with “IPCSG” in the subject line at spender@alum.mit.edu
NETWRKING

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@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: http://ipcs.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.

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.