PACT INC

Patient Advocates for Advanced Cancer Treatments

PROSTATE CANCER COMMUNICATION

VOLUME 33, NUMBER 1 • SPRING 2017
FOUNDER: LLOYD J. NEY, SR.
FOUNDED 1984

We are changing to a 32 page newsletter format 3 times a year which will save us approximately $14,000 per year. You will still receive the same amount of information and content, just in a different delivery format. A 24 page newsletter - 4 times per year is 96 pages, also a 32 page newsletter - 3 times a year is 96 pages. We'd love to hear your comments about this change, please let us know!

INSIDE:

Life Without Prostate Cancer:
Imagine The Possibilities!

PAACT INC

Patient Advocates for Advanced Cancer Treatments

PROSTATE CANCER COMMUNICATION

Published Quarterly by: PAACT, Inc.
Patient Advocates for Advanced Cancer Treatments
11555 Jadon Ct NE
Sparta, MI 49345-8155

President —Richard H. Profit Jr.
Editors….Richard H. Profit Jr./Molly Meyers
Manager of Business Operations — Molly Meyers
Webmaster —Omega Systems
Printer — Rogers Printing, Inc.

Postmaster: Send address changes to:
PAACT, Inc.
PO Box 45 • Sparta, MI 49345

Phone: (844) PAACT4U • 616/453-1477 • Fax: 616/453-1846
E-Mail: paact@paactusa.org or paact@paact.help
PAACT Web Page & Newsletter: http://www.paactusa.org
or http://www.paact.help

We want to thank those of you who have made special donations to PAACT. Please remember that your gifts are tax deductible (Federal ID# 38-2763817), because we are a 501 (c)(3) non-profit corporation.

EDITOR:
Articles authored by other than the editor may not fully reflect the views of the corporation but are printed with the understanding that the patient has the right to make his own interpretation of the efficacy of the information provided.

In an effort to conserve space and be able to insert as much material as possible in the newsletter, references from various articles are intentionally omitted. If you would like to obtain those references, please contact PAACT, we keep all of the original articles and the references used on file.

TABLE OF CONTENTS

PAACT OFFICE: PO Box 45 • Sparta, MI 49345

USPS Address Forwarding has EXPIRED!
Do *NOT* use OLD ENVELOPES or OLD ADDRESS!

Please make a note:

~~1143 Parmelee Ave NW,~~
~~Grand Rapids, MI 49504~~

CORRECT MAILING ADDRESS FOR PAACT:

PO Box 45, Sparta, MI 49345 *or*
11555 Jadon Ct NE, Sparta, MI 49345

If anyone gets mail returned, please forward on to the NEW address or contact us at 616-453-1477 from 8-5, e.s.t. or by email at paact@paactusa.org or paact@paact.help.

Thank you for your understanding and loyalty.

Please consider a tax-deductible donation to help support this FREE newsletter which reaches over 20,000 people.

Donate online at www.PAACT.HELP, or call Molly at (844) PAACT 4U.

TAX DEDUCTIBLE

PAACT is a 501 (c)(3) non-profit corporation.
(Federal Tax ID# 38-2763817)

WHAT THE HECK HAS BEEN GOING ON IN MY WORLD-PART 75!

Mark A. Moyad, MD, MPH, University of Michigan Medical Center

Unpaid and generally unappreciated and unloved consultant to PAACT despite the fact that this is the 75th time in a row I have written for this newsletter free of charge. You would think that I would at least be given a complimentary PAACT car or PAACT pen or just something complimentary by now!!???

Note: A total of 75 times in a row and for almost 20 Freakin years of my precious life I have written, volunteered and worked my fingers to the skeleton for this newsletter/organization, and I have yet to receive any personal financial compensation or personalized classic timeless gifts such as; an official PAACT wallet to put my new Outback Steakhouse gift card inside, because I did actually receive an Outback gift card in a PAACT envelope, but it was not a gift from PAACT. Where or why did I get the Outback Steakhouse gift card? It was NOT from any of my Australian friends either and again not from my PAACT brother and sister, but rather from a reader of this column! Thanks to benevolent and ever kind and giving reader Dr. Ford III for this wonderful and thoughtful carnivorous gift. Dr Ford III, you are a fine American and may you win the lottery and hire me as your personal doctor with a starting salary of 1 million a year + benefits, like free 50-yard line seats to all Michigan Football games in 2017 along with unlimited beer, popcorn, chips, and red licorice before, during and after the game! Oh and my wife needs a new car. Thanks!

I WANT TO THANK YOU AGAIN FOR CONTINUING TO MAKE "THE SUPPLEMENT HANDBOOK" a best-selling book even after 2 years and it was just translated in Polish (no kidding). YEAH!! THANK YOU!!! Second, if you have not picked up a copy, please get one on Amazon.com (the very cheapest place to procure a copy) to support my eventual unlimited beer and Netflix fund. If I can make enough money, I want to buy a house next to Tom Brady so we can be best friends! I know we would be like close brothers from another mother. We would spend every day talking about sports, the prostate, and throw a football around in our back yards (he would throw and I would catch of course) and have outdoor barbecues together and make fun of the NFL commissioner. I can't wait! I am so excited, but without your donations, my dream can never be a reality! So, what are you waiting for? Please give to the newly formed "Moyad-Brady Are Going to Be Best Friends" Fund today!

350) Time to put individual selenium dietary supplements to bed especially in the area of cancer prevention and treatment (aka put them in the garbage please)? Yup!

(Reference: Goossens ME, et al. European Journal of Cancer 2016;69:9-18).

Bottom Line

How much longer will researchers spend money, time and energy on selenium supplements to prevent cancer or prevent cancer recurrence! It failed another Phase 3 trial and who even knew?! I bet you most of the people reading this column had no idea it failed yet another cancer phase-3 trial in the past few months! Why didn't you hear about it? It's because it's a boring and a redundant story! Yet, you should know about it because it's a lesson of how "less is at times more" when it comes to certain supplements for cancer treatment. This does not mean selenium supplements have no role in medicine but it does mean it has been a loser in the area of cancer prevention and treatment (especially prostate cancer folks).

What else do I need to know?

What is the difference between a complete loser and a selenium supplement? NOTHING!!! The problem is this story is so redundant and boring and so redundant and boring (see what I did there - repeated the word redundant - man I am smart and crafty) that I didn't see it in any newspaper or tweet, but you will read about it here! 100s of millions of dollars have been spent on this dietary supplement to prevent or treat cancer and basically ALL of these expensive phase 3 studies have failed and/or suggested that selenium might actually increase the risk of some cancers, like prostate cancer and skin cancer, when taken in excess (not from a multivitamin folks - just the individual supplements of 200 micrograms). Well, in Europe there was an ongoing phase-3 randomized trial called "SELEBLAT" where participants took 200 micrograms of selenium yeast or placebo to reduce the risk of bladder cancer returning after treatment. The study involved patients from 14 medical centers in Belgium! Yeah Belgium! I gave a cancer talk there many years ago and came very close to moving there for a few years afterward because the beer and chocolate were so amazing! OMG! Sorry, I digress…back to selenium. Where was I…oh yeah!

Yup, that is right! Bladder cancer! First selenium fails in prostate so, now it gets tested in bladder cancer. Arghhhhhh (this is a symbol and sound of complete frustration similar to the feeling I had when the referees cheated in the Michigan and Ohio State football game in 2016 to give the Buckeyes an edge), the urologic pain of it all! It is like passing a kidney stone and having a headache at the same time. Anyway, after the smoke cleared the researchers from this latest phase 3 clinical trial concluded their findings by stating the following:

"Selenium supplementation does NOT lower the probability of recurrence in bladder cancer patients." (Okay I capitalized the word "NOT")

Selenium has not demonstrated an ability to reduce the risk of prostate, bladder cancer, skin cancer, or blah, blah, blah. In fact, all it has done is hemorrhage taxpayer money and I feel bad for the patients in these clinical trials. The initial thought was good in testing it to see if it helps, but more and more global trials

kept popping up and failing and you just have to wonder why we keep doing these studies???!!! And, there is another one similar to SELEBLAT going on in the United Kingdom called "Selenib" right now! I mean you would think that just by sheer luck one of these many trials would show something positive but they haven't. Man, this is like a bad high school or college relationship - time to move on and find a new partner because this relationship is bad for the both of us! Now, I'm not implying anything here personally, despite being stood up at my senior prom, which did hurt my feelings, but I never tried to ask this selenium supplement (aka person) out again that is for sure. Everyone reading this column probably had a selenium supplement or two in their lives and I bet you that you are glad you parted ways from that supplement/person right? Except for some of us in the urology community! Some of us just like to get stood up at the prom over and over and over again and never want to move on! Man, what gluttons for sheer relationship punishment! The prom is over folks, it's time to move on to a new supplement or drug (same thing).

Look, selenium in 2017 scares me for a few reasons. First, it has consistently failed so many clinical trials and even suggested it could encourage the growth of some tumors, including prostate cancer in the U.S. SELECT trial in men that were already getting enough selenium from their diets. You see in the 1990s many U.S. men and women and dogs (okay I threw the word "dogs" in there because they also have a prostate and never get enough attention when it comes to prostate health) were deficient or insufficient in selenium but then something amazing happened. Many companies decided to add more and more selenium to their foods and especially multivitamins. Heck, when I was a kid (not that long ago - I am 21 years old + 31) my multivitamin didn't even have selenium in it, but turn the clock forward to the year 2000 and beyond and you can't find a multivitamin without selenium folks! In other words, these U.S. studies are showing that we are getting plenty of selenium today, which is also, why many men's multivitamin's recently REDUCED their amount of selenium in them! Smart! Still, many countries in the world don't have selenium blood levels of their population as high as the U.S. - Belgium and the United Kingdom are two examples. You would hope that this stuff might work in those places…nope! Not so far.

The second reason I'm scared of selenium is that it's not doing diddly squat (aka nothing at all) for cancer patients in general and could be doing harm. Thirdly it could be increasing the risk of skin cancer recurrence or diabetes or…yes it could! Now, let me reiterate this does not mean selenium is worthless across all medical specialties. It's being studied in the area of thyroid diseases and multivitamins with selenium appear to be safe. Yet, for cancer patients? It's time to break up with selenium supplements, just like you need to break up with a partner from a bad relationship. Don't get stood up at the prom twice people! Once it happens it's time to move on especially after one of the largest and most important dances of your life (that is my analogy of a negative phase 3 trial). So, when I run for President in 2024 and win, my first order of business will be to eliminate funding for selenium supplement clinical trials in the area of cancer. Oh, man! Can't wait!

351) Chondroitin sulfate dietary supplements deserve some attention people! Is anyone listening to me??!! Why aren't these supplements getting attention that is more positive? Time to change things now!

(References: Kantor ED, et al. Int J Cancer 2016;139:1949-1957.; and Tsai CY, et al. J Cell Biochem 2009;108:489-498; and Chesnokov V, et al. Cancer Cell Int 2014;14:45.; and Singh JA, et al. Cochrane Database Syst Rev 2015;1:CD005614)

Bottom Line

Research from Memorial Sloan Kettering, Harvard and other medical centers suggests that glucosamine and chondroitin supplements together may have anti-inflammatory properties (actually it appears that chondroitin could be providing much of the benefit if it's real), and they could also reduce the risk of certain cancers, such as colorectal cancer, from a very large U.S. prospective study of health care professionals! Wow! However, the fact that these supplements do NOT appear to increase the risk of ulcers, heart attacks, hypertension, heart failure or countless other problems like many of the pain relievers, is why I am so excited about these supplements! What? Yes, it's time to bring a little respect to the dietary supplement that tends to be such a piñata for so many bone headed "experts" not providing an objective benefit-to-risk analysis.

What else do I need to know?

When I hear arthritis "experts" say negative things about some of the low cost arthritis dietary supplements explaining that they have only some mild or moderate evidence, and in some studies don't work as well as a placebo, I giggle really loud and then I get as angry as a dog being taunted by a squirrel (in the animal world that's really angry).

What's the problem here? These dietary supplement, all or nothing haters (in other words they give such broad all or nothing recommendations like supplements don't work, but don't provide the specific context - who does that?), ignore some of the more interesting clinical trial research that suggests they might slow the progression of arthritis and/or that they have been found to be overall SAFE in clinical trials. That's the point my friends! That's the point that gets missed and dismissed. They don't mention the extreme problems with the conventional options in this area of medicine. I'm a big fan of drugs when needed but painkillers are damaging too many people in the U.S. and around the world. For example, opioid drugs are the number 1 cause of unintentional drug overdose that leads to death in the U.S. and acetaminophen (Tylenol…) is the number 1 cause of acute liver failure in the U.S. And, the other over the counter (OTC) painkillers, including ibuprofen are now associated with increases in heart failure (per FDA), heart attacks, hypertension, ulcers, blah, blah, blah, even with short-term use in some people. So, if you can find ANYTHING that can reduce chronic dependence on high or regular doses of painkillers then this is a good thing right!? If it works, just a little or a lot better than a placebo and it's as safe as a placebo, then that's a good thing right? We need all types of options to help patients.

For example, weight loss is one of the best ways to reduce the dependence on and dosage of pain killers for arthritis and could reduce some side effects of cancer treatment (see later story on

neuropathy), but as much negativity as I hear about whether or not supplements work for osteoarthritis, again, I never hear of serious toxicity associated with these dietary supplements such as glucosamine and chondroitin. Now, in one of the largest credible databases in the U.S. (aka the current study I am writing about today also known as "NHS" and "HPFS") the use of glucosamine and chondroitin supplements in COMBINATION was "associated with a statistically significant, 23% reduced risk of colorectal cancer." This finding was also found in some other observational studies.

NHS is an ongoing prospective study established in 1976 with over 121,000 registered nurses living in 11 states and the HPFS is an on-going prospective cohort study of over 51,000 U.S. male health professionals. The average baseline age of NHS and HPFS is 68 years and 67 years and a BMI of 26. There was a 21% reduction observed for any use of glucosamine and a 23% reduction in colorectal cancer risk found for any use of chondroitin supplements. Use of glucosamine without chondroitin was not associated with a reduced risk of cancer, but the use of glucosamine with chondroitin was significantly associated with a reduced risk of colorectal cancer. Aha! Perhaps the chondroitin is doing all the work?

It's interesting that some laboratory evidence supports a potential anti-inflammatory impact of these supplements including the potential to reduce TNF-alpha, IL-6, COX-2, CRP and on and on it goes! Preliminary lab studies show the ability of these ingredients to suppress prostate cancer growth (see references at the beginning of the article - I am too lazy as a 20-year volunteer to retype them again). HOWEVER, do I really believe glucosamine and chondroitin prevent and fight cancer? I HAVE NO REAL IDEA FRIENDS! There has been some concern that these osteoarthritis supplements encourage the growth of prostate cancer, but that evidence has not only been non-consistent but weak and it doesn't seem to make sense given what we know about these supplements right now.

Again, I think it's amazing that some "experts" that bash these supplements, somehow consider them a failure if they cannot beat a prescription or over the counter pain killer for pain relief, but again they fail to realize that this weakness is also their greatest strength, which is their safety along with some mild to moderate efficacy! (I love to underline for emphasis, which is kind of like an addiction similar to Double Stuff Oreo Cookies or McDonalds French Fries - I can't get near them or else they go straight into my belly - that is my true weakness in life along with the PAACT folks smiling and telling me I cannot quit writing for the newsletter because they would not survive - what a bunch of suck ups).

Does it really matter that glucosamine and chondroitin may or may not work as well as NSAIDs (aka pain killers) especially if the safety is superior to NSAIDS? You can decide - along with your doctor, but if indeed, they contain anti-inflammatory impacts and they might reduce the risk of colorectal cancer, then perhaps they should get more attention in prostate cancer! Who knows! Still, what many of you reading this column right now may not know, is for certain types of bladder pain syndromes these supplements/compounds are being studied as an option for pain relief with some success. So, they already have an interesting urologic track record in reducing pain and inflammation so, even though it's getting more attention in colorectal cancer, perhaps this article will help to give it some attention in urology and other areas of oncology. One can only dream!

By the way, recently a 2-year study of chondroitin sulfate, up against the drug Celebrex (not a cheap drug except everywhere outside of the U.S.), was completed (Pelletier JP, et al. Arthritis Res Ther 2016;18:256….study was done in Montreal - yes they also have good beer and a hockey team… it is Canada for goodness sake) and it was found that BOTH WERE EQUALLY EFFECTIVE AT REDUCING OSTEOARTHRITIS SYMPTOMS (pain, stiffness, physical function…). Chondroitin was given at 1200 mg per day (three 400 mg capsules) or Celebrex 200 mg daily (3 capsules - 1 actual pill and 2 dummy pills to reduce bias) for 2 years! In fact, those taking chondroitin had less cartilage volume loss compared to Celebrex in one part of the knee. So, Celebrex may work better as needed or on demand, but chondroitin (from animal cartilage like bovine trachea - yuck!) might be equal or better when taken long term as a preventive pill or for future studies (hint hint).

The bottom line is that chondroitin sulfate (and perhaps glucosamine) deserves more attention and objectivity. One of the many reasons I like to work, for free, for PAACT despite everything telling me to charge them significantly for my current and past services (you got 10 million dollars brah?) is that you get both sides of the story here. It's so easy to apply a broad brush opinion toward supplements as either all good or all bad in medicine, but that just reflects a lack of education in this field of medicine when it comes to supplements. Supplements that work are essentially drugs and can work in one area, but can also be worthless and even dangerous in another area. For example, earlier you learned that selenium and certain cancers don't mix, but the selenium supplement could have a role for some patients with autoimmune thyroiditis (that is a whole other story). And, vitamin E and prostate cancer don't mix but it's clearly used in ophthalmology as part of a macular degeneration treatment & even in Alzheimer disease - it has 2 major positive clinical trials along with standard treatment. My point is, that if someone tells you a certain supplement is completely worthless or completely effective or completely safe throughout all of medicine it is really a reflection of poor education in this area. Similarly, if someone told me a certain drug had no role across the board, worked for everything or came with no toxicity, then I would be skeptical. Does chondroitin have a role in arthritis? Yes! And perhaps in some other areas of pain, but quality control is an issue and which drugs it can be safely or not safely combined with, needs a lot more research. Still, it's interesting isn't it? Still, from cow trachea? Grosssssssssss!

352) One single multivitamin pill per day could be heart healthy and prostate healthy? Yup! But, more than one multivitamin per day could be bad news!

(Reference: Rautiainen S, et al. J Nutr 2016; 146:1235-1240.)

Bottom Line

Multivitamin use in healthy physicians could lower the risk of major cardiovascular events. A multivitamin a day may be heart

healthy. So, if it might help doctors then that's a good thing right!

What else do I need to know?
A recent randomized trial of a daily multivitamin in men, found a significantly lower risk of cancer versus placebo with controversial results on heart health (that trial was called the "Physicians' Health Study II or PHSII). And, it appeared to be safe in men previously diagnosed and treated for cancer (including prostate cancer). However, that means there must have been a PHS I trial before this PHS II trial right? Yes, and they are still following participants from that study.

So, researchers wanted to determine the impact of multivitamin use in the Physicians' Health Study I that were free of cardiovascular disease (CVD) and cancer at baseline or the beginning of this study. In multivariable-adjusted analyses, a self-reported duration of 20 years or more of multivitamin use was associated with significant 44% reduction of cardiovascular disease (CVD) events. Multivitamin use was also associated with significant 14% reduced risk of cardiac revascularization (reduced risk of needing a cardiac procedure and that's a good thing). This long-term prospective study of initially healthy men, demonstrated that multivitamin use for 20 or more years was associated with a lower risk of major CVD events.

Also, it's interesting that some "experts" claim multivitamins are worthless, yet in the only major global randomized trial of multivitamins versus placebo (Physicians Health Study II) there was a significant reduction in the risk of cancer (primary endpoint) and a lower significant risk of fatal heart attacks in men with no previous history of heart disease, but this could have been due to chance because there were not that many fatal heart attacks in this clinical trial (thank goodness). And, there was also a significant reduction in the risk of a cataracts (secondary endpoint) and the multivitamin used was of low cost, and safe as a placebo overall (THEY USED CENTRUM SILVER - and "no" I have never worked with them or been paid by them).

So now along comes this prospective look or cohort from a randomized trial of aspirin versus placebo or the first Physicians Health Study (PHS I) and long-term multivitamin use in healthy physicians from that trial and it appears to be associated with a lower of CVD. So, a multivitamin a day in healthy men appears to be either healthy or of no benefit and low cost and could reduce some subtle deficiencies (like B12) even in very healthy men so where are those experts now?

Still, there should be a warning. There has been no research to suggest more is better and in fact, more than one multivitamin pill per day has been associated with a higher risk of aggressive prostate cancer in some of the largest studies to examine that issue (Lawson KA, et al. J Natl Cancer Inst 2007;99:754-764. NIH-AARP Study). So, here is another lesson in "less is more" and "first do no harm." So, currently when I see prostate cancer patients that are taking packets of multivitamins (2-5 per day) I simply exercise my opinion and tell them I don't think this is good move. It's better to be safe than sorry (hey I just made that saying up and I am sure no one has ever said that before – I'm going to patent it and be rich)!

353) Fat to lose fat and fight cancer! Maybe! It's an option for some of you out there! Remember, I also love exclamation points!!! They are my clear drug of choice in the punctuation world. I can never get enough!!!
(Reference:Veum VL, et al. Am J Clin Nutr 2017;105:85-89; and Tan-Shalaby JL, et al. Nut Metab (Lond) 2016;13:52.)

Bottom Line
High fat diets may be heart healthy. And, high-fat diets should receive more consideration for weight loss and as a potential anticancer option used along with conventional treatment.

What else do I need to know?
Dietary fat used to be the ugly duckling, no one wanted to touch it. It was blamed for everything wrong in the world including weight gain and heart disease and probably even global warming. However, this was not based on sound research, but rather on opinion and indirect association. In other words, since fat carries more than twice the number of calories per gram versus protein and carbs then it must be bad for you if you consume it in large quantities, but perhaps we got it wrong! Fat can make you lose fat in the short-term and it's getting exciting to research as an anticancer potential option.

So, along comes this beautiful preliminary study to determine the impact of a very high-fat, low-carbohydrate (VHFLC) or low-fat, high-carbohydrate (LFHC) diet for 12 weeks. A total of 46 men (aged 30-50 years) with a BMI greater than 29 were randomly allocated to VHFLC or LFHC, and both diets were equal in daily calories (approximately 2090 cal/day), protein (17% of calories) and emphasized low-processed, lower-glycemic foods. CT scans were used to quantify fat mass, which is cool because it helped tell researchers what was going on in the inside when dieting, not just the outside.

Interestingly, the intake of carbohydrate, total and saturated fat were 51%, 29%, and 12% of calories in the LFHC diet and 11%, 71%, and 34% of calories in the VHFLC group. No difference occurred in intakes of protein and polyunsaturated fatty acids. Both diets similarly reduced waist circumference (11-13 cm = 4-5 inches!!!), abdominal subcutaneous fat, visceral fat mass, and total body weight (11-12 kg = about 25 pounds!!!). Both groups reduced triglycerides and LDL ("bad cholesterol") decreased in LFHC and HDL ("good cholesterol") increased in VHFLC. Groups also showed similar decreases in insulin, and blood sugar. Dietary fat did not appear to acutely increase adipose tissue or metabolic syndrome in humans.

Consume fat to lose fat? This is getting interesting because even randomized trials are beginning to demonstrate that controlling calories regardless of the source may be the secret to successful weight loss. There was a dramatic increase in saturated fat consumption in the high-fat group, which helps to increase HDL but also can increase LDL. Regardless, please remember that dramatic weight loss occurred in both dietary groups with approximately 25 pounds lost in just 12 weeks! It appears it's time to realize that high-fat diets (aka ketogenic diets) have a role for weight loss and now could have as much of a chance in helping some cancer patients as a low-fat or any other type of diet. High-

fat intake should really be called "controlled or reduced calorie" intake, because that's what it does in general when it's successful! Hey, just like any other successful diet plan!

In the meantime, the concept of robbing some of the fuel used by some aggressive cancers (blood glucose) and instead using ketones (a result of high-fat dieting) that cancer cannot use as fuel in some cases is going into mainstream clinical research, from brain tumors to melanoma, with some early suggestions that some people might benefit (emphasis on might). The first goal is obviously to lose some weight if needed and this end might justify the means. As I constantly like to say, until I am Go Blue in the face, diet should fit personality and circumstance. And, some people out there not able to tolerate other diet plans, could find some success on a high-fat and low-carb dieting plan for weight loss. Whether or not they will ultimately reduce the risk or progression of some cancers remains to be seen but it's getting interesting.

354) Wait? Exercise and weight loss could reduce the risk of one of the nastiest side effects of chemotherapy for prostate cancer!?! Why not! It appears this could be the case in breast cancer using the same class of drugs!

(Reference: Greenlee H, et al. Int J Cancer 2017; published ahead of print)

Bottom Line

Obesity and less exercise may increase the risk of chemotherapy-induced peripheral neuropathy (CIPN). Prostate cancer patients should also be told that lifestyle changes could reduce some docetaxel and other chemotherapy side effects.

What else do I need to know?

Lifestyle parameters could impact CIPN but this hasn't been adequately studied. Thus, analyses involving 1237 women with breast cancer that received taxane (taxotere for example - same chemo drug used in prostate cancer) treatment and provided information on symptoms of neurotoxicity was just published. CIPN was evaluated at baseline, 6 months and 2 years using the Functional Assessment of Cancer Therapy-Taxane Neurotoxicity (FACT-NTX).

At baseline, 66% of patients were overweight or obese and 30% had documented low levels of physical activity. Increased CIPN was 2.37 to 3.21 ($p = 0.03$ and $p = 0.003$) times more likely to occur in overweight and obese patients versus normal weight patients after 2 years. CIPN was less likely to occur in highly active patients versus less active patients at 6 months (44% reduction, $p = 0.03$) and 2 years (57% reduction, $p = 0.02$). Obesity and low levels of moderate to vigorous physical activity were associated with worse CIPN in breast cancer patients receiving taxane chemotherapy.

Here's the deal folks! I love to follow the breast cancer research because it can provide many insights into what can and cannot help reduce the risk of side effects from cancer treatment. Whether it's the best drugs to use to reduce hot flashes or the impact of exercise and diet, the breast cancer research is massive and awesome and can provide wonderful hints into what might work in prostate cancer.

CIPN is not a pleasant side effect, so anything that can be done to reduce it would be critical. Most of the prescription medications used offer little clinical benefit and countless side effect profiles, while many supplements could actually make it worse so what's left here? Some oncologists use a type of cooling of the feet and hands while receiving chemotherapy to reduce the risk and extent of the neuropathy that these drugs can cause, but we have to offer more. Nerves are so, so delicate and can be damaged so easily and when injured need a lot of time and effort to recover. Perhaps weight loss and exercise keeps nerve tissue receiving an adequate blood supply and induces healing mechanisms, also allowing better control of glucose and insulin levels and ultimately minimizing damage. Approximately 45 minutes per day (not easy) or more of moderate-to-vigorous physical activity was associated with less CIPN.

It's interesting because the world of peripheral neuropathy or nerve damage to the hands and feet (and other areas of course) is so well known in diabetes and, patients and health care professionals push for better control of weight, more exercise and blood sugar control to reduce this damage. And, now along comes some good research to suggest cancer patients following these same behaviors could reduce the risk of this condition. GOOD STUFF!

355) Curcumin/turmeric supplements cure everything?! Come on man! Do these supplements come with a catch? Of course they do! As does everything in life!

(References: Thomas R, et al. Prostate Cancer Prostatic Dis 2014;17:180-186.; and Mahammedi H, et al. Oncology 2016;90:69-78.; and Tang M, et al. Am J Clin Nutr 2008;87:1262-1267.; and Ghosh Das S, et al. Plant Foods Hu Nutr 2012;67:186-190.; and Hejazi J, et al. Nutr Cancer 2016;68:77-85.; and Epelbaum R, et al. Nutr Cancer 2010;62:1137-1141.)

Bottom Line

One of the hottest supplements in the U.S. is turmeric and/or one of the potentially active ingredients found in this spice known as "curcumin." It's an anti-inflammatory love fest, darling that appears to have preliminary data that it fights cancer, arthritis, depression and blah, blah, blah, but what if it also increases the risk of kidney stones (especially turmeric supplements), did not work in one recent prostate cancer study, and comes with several other issues!?! Well, that would be called…hmmm, perhaps objective reporting or just real life.

What else do I need to know?

When someone tells me any supplement or drug (same thing) works for countless health conditions and has no side effects, then my BS meter goes up and I'm done listening. After doing what I do - for 30 years now (arguably longer full time than any other person - I love to say that) every time someone tells me there is no catch to anything, it has simply never been true! So, let's get back to this spice and let's spice things up a bit.

Turmeric contains a compound that is responsible for the yellow color of this spice and it has some ingredients that appear to have anti-inflammatory effects, but that alone should not get you excited because most spices and basically all fruits and veggies have some "anti-inflammatory" effects. Anyway, the name of the yellowing compound in turmeric is "CURCUMIN." It has showed

some preliminary promise in localized prostate cancer as a part of a supplement to reduce PSA and has recently been combined with chemotherapy for castrate resistant prostate cancer (CRPC) in a new small study. Still, this is preliminary research and not convincing research that curcumin is having this impact, because it has been combined with drugs or other compounds.

There's also preliminary research to suggest that it could help in the treatment of depression and even different types of arthritis. Yet, it's tough to find someone or something that tells you the catch with turmeric and/or curcumin. So, what's the catch Moyad? The yellow can stain your new clothes and face? Nope that is endearing. Is it that it's not always easy to pronounce the word "turmeric?" Nope! So, then what's the catch with turmeric supplements? They are high in soluble oxalates, which means they could increase the risk of kidney stones (curcumin not as much, but this has not been well tested and researched).

And, in another recent study with prostate cancer patients receiving radiation treatment, curcumin appeared to have no impact, but this is also preliminary short-term research. In most of these other cancer treatment studies the dosages being used are no joke, for example, 6000 mg a day with chemotherapy and that equates to 12 capsules per day, and in some cases more and some cases slightly less. Come on man!

So, the potential for toxicity is there with these higher dosages for example nausea, diarrhea or something else including the potential for a change in blood cells when given IV (not orally). This has caused some cancer trials to be stopped early or dosages to be reduced because of side effects (see Epelbaum R, et al above). Again, when you are combining curcumin with some of the most effective and toxic chemotherapy drugs, then it's hard to tell what side effect is actually due to the curcumin because the other drug has so many side effects it can mask the side effects of the supplement.

I'm excited to see what curcumin could do at 500 mg or 1000 mg or 1500 mg - similar to the dosage being tested in other medical conditions outside of cancer. We're doing no one any favors when we don't cover the potential side effects of any supplement. Don't get me wrong I'm excited about the role of curcumin in some areas of medicine, but I'm not so over the top excited that it causes me to fail to mention the catches!

356) Hey Dr. Moyad I exercise as much as anyone and all my friends offer me "Creatine Supplements" but do they really do anything? No, if you are older and maybe if you are young, but you're not supposed to use them when really, young, and keep watching clinical trials!?! What is Moyad talking about?!

(References: The Supplement Handbook. Shameless Plug-Moyad; and Simon DK, et al. Clin Neuropharmacol 2015;38:163-169 and see other reference in the story)

Bottom Line

Creatine supplements have shown some potential to enhance explosive and quick exercises but for others that like endurance or longer aerobic exercises, or those that like to lose weight, or appear to being losing weight, then creatine supplements are not for you. The good news about this supplement is that it appears to be safer in adults and patients than we once thought, and further good news, is that it's being tested in major clinical trials right now to improve muscle performance in those with muscular and/or neurological diseases (although it just failed a major phase-3 like clinical trial in Parkinson's disease called "NET-PD" creatine trial where patients received 10 grams per day for about 5 years versus placebo). If I had my druthers I would encourage prostate cancer patients to use a protein powder with a variety of amino acids from plants (pea protein, soy, hemp, brown rice…) or animal-based (egg white, casein, whey…) flavored protein powder instead of creatine supplements to lose weight and/or improve muscle protein synthesis.

What else do I need to know?

The reason creatine supplements are again in the news is that recently a paper was published (Herriman M, et al. Pediatrics 2017; February) where a caller pretended to be a 15-year old boy customer, and 164 of the 244 health stores/sales attendants contacted (67%) on the phone recommended creatine and 10% recommended a testosterone booster supplement! Why did this get so much attention? It's because below the growing age (before 18-21 years of age) these supplements are not recommended, because they have not proven to be safe and could impact growth or development in some way. And, yet there it was…all these sales attendants still recommending it to kids less than 18 years of age!

It's weird right (HERE COMES A MAJOR DOSE OF MOYAD SARCASM), because it's almost as if these supplement shops are a business and not a non-profit free clinic so, it almost seems that they also exist to turn a big profit and stay in business?! In other words, come on man! Of course, these results are not surprising to me. You are calling businesses that are major suppliers or sellers of creatine and they make money from creatine, and somehow you think they are going to discourage the use of creatine! Geeessssh! And, this interesting research study concluded by stating that pediatricians need or should get more involved in recommending safer and healthier alternatives for athletic performance compared to creatine. OH, THIS IS FUNNY!! I love how twisted the world really is at times. So, here is a supplement (creatine) NOT really discouraged by any major athletic entity like the NCAA or IOC and somehow pediatricians and other doctors need to rescue the problem?! What!! Why is the answer to so many of these supplement problems "your doctor needs to step it up" when currently doctors have to see countless patients daily, sit on a computer during a good portion of your visit and have less time than ever before per patient? And, to top things off the actual objective education on supplements to physicians and other health care professionals is still poor and needs more attention. We need to quit seeing problems in medicine and suggest doctors should fix it, when currently doctors are inundated with trying to fix so many problems that others have created for them. In other words, simply more research on some of these supplements, and what they can and cannot do is needed. I mean it's not as if the world is testing creatine in athletes below the age of 18 and appearing to claim some benefit (MORE SARCASM…see Yanez-Silva A, et al. J Intl Soc Sports Nutr 2017;14:5-a study of 17

year olds taking creatine to enhance their soccer skills with the following conclusion at the end of the study: "There is substantial evidence to indicate that a low-dose, short-term oral creatine supplementation beneficially affected muscle power output in elite youth soccer players."…YEAH LIKE THAT IS GOING TO DISCOURAGE YOUNG PEOPLE).

So, let's try and make this short and sweet and get away from the chaos for a second. Are creatine supplements an option for some people? Yes! However, not that many people can really benefit but there may be some exceptions. Creatine is actually well produced in the human body already from a few amino acids (Glycine and Arginine and Methionine), so if you like to consume some protein/amino acids then the body loves to make its own creatine (another amino acid). For example, meat and fish contain high amounts of creatine (Greek word for meat = "Kreas") so vegetarians will see a potentially greater response when trying this supplement. Still, the kidney and liver and even the pancreas like to make creatine, and it is primarily stored in muscles and about 1.5-2% of body creatine is converted to creatinine daily (you have seen "creatinine" on your lab reports as one measure of kidney function). Creatine serves to regenerate ATP, or what that means is it's converted into Creatine Phosphate or Phosphocreatine, stored in muscles, and used for energy.

Creatine has been proven to be of some benefit for High-Intensity Training (HIT) and explosive exercises (sprinting, football, baseball…you know sports we wish we could all play as we age), and it could help slightly with strength and muscle mass. What this essentially means is that INTENSE REPETITIVE EXERCISE LASTING LESS THAN 20-30 SECONDS SUCH AS SPRINITING OR LIFTING WEIGHTS OR HIGH JUMPING then creatine has shown some improvement with strength and lean muscle mass improvements. In reality, it appears more beneficial for young folks (21 and over) that use this substance with these exercises and in reality, there has been some research to suggest SLOWER TIMES WITH ENDURANCE RUNNING PERFORMANCE when using these supplements. So, if your main thing is endurance and aerobic exercise that takes some time, then this is not the supplement for you. This is one reason why I do NOT use creatine before, during or after any of my runs or basically, I never use it at any time, but I love to eat meat and fish. And, I currently have no intention of being an Olympic High Jumper any time soon (although when I saw a mouse in our basement the other day I jumped really high and hit my head on the ceiling so perhaps I should rethink my future career options). Most clinical studies start with a loading dose of 20 grams and then shift to 5-10 grams per day as a maintenance dosage.

So, let's talk about some other catches that you don't get to hear about as much. Creatine can help you GAIN WEIGHT because it can suck in more water and create more water weight. Creatine is an "osmotically active substance" that also pulls water into muscle cells and then potentially increases protein synthesis and muscle fibers can grow, but you run the real risk of increasing your water weight if you do not step up your exercises with creatine. Yikes! Creatine is also recommended by some experts to be combined with fruit juice because the combination raises insulin levels due to the sugar and drives even more creatine into muscle cells! So, you can see why a younger and thinner population of people might want to give this a try for the heck of it instead of say the people that read my PAACT column (including my old self).

There is also research to suggest that increasing your supplemental intake of creatine could suppress or reduce your body's ability to make its own creatine. This is a big potential catch! And, because it can be converted to creatinine then those with kidney and liver diseases are also told to not take this supplement. Keep in mind that some creatine supplements are not proven pure or unadulterated and could actually contain creatinine in them!

There are many clinical trials ongoing with creatine in those with heart failure or muscular dystrophy…again situations where a muscle might require a little assistance. However, I will not lie to you, but after it failed a MAJOR phase-3 Parkinson trial and did not beat placebo, I was really sad and disappointed and lost my enthusiasm for this supplement in medicine until other clinical trials are to be completed and hopefully show something different. Now there is a new concern. Creatine use in those with high caffeine intakes appeared to be associated with an INCREASED progression of Parkinson disease (Simon DK, et al. Clin Neuropharmacol 2015;38:163-169)! Yikes! Now, this is observational and not proven, but it's reason enough to be concerned in those with Parkinson disease.

Still, let me leave you with a glass of creatine half-full message! Numerous clinical studies including one of 72 year old overweight men continues to suggest some advantage to even small amounts of protein supplementation and working out (Murphy CH, et al. Am J Clin Nutr 2016;104:1594-1606). In other words, many protein powders today taste amazing (my favorite is "Jay Robb" and no I have never talked to or been paid by this company, but it's a clean product that tastes amazing) and have many amino acids that could help enhance muscle protein synthesis. In a future issue, we will go into this in more detail because not only does it potentially increase your own creatine production in the body but it helps to increase protein intake as we age (which some of us simply need more of with aging). Again, we will discuss this more in the future, because I need you to be incredibly excited about reading another column in the future and potentially increasing my beer and Outback steak house food fund! Oh Boy!

THAT'S ALL FOLKS…. See you in SUMMER, when I will write about many other serious issues and give timeless advice in the next newsletter, such as why it is never smart to juggle knives, chainsaws or porcupines as a hobby, or why it is never smart to use the word "prostrate" when you mean "prostate," or why it is never smart to walk on the Ohio State University Campus and yell "Go Blue Forever" or "Harbaugh is going to own you next year and every year after that," and why it is never smart to wear a tight Speedo bathing suit after the age of 50, or why it is never smart to steal your friends Viagra pills and replace them with blue laxative pills if you still want to stay friends, and why it is probably never smart to ask your friends at your next dinner party if they all want to do Kegel exercises together just for fun instead of play scrabble.

PROSTATE MRI AND TARGETED BIOPSY: FINDING THE CANCER THAT COUNTS

Arvin K George, MD
Assistant Professor - Michigan Medicine
Department of Urology – Division of Urologic Oncology

Prostate cancer remains the most common cancer in men, outside of skin cancer, with an estimated 161,360 new cases to be diagnosed this year in the United States alone. One in seven men will be diagnosed with prostate cancer in their lifetime, however the vast majority who are diagnosed will not die from it. Distinguishing aggressive from indolent (non-aggressive) prostate cancers remains an important clinical problem.

How do we diagnose prostate cancer?

Prostate specific antigen (PSA) is a protein made by the prostate that can be detected by a blood test. It has been used to assess a man's risk of prostate cancer with higher levels suggesting the need for a prostate biopsy. PSA can rise for any number of reasons including a urinary tract infection, inflammation of the prostate (prostatitis), an enlarged prostate, and even after sexual activity. Therefore, an elevated PSA does not in and of itself reliably indicate the presence of cancer, and as such, a biopsy is required for a definitive diagnosis.

The current gold standard in diagnosing prostate cancer is a transrectal ultrasound (TRUS) guided 12-core prostate biopsy. It involves placement of a TRUS probe followed by a systematic but non-targeted sampling of the prostate. The tissue obtained does not represent specific areas of the prostate that are more likely to harbor cancer, but rather random areas that are thought to be representative of the entire prostate. This technique may be equated to shooting (biopsy) fish (prostate cancer) in a barrel (prostate) with your eyes closed. If a fish doesn't float up, it doesn't mean there is not one in the barrel. Unfortunately, this approach results in up to 75% of men having a negative biopsy, and in those where prostate cancer is found, one third will have low-risk prostate cancer that will not affect them in their lifetime.

Widespread PSA screening instituted in the 1980's, had the benefit of diagnosing men with early stage disease, but has subjected a large proportion of men to a biopsy in which no cancer is found, and identified cancers that will be treated even though they are unlikely to cause harm. This has significantly limited the benefit of PSA screening and resulted in a broad scaling back of widespread PSA testing.

Should I get my PSA tested?

Rather than instituting screening for all men, it should be performed after a candid discussion regarding what the test shows and the risks and benefits of prostate biopsy and treatment. It is not recommended for men >70 years old or men who have a life expectancy of <10 years. In order to maximize the benefit of screening, a number of things should be considered. Do my other health issues take precedence? Do I have risk factors (African American race, family member with prostate cancer) for prostate cancer? The conversation surrounding screening can at times be confusing and dialogue with your doctor is important. If prostate cancer is found, a number of excellent treatment options exist including surgery, radiation, and newly emerging focal therapy options that treat the cancer alone rather than the entire prostate.

Prostate MRI

An elevated PSA suggests an increased risk of prostate cancer but provides limited information on how aggressive it is, or where in the prostate it is located. A prostate biopsy removes 12 cores of tissue for analysis, but only samples approximately 1/100,000 of the prostate without providing information on areas that were not sampled. The medical community has worked to identify better ways in which to not only diagnose prostate cancer but also find prostate cancer that is aggressive. A number of new tests that look at proteins and changes at the DNA level have been introduced and resulted in incremental improvements over PSA alone. Few have demonstrated the ability to transform the diagnosis of prostate cancer like prostate magnetic resonance imaging (MRI).

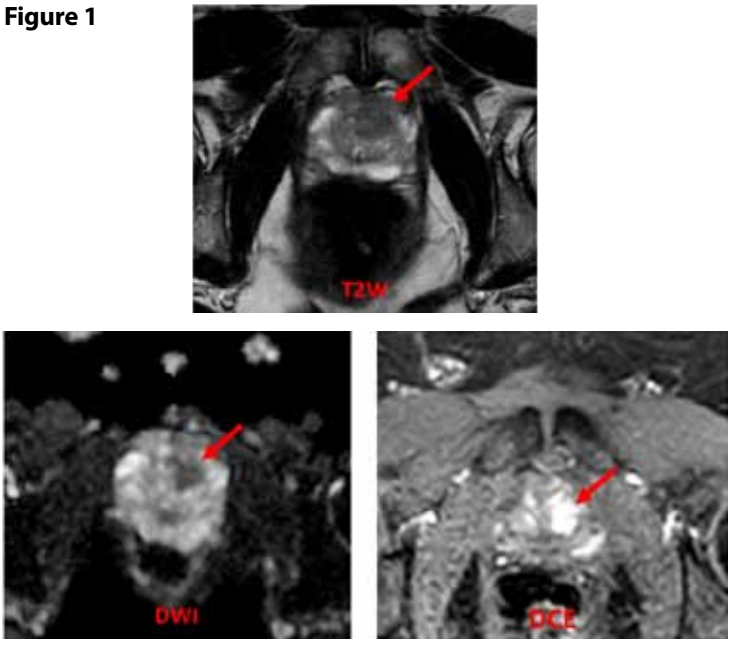
MRI has been around for many years though improvements in technology have allowed for clearer pictures of the prostate that help doctors find areas as small as 3mm that are suspicious for prostate cancer. A prostate MRI is a 30 minute scan that provides detailed images of the prostate anatomy and information on how different areas of the prostate tissue are functioning. It is performed with the administration of intravenous contrast to visualize blood flow to the prostate. If a prostate MRI is to be done after a prior biopsy, it is obtained a minimum of 6-8 weeks after the biopsy to allow for bleeding within the prostate to resolve so that it will not affect the quality of the images. An MRI with gadolinium contrast can be safely repeated after 1 week if necessary.

It consists of a number of scans combined into one, each of which yields different information on the prostate tissue. The three major components of prostate MRI that enables doctors to see areas of cancer are T2-weighted imaging (T2W), diffusion-weighted imaging (DWI), and dynamic contrasted enhanced (DCE) imaging (Figure 1):

T2W – shows 'dark spots' in the prostate that are suspicious for prostate cancer

DWI - measures the movement of water between cells in tissue. If water cannot move freely within a specific area of the prostate, it signifies more numerous and tightly packed cells that may represent cancer.

Figure 1



62 year-old man with a PSA of 8.7. He underwent a random 12-core biopsy which revealed 1 of 12 cores positive for Gleason 6 Prostate Cancer. He underwent a prostate MRI to determine if any aggressive cancer was present. T2-weighted imaging, diffusion weighted imaging, and dynamic contrast enhanced imaging demonstrated a suspicious lesion in the anterior prostate that was targeted on fusion-guided biopsy (Figure 2).

DCE - measures the degree of blood flow. If a specific area receives blood flow before the rest of the tissue, it implies an increased concentration of new blood vessels that can occur where prostate cancer develops.

Each sequence by itself provides limited information, but together the presence of findings in a similar region in all three are strongly indicative of the presence of cancer. Not only can it show when cancer is present, but it can exclude the presence of prostate cancer, potentially without the need for a biopsy. A recent study in the Lancet demonstrated that in men with a negative MRI, no aggressive cancer was present in 89% of cases who went on to receive a biopsy.

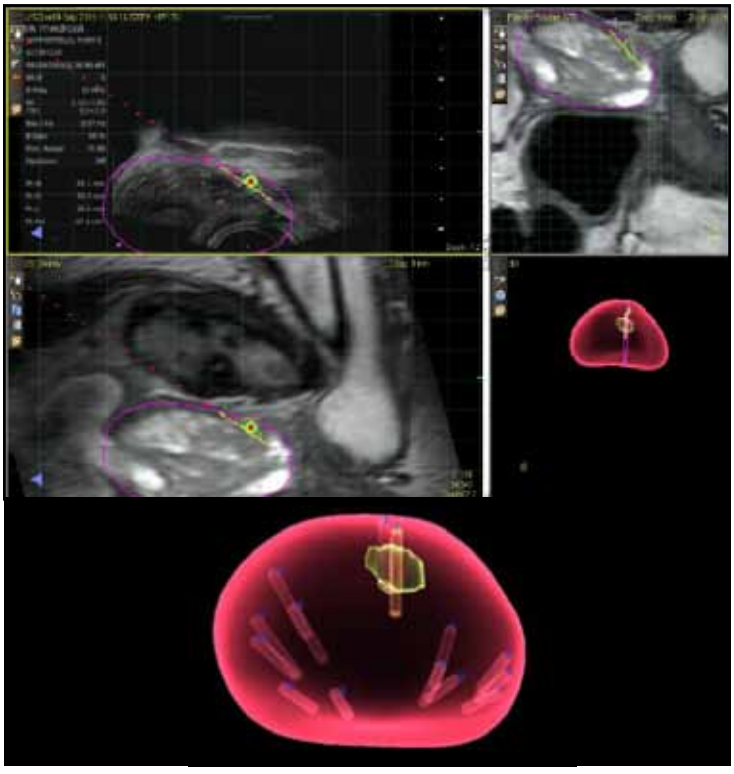
The use of prostate MRI has expanded as we learn more about its benefits. Currently, it is used in men who have had a negative standard TRUS biopsy, in men who have been diagnosed with low-risk prostate cancer who wish to pursue active surveillance (careful monitoring), and those who have chosen definitive treatment with surgery or radiation. In men who are candidates for active surveillance, prostate MRI is performed to ensure more aggressive prostate cancers are not hiding elsewhere in the prostate. In men who are undergoing treatment, prostate MRI is able to aid treatment planning, to guide the surgeon or radiation oncologist.

Targeted prostate biopsy

TRUS biopsy of the prostate does not target areas suspicious prostate cancer. Rather, it randomly samples the prostate with the hope that it will find cancer if it is present. In some men, a standard biopsy is enough to obtain a diagnosis. Unfortunately, in some men, the results are inaccurate and they may go undiagnosed (or misdiagnosed) until curative treatment is no longer possible.

Transrectal ultrasound allows for visualization of the prostate, but rarely gives information on where cancer may be hiding. The pictures are of low quality, subjective in interpretation, and only serves to ensure the biopsies are equally spaced. The diagnostic information provided by prostate MRI can now be used to assist doctors during a prostate biopsy. A magnetic resonance/ultrasound fusion-guided prostate biopsy allows the MRI images to be overlaid (or fused) on top of the ultrasound (US) images during the biopsy to allow sampling of the suspicious areas on MRI even when it is not apparent on US alone - shooting fish in a barrel with your eyes open. The UroNav™ fusion biopsy platform is an electromagnetic navigation system that co-registers (lines up) the prostate MRI with the prostate US (Figure 2). It guides the urologist to target the area of suspicion on MRI and records the coordinates of where the needle went into the prostate, providing detailed information regarding the location of the cancer for future treatment.

Figure 2



The UroNav Fusion Biopsy system was used to sample the suspicious lesion. The top screen demonstrates the US and bottom screen shows the MRI. A bullseye target is placed on the suspicious area for the doctor to perform a targeted biopsy. The right screen shows the final biopsy locations. The 12-core biopsy alone would have missed the lesion. The patient was found to have high risk Gleason 4+5=9 prostate cancer on his targeted biopsy, and again a single core of Gleason 6 on his random biopsy. He went on to successfully have a robotic-assisted radical prostatectomy and has an undetectable PSA.

MR/US fusion-guided biopsy, also known as a targeted prostate biopsy, has been shown to be superior to a standard TRUS biopsy

alone. The ability to 'see' what is being biopsied and specifically targeting areas that are much more likely to harbor prostate cancer has significantly improved our ability to detect and diagnose prostate cancers that are traditionally missed. A study in the Journal of American Medical Association provided the most definitive evidence supporting the benefit of targeted biopsy. In a study of more than 1000 patients, targeted biopsy *detected 30% more aggressive prostate cancer* than standard TRUS biopsy, while *decreasing the detection of low-risk prostate cancers by 17%*. The ability to find cancers that are potentially lethal (that standard biopsy misses) while at the same time avoiding the diagnosis of low-risk cancers that do not require treatment is why prostate MRI is such a powerful tool.

This has been especially useful in men who have a negative standard TRUS biopsy. The concern that prostate cancer remains undiagnosed in these men is significant. A prostate MRI followed by targeted biopsy in those with suspicious areas provides confidence in a final diagnosis. A repeat biopsy using an MRI-targeted approach can identify significant prostate cancers in 11-54% of patients. If a targeted biopsy is negative, the patient is given reassurance that an aggressive cancer is not being missed. If the biopsy is positive, it allows for appropriate curative treatment where necessary.

Challenges in Prostate MRI and Targeted Prostate Biopsy

Despite its promise, obtaining a *high-quality* prostate MRI and *accurate* targeted prostate biopsy is difficult. Obtaining prostate images that are of sufficient quality for diagnosis are a challenge as newer scanners are required and the machine settings must be adjusted for the specific study. Additionally, given its novelty, there are few experienced radiologists who have the specialized training and expertise to interpret prostate MRI. Dr. Matthew Davenport at Michigan Medicine who specializes in prostate MRI, has lead the charge in training additional radiologists in the state with the goal of being able to offer this valuable service to more patients. Finally, performing a fusion biopsy requires specific training in the procedure and without such training, it can give incorrect results that are thought to be accurate. These challenges remain on both a state and national level and it is essential to ensure that patients have access to high-quality imaging, expert interpretation, and urologists with sufficient experience in MR/US fusion-guided prostate biopsy.

Active Surveillance for Prostate Cancer

We have learned a tremendous amount about prostate cancer over the last 20 years. We now know that in certain patients, low-risk prostate cancer can be managed with active surveillance. Low-risk prostate cancer is extremely unlikely to spread outside of the prostate and almost never results in death from the disease. Active surveillance consists of regular PSA testing every 6 months and repeating a prostate biopsy every 1-3 years to ensure the cancer has not become more aggressive or grown in size. Active surveillance provides patients the option of avoiding major surgery or radiation (and the side effects associated with treatment) if and only until it does progress, while not losing the window of opportunity for curative treatment. In patients initially managed with active surveillance 63% and 55% remain without treatment at 10 years and 15 years, respectively.

The success of active surveillance is dependent on ensuring that only low-risk prostate cancer exists in the prostate. Prostate MRI and targeted biopsy can be used as a confirmatory test to ensure that a man with low-risk prostate cancer does not have more aggressive prostate cancer elsewhere in the prostate missed during a random TRUS biopsy. In patients initially diagnosed with low-risk prostate cancer who go on to have a targeted biopsy, 30% will have higher-risk prostate cancer found that requires more aggressive treatment. However, as this technology is not widely available, it is not always offered to men in whom it would be of great benefit.

The Michigan Medicine, Department of Urology, now offers a comprehensive Prostate Cancer Active Surveillance Clinic at the Livonia Center for Specialty Care. Patients have access to state-of-the-art prostate cancer care including consultation with a Urologic Oncologist (Urologist with sub-specialty training in genitourinary cancers, and specific focus on prostate cancer), management of erectile dysfunction (Urologist with subspecialty training in Male Reproductive Medicine and Sexual Health), management of urinary symptoms, and nutrition counselling, all within the same setting. Additionally, all patients are offered additional services including prostate MRI and fusion-guided prostate biopsy, evaluation with novel genomic testing, and participation in cutting edge research. This resource represents the only one of its kind in the state.

Focal Therapy for Prostate Cancer

The conventional treatments for prostate cancer include robotic and open surgery, various forms of radiation, and cryotherapy. These options, treat the entire prostate, even if there is only a small focus of prostate cancer. The treatment of the entire prostate comes with the potential for significant side effects which include impotence, urinary incontinence (leakage of urine), worsening urinary symptoms (frequency/urgency/pain with urination), bleeding into the urinary tract, and rectal/bowel irritation.

Focal therapy for prostate cancer, also known as partial gland ablation, aims to only treat the area of the prostate which is affected by the cancer while leaving unaffected areas intact. Historically, focal therapy was used sparsely, but the ability to 'see' the prostate cancer with prostate MRI, and improvements in treatment technologies have demonstrated potential. Treating only the cancerous area, in early studies has demonstrated a much lower rate of the side effects mentioned above, specifically an extremely low rate of impotence and urinary leakage.

A number of focal therapy options exist. These include various ways to ablate (destroy) the prostate tissue that has cancer. High-intensity focused ultrasound (HIFU) has shown significant promise and the treatment can be guided by MRI in a similar fashion to a fusion biopsy resulting in a 'targeted' focal treatment. However, the treatment is not suitable for all men and is determined by an Urologist with expertise in the area.

The Michigan Medicine Department of Urology will offer HIFU targeted prostate cancer treatment to select patients in whom it is appropriate, a novel therapy that will allow cancer control with minimal side effects. Dr. Ganesh Palapattu, Chief of Urologic

Oncology at Michigan Medicine states "We are excited to offer this novel technology to treat select men with prostate cancer. Our goal is to be able to effectively treat prostate cancer with modest side effects. HIFU represents one such option that may prove useful for some men."

How do I get a Prostate MRI or Fusion Biopsy?

The Michigan Medicine, Departments of Urology and Radiology have implemented a prostate imaging and fusion-guided prostate biopsy program in the last 3 years. It was the first to introduce this novel technology to the state of Michigan and to date has the greatest experience in the region. As a leader both nationally and internationally in prostate cancer care, Michigan Medicine doctors have been training others in the region in this technology. If you are interested in prostate MRI and targeted prostate biopsy, you may contact the Michigan Medicine Comprehensive Cancer Center for a consultation at (734)-647-8903 or request an appointment online at http://www.mcancer.org/cancers-and-treatments/online-appointment-request.

3D BIOPSY AND NANOKNIFE® TREATMENT SIGNALS BEGINNING OF NEW GENERATION OF MINIMALLY INVASIVE, LESS TOXIC, PROSTATE CANCER TREATMENT WITH LOWER TOXICITY THAN CURRENT METHODS

Israel Barken, MD

Irreversible electroporation (IRE), also called NanoKnife® Treatment is a new effective treatment method for prostate cancer, that is clinically proven to minimize side effects such as impotence and incontinence. Dr. Michael K. Stehling has treated the most prostate cancer patients in the world using this image guided treatment, while generating the best therapeutic results.

At the Prostate Center of Offenbach, Germany (www.prostate-center.org) which he founded in 2010, Stehling has treated hundreds of patients at every grade and stage of prostate cancer, and helped to advance the use of image guided treatment technologies worldwide. Prof. Stehling is internationally recognized as a leading expert on image guided tumor ablation treatments. He is the most experienced practicing doctor in the field of image guided tumor ablation with IRE of the prostate, having treated the largest number of patients, while generating the best therapeutic results worldwide.

"The patients we have treated at The Prostate Center have had their cancers destroyed without the need for surgery, with a low incidence of side effects and in most cases have been back on their feet the next day," said Dr. Stehling. "Data confirms what we see every day, we have a very attractive approach for patients who are concerned about quality of life challenges and are considering options for the treatment of localized and late stage prostate cancer," he said.

Current treatment methods for prostate cancer often lead to impotence (loss of erection ability) and incontinence (loss of bladder control) in the majority of men.

Unlike other treatment procedures for prostate cancer, image guided or IRE only destroys cells; vital tissue structures are not affected, making IRE the first tissue-selective form of therapy. This is significant considering that up to 70% of all men are impotent after having radical therapy and 10-50% are incontinent.

NanoKnife® Treatment uses strong electric fields that cause cells to die without exposing the tissue to radiation or heat. IRE is precision guided and reliably destroys cells within the treatment field, but important anatomical structures in and around the prostate such as nerves, the intestinal wall, the sphincter, veins and arteries are spared. Potential issues with erection and bladder control and other side effects are reduced while healing time is minimal, making it an ideal method for focal prostate cancer therapy and for men concerned about quality of life challenges.

A recent analysis of clinical data from over 200 patients treated by Dr. Stehling, found that IRE allows for faster recovery times and lower side effects in all stages of prostate cancer. Data from the study, which was conducted at the Prostate Center also found that the most common side effects were either eliminated or greatly reduced using image guided treatment.

During the study, Dr. Stehling and his team of researchers evaluated data from 265 patients with primary (stages T1-T4) and recurrent PCa after surgery, radiation therapy and HIFU. Initial tumor control was achieved in all patients, and during the follow-up period of up to 4 years, the recurrence rates were 0/55 (Gleason <7), 3/117 (Gleason 7) and 10/67 (Gleason >7). There were no IRE-related complications and toxicity was extremely low: 27 patients reported a transient reduction of erectile function (EF) (resolved after 6-8m), 15 a permanent reduction and 2 a permanent loss of EF.

Throughout the study, there were no cases of IRE-related incontinence, even when the lower urinary sphincter was included in the treatment field. Incontinence is one of the most common adverse side effects

of current treatments for localized prostate cancer and can have a substantial impact on quality of life. The NanoKnife® Treatment also had very low toxicity on the rectum and bladder, even in cases of advanced cancer infiltrating these structures in patients who were not candidates for surgery or radiation therapy anymore.

"Treating prostate cancer with minimal pain and minimal risk of impotence and incontinence, even in patients with advanced and recurrent cancer, with a one-time, one-day treatment, until recently, was unthinkable," Dr. Stehling said. "The cutting edge technology of IRE makes this a reality."

When multimodal and three-dimensional MRI images are used, cancer loci in the prostate can be identified and localized with pinpoint accuracy and a detection sensitivity of at least 85%.

A prostate MRI also shows whether the carcinoma is only present in the prostate or has infiltrated nearby tissue (local staging). Ultrasound, computer tomography (CAT scans) or PET/CTs are not able to do this.

A 3-d biopsy is more than three times as accurate as standard biopsies, is three-dimensional, MRI-guided, precise, under general anesthesia and without risk of infection. It overcomes all of the drawbacks of rectal punch biopsies and, in conjunction with MRI, is becoming an essential tool for every type of focal therapy (therapy targeted at cancer locations or "foci").

The Prostate Center, has further developed this type of biopsy especially for NanoKnife® treatment. Using "Histo-Modelling®," the center relies on biopsy data to create an interactive 3-d model of the prostate that shows the distribution of all cancer foci and how dangerous each is (Gleason score).

"Up until now, simply knowing that there was cancer somewhere in the prostate was enough to set radical therapy in motion," Stehling said. "This is because no attention was paid to the exact characterization of the tumor. If the prostate is to be spared, the physician must know before treatment begins where in the prostate the tumors are and how dangerous each tumor is."

The once-in-the-world experience with this new technology together with a strong focus on Magnetic Resonance Imaging (MRI) makes this pioneering treatment something that should be considered as an alternative to common treatments.

Because of the disadvantages of radical therapy, prostate cancer therapy is beginning to be seen in a different light. It is plausible that irreversible electroporation (IRE – NanoKnife®) can and will completely replace current surgical and radiation methods.

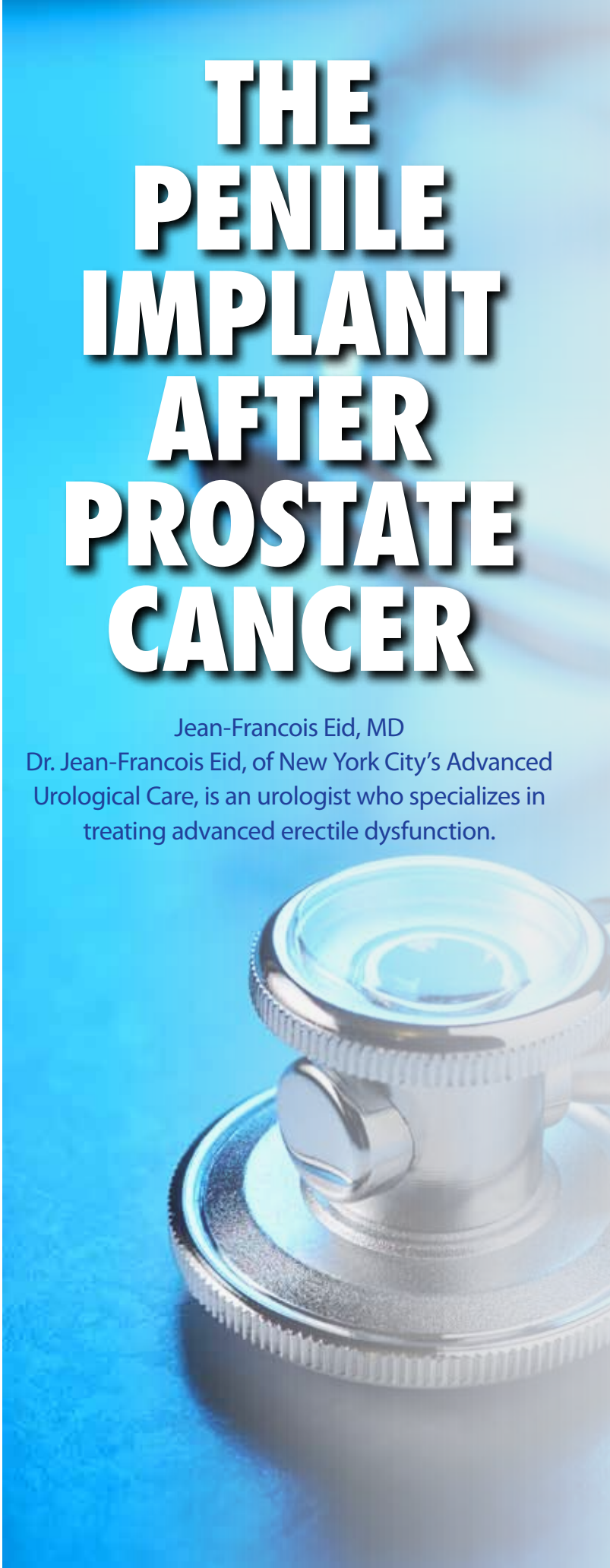
For further questions about Electroporation and prostate cancer, call PCREF at 619-906-4700 or write to Info@pcref.org.

Michael K. Stehling, MD, PhD - Professor of Radiology, Lecturer at LMU Munich, fmr. Associate Professor of Radiology at Boston University, USA.

THE PENILE IMPLANT AFTER PROSTATE CANCER

Jean-Francois Eid, MD

Dr. Jean-Francois Eid, of New York City's Advanced Urological Care, is an urologist who specializes in treating advanced erectile dysfunction.



Prostatepedia spoke with him recently about penile prostheses after prostate cancer. *Article originally appeared in Prostatepedia – September 2016, Volume 2 No. 1.* For information on Prostatepedia go to prostatepedia.net.

How did you come to focus on erectile dysfunction?
Dr. Eid: I became interested in erectile dysfunction as a medical student. Back in the early 1980s, I heard an urologist lecture about penile implants. During my residency at New York-Presbyterian Hospital, we had an ultrasound machine in the department of urology. Nobody was using it, so another Urology Fellow and I started using the machine to do blood flow studies on patients with erectile dysfunction.

I became interested in using penile injections to provide patients with erections. I went from being interested in the diagnosis of erectile dysfunction to being interested in treating patients with penile injections. Back in the 1980s, we didn't have pills like Viagra and Cialis. We didn't really have any options that worked.

Throughout my training, I always preferred delicate reconstructive procedures that needed fine, precise work, rather than extirpative procedures to remove a big tumor. I found extirpative procedures to be less technically challenging. My work continues to fascinate me. The patient evaluation requires thorough history-taking and some psychological insight, which is something I enjoy doing. At the same time, you want to make the patient feel comfortable; erectile dysfunction is a somewhat personal and delicate issue. There is a little art and empathy involved in communicating with someone suffering from erectile dysfunction.

I find it extremely gratifying to make somebody potent again without leaving any traces of the surgery. My goal is to conceal and hide the implant so the patient feels completely normal.

When a man has erectile dysfunction, he thinks about it all the time. It's not something that affects him only in the bedroom. After a while, it fatigues, occupies, and depresses the brain. Every time he sees a love scene in a movie theater or he goes out to have drinks with friends or somebody makes a joke or he sees an attractive person, he is reminded that he has erectile dysfunction. It depresses men tremendously.

The first thing a patient will say after he gets a penile implant is, "I'm a new man. I feel so free. You gave me a new life." It's sort of bizarre, because you would think that somebody would say that if you saved them from cancer or from a heart attack and not from erectile dysfunction.

How does a penile prosthesis work?
Dr. Eid: There are two types of penile implants. One type of penile implant, is always firm and is called a semimalleable implant. The other is a saline-filled inflatable implant.

The inflatable implant was invented in 1973 and FDA-approved in 1975. It consists of two cylindrical plastic tubes that are placed inside the shaft of the penis and are connected to a pump that is concealed inside the scrotal sac. The pump is connected to a small reservoir the size of a Ping-Pong ball that stores the saline when an erection is not needed. The saline fluid is transferred into the cylinders by activating the pump when the patient is interested in being sexually active. It's a hydraulic device that is manually activated. It mimics a physiological erection, while also allowing the penis to become flaccid when an erection isn't needed.

There are two manufacturers, both in the state of Minnesota. Boston Scientific is in Minnetonka. Coloplast is in Minneapolis.

In which patients is the inflatable pump used?
Dr. Eid: This is a great treatment for advanced ED that does not respond to medications such as Viagra or Cialis. In order to optimize the outcome, we have every possible device size available in the operating room; the penis is measured during the procedure, and the correct cylinder size placed in order to maximize the size and quality of the erection. It's difficult to tell which implant is appropriate for which patient until then. The choice of device brand depends on the patient's anatomy, his age, his partner's age, his manual dexterity, whether he has scar tissue, his body habitus, etc.

There are some special considerations for prostate cancer patients regarding reservoir placement (the little Ping-Pong ball-like structure that stores the saline fluid). After robotic prostatectomy, surgeons do not close the peritoneum, which is a layer of tissue that separates the abdominal cavity from the pelvis.

Therefore, in order to safely place the reservoir, I perform a second separate incision about one to one-half inch either on the right or the left side of the lower abdomen. The reservoir is then placed from above, underneath the abdominal muscles, and the tubing is tunneled into the scrotal sac to connect with the pump tubing. A separate incision is unnecessary for patients following radiation therapy and is only needed for patients following robotic prostatectomy.

Are there any other considerations for prostate cancer patients?
Dr. Eid: The data on potency after prostate cancer surgery varies tremendously. If you look at the European data published by independent third parties, post-surgery erections returned to normal in fewer than 10% of men. Another 20% responded to pills like Viagra or Cialis. Seventy percent of men after robotic prostatectomy do not respond to oral medication.

Patients need to know that if they wait for more than two years after surgery and recovery of erections hasn't occurred, then it's appropriate to consider a penile implant.

Some patients do use penile self injections. There are two types of penile injection medication. Caverject and Edex are FDA-approved and can be purchased in drug stores. These injections are safe for long-term use.

There are other types of medications, such as Trimix (mixture of papaverine, phentolamine, and prostaglandin E1), which are not FDA approved for penile self-injection but are most often used by post-prostatectomy patients. Penile scarring, deformity, and shortening will occur over the long run. Trimix should only be used for a couple of years while waiting to see if recovery of potency will occur.

How long does a penile implant last?
Dr. Eid: Penile implants will last anywhere from 15 to 20 years. But when they break, they are easily replaced.

Infection of the device is the most dreaded complication and occurs because of bacterial contamination of the implant during the surgical procedure. The rate of infection varies according to surgeon's talent, experience, and surgical volume. This can be as high as 15% or as low as 2%. Our infection rate is 0.47% based on 3,028 consecutive implants since January 2006. We update our data on a regular basis.

Specialists will have a much lower infection rate. It's important for patients to seek out the most experienced doctor. Think of a penile implant as one would a root canal procedure. You want to see a root canal specialist, rather than a general dentist for it.

Seeing a specialist is very important, because it minimizes the risk of infection, maximizes the size of the penis, and optimizes the placement of the pump and concealment of tubing and incision. Specialists also make smaller incisions, which reduce areas of skin numbness, preserving sensation and ability to achieve orgasm.

Do you advise patients to specifically ask about infection rates when evaluating doctors?
Dr. Eid: Yes, but very few places actually track their infection rates and it's often difficult to obtain this data.

How should patients evaluate a specialist?
Dr. Eid: There are clues to look for. If you walk into a doctor's office and you don't see any information on penile implants, then you can guess that not a lot of implants are being performed by that practice.

If the doctor sees female patients as well as male and performs mostly general urological procedures, then this automatically indicates that the physician hasn't done a lot of penile implants. (There just isn't enough time in the day to do all these things.)

If the doctor has assistants do some of the ED evaluation and some of the medical treatment of erectile dysfunction—a physician assistant does the penile injections—then you know that the doctor is not really involved and interested in treating erectile dysfunction. He will not have the opportunity to discuss penile implants with many patients.

If you ask about penile implants and the doctor doesn't volunteer a list of patients who already have had a penile implant placed by his practice that you can talk to, this also would indicate that not a lot of implants are being performed there.

If the doctor doesn't have models of all the different types of implants that you can look at and manipulate, and if you ask for information on penile implants and all you get is a pamphlet from the company itself and nothing written by that physician, then this also indicates that the procedure is not frequently performed in that practice.

If you schedule the procedure and find that the staff doesn't really know about insurance reimbursement, that's also a clue that they're not frequently scheduling the implant procedure.

If you ask the doctor, "Do you like to have a representative from the company there during the procedure?" and he says yes, then, you know that he is not going to have a choice of which implant to use. (If a representative from one company is there, the doctor is less likely to use an implant from another company, even if the other company's implant fits you better.)

If you ask directly about infection rates, he may say, "My infection rate is very low." But looking for clues is a much cleverer way of finding information about how many implants a doctor actually does.

How much does an implant cost? Is it usually covered by insurance?
Dr. Eid: These devices have been around since 1973 and the procedure is reimbursed by most commercial insurances including Medicare.

More recently insurance plans have increased their deductibles and some will play games. They claim to cover the procedure, but won't pay for the implant device. This is a newer occurrence and is absurd.

If a patient is paying cash, the device itself costs from $8,000 to $10,000. When you add the cost of the operating room, anesthesia, and the surgeon's fee, it can add up to about $25,000, depending on the facility used.

It is recommended to have this procedure performed in a clean outpatient ambulatory surgery center and to avoid a hospital stay. Ambulatory facilities charge less than hospitals. (The operating room and anesthesia fees are much cheaper.)

I suppose if the device lasts 20 years, $25,000 isn't a bad deal.
Dr. Eid: No, it's not. There are a lot of other medical procedures that are much more expensive.

Is there anything else men should know about the penile implant or other options available to treat erectile dysfunction after prostate cancer?
Dr. Eid: One feels completely normal with a penile implant. Everything is preserved; nothing is removed from the patient to put in the penile implant. Also for many, the implant restores a fuller penile anatomy. The penis doesn't retract when the implant is not in use, so the flaccid penis appears larger.

After prostatectomy, some patients will have difficulty with urination if the patient is overweight and the penis retracts. A penile implant will also help in this situation.

Patient and partner satisfaction with penile implants is greater than 90%, but as with any medical procedure, seek the most experienced physician you can find in order to maximize chances of success.

A NEW AND SAFER IMAGING AGENT FOR PROSTATE MRI

Dan Sperling, MD

Multiparametric magnetic resonance imaging (mpMRI) of the prostate is a singular factor in changing the prostate cancer (PCa) detection, diagnosis and treatment landscape. It has been shown to be highly significant and specific in detecting significant prostate cancer. The use of more than one imaging parameter, or functional sequence, allows us to characterize abnormal tissue as a tumor. In effect, mpMRI gives us a unique portrait of each patient's cancer that guides biopsy and treatment decisions.

Employing multiple parameters (T2 weighted imaging, diffusion weighted imaging, spectroscopy, dynamic contrast enhanced) in combinations of two or more is essential for accurate classification of abnormal tissue. There are benign conditions that can readily confound or confuse the reader, because they may share certain image-based aspects of PCa. However, mpMRI transcends that possibility because each parameter looks at particular tell-tale cancer features. Thus, the combination together enables us to distinguish benign abnormalities such as prostatitis or hyperplasia (BPH) from malignancy.

One of the functional parameters that is routinely included in a prostate scan is dynamic-contrast enhanced MRI (DCE-MRI). The value of DCE-MRI is the identification of a tumor's blood supply. A tumor has the ability to generate new blood vessels (called angiogenesis) by which to sustain itself and feed its growth. However, these blood vessels are less organized and more permeable than healthy blood vessels. With DCE-MRI, we use an IV infusion of a contrast agent that will clearly register on the images. Once in the bloodstream, we run a closely timed sequence of scans as the agent infiltrates blood vessels in and around the prostate gland within seconds, then washes out. The way in which these vessels take up the contrast agent and the speed with which it washes out is revealed, and we can time it by the series of scans.[1]

For DCE-MRI of the prostate, a gadolinium-based contrast agent is used. Gadolinium is a soft, silvery white chemical element. For it to show up during the MRI, the atoms are bonded with special molecules that preserve its imaging properties while overcoming any toxicity. Gadolinium is considered very safe for adults. However, the use of gadolinium-based agents is restricted to those with healthy kidney function, since kidneys do the work of flushing out all gadolinium via urine within 24 hours of administration. This means that those with poor kidney function, as measured by a simple blood test, cannot undergo the DCE sequence. Thus, we may miss an important clue regarding tumor activity and extent. In addition, in 2015 clinical evidence was reported that some types of gadolinium-based agents may deposit a very small amount of gadolinium in the brain where it may remain for years.[2] Needless to say this was very concerning now that we depend on the advantages of mpMRI to best meet our patients' needs.

However, there is cause for optimism since its increased safety allows use with a wider range of patients. A growing number of centers of radiologic excellence, including ours, now make Dotarem available for prostate mpMRI because of its increased safety features.

In March, 2013 the U.S. Food and Drug Administration (FDA) approved the use of a gadolinium-based contrast agent called Dotarem or gadoteric acid (released in 1989 by Gueret Pharmaceuticals, France). Dotarem was already widely used in Europe and other countries around the world. It was originally developed for neurological MRI of the delicate brain and spinal cord structures of the central nervous system because it doesn't deposit residue in the brain. This also made it safer for use even in children and those with compromised kidney function.

The use of Dotarem in mpMRI of the prostate is slowly on the rise. For example, the authoritative Dutch team out of Radboud University Nijmegen Medical Center, with whom our Center frequently collaborates, used Dotarem for its clinical study of mpMRI and early risk stratification of candidates for Active Surveillance.[3] It was likewise used by a Dutch-U.S. team to discriminate between prostate cancer and benign conditions that can be mistaken for prostate malignancy.[4]

As with all gadolinium-based contrast agents, Dotarem comes with safety warnings regarding dosage and the need to ensure that patients do not have significantly high-risk kidney issues. However, there is cause for optimism since its increased safety allows use with a wider range of patients. A growing number of centers of radiologic excellence, including ours, now make Dotarem available for prostate mpMRI because of its increased safety features.

(Endnotes)
1 Verma S, Turkbey B, Muradyan N, Rajesh A et al. Overview of dynamic contrast-enhanced MRI in prostate cancer diagnosis and management. Am J Roent. 2012 Jun;198(6):1277-88.
2 https://www2.rsna.org/timssnet/media/pressreleases/14_pr_target.cfm?ID=810
3 Hoeks C, Somford D, van Oort I, Vergunst H et al. Value of 3-T Multiparametric Magnetic Resonance Imaging and Magnetic ResonanceYGuided Biopsy for Early Risk Restratification in Active Surveillance of Low-Risk Prostate Cancer. Invest Radiol 2014;49:165-172.
4 Litjensa GJ, Elliott R, Shihc N, Feldman M et al. Distinguishing prostate cancer from benign confounders via a cascaded classifier on multi-parametric MRI. Medical Imaging 2014: Computer-Aided Diagnosis, edited by Stephen Aylward, Lubomir M. Hadjiiski, Proc. of SPIE Vol. 9035, 903512· © 2014 SPIE · CCC code: 1605-7422/14/$18 · doi: 10.1117/12.2043751.

ADDING MULTIPARAMETRIC MRI TO PROSTATE CANCER SCREENING WILL SAVE LIVES AND MONEY

Robert Princenthal, MD • Rolling Oaks Radiology
Ventura County, California | 805-778-1513

In recent years, recommendations for prostate cancer screening have been caught amidst growing controversy. The utility of prostate-specific antigen (PSA) blood testing, the most prominent front-line screening exam for prostate cancer, has been heavily critiqued. Meanwhile, numerous men present with incurable late-stage prostate cancer while men with low-risk, indolent disease receive treatment that offers little benefit in terms of health outcomes. Prostate cancer patients and their physicians have long sought an alternative to the current standard of care in prostate cancer detection and diagnosis. Multiparametric MRI is an emerging technology that could be added to PSA-based prostate cancer screening to improve diagnosis and management.

Controversy Surrounding Prostate Cancer Screening

PSA is a protein produced by the prostate gland. PSA is present in the blood of most healthy men, although normally at low levels. However, PSA levels can become elevated in men with prostate cancer and other prostate conditions.

Researchers identified PSA as a potential biomarker for prostate cancer in the 1970s. PSA tests were initially used to monitor the progress of disease in men already diagnosed with prostate cancer. In the early 1990s, additional research showed that PSA tests could be used as a first-line screening exam for prostate cancer. The standard of care in prostate cancer detection and diagnosis remained largely unchanged in the following two decades.

Pros & Cons of PSA Testing

PSA blood tests provide useful information about prostate health and have helped to save many lives from prostate cancer. With PSA-based screening available, prostate cancer mortality rates dropped by more than 40 percent from 1991 to 2009. However, the conventional process for detecting and diagnosing prostate cancer can be improved.

Despite the benefits of PSA-based screening, the standard of care in prostate cancer diagnosis has been somewhat crude over the past two decades. PSA levels are a volatile biomarker. They can fluctuate for numerous reasons besides the presence of cancer. Prostate enlargement, infection and age can all affect PSA levels.

In the past, a PSA level of 4 was commonly used to determine which men should be biopsied. This benchmark is somewhat arbitrary and others suggest an even lower benchmark of 2.5.

- **15 % of men with PSA levels less than 4 will have prostate cancer.**
- **25 % of men with PSA levels between 4 and 10 will have prostate cancer.**
- **More than 50 % of men with PSA levels of 10 or more will have prostate cancer.**

While PSA testing is imperfect, it can be useful. Rather than using a PSA level of 4 to triage men for biopsy, doctors could consider PSA levels along with other factors. These include rate of PSA level increase and size of prostate at initial screening.

TRUS Biopsy

The second step in the conventional process for diagnosing prostate cancer has required transrectal ultrasound (TRUS) biopsy. TRUS biopsy is far from perfect as a diagnostic exam. During this procedure, around 12 or more biopsy needles are fired into the prostate in relatively blind fashion to draw tissue samples for testing. The grey scale ultrasound used in the TRUS biopsy is not effective at detecting cancer cells, or specific nodules within the prostate, so there is no real attempt to biopsy suspicious areas in a targeted approach.

More than 1 million TRUS biopsies are performed each year. Up to two-thirds provide no useful clinical data. Many men without prostate cancer are indeterminately biopsied based on PSA levels alone or clinically insignificant cancers are identified by chance. In other instances, important cancers are missed due to the inadequacy of TRUS biopsy. Additionally, roughly one-half of cancers diagnosed by TRUS are inappropriately sampled and under-graded. For instance, a higher-grade, Gleason 7 cancer could be misrepresented as a low-grade, Gleason 6 cancer.

If an initial TRUS biopsy does not detect cancer and PSA levels remain elevated, men are often asked to return for repeat transrectal biopsies once per year or less. Each repeat biopsy puts men at additional risk for complications, such as bleeding or infection – even erectile dysfunction. In addition to causing unnecessary harm, repeat biopsies can become costly. This process repeats itself year after year until cancer is finally detected or until a man becomes too frustrated to continue.

Active Surveillance or Treatment?

To complicate prostate cancer screening, many prostate cancers can be safely monitored rather than treated. Most prostate cancers are low-grade (Gleason 6), slow-growing cancers that will not cause harm for many years. However, the early detection and treatment of high-grade, aggressive cancers is critical to achieving the best possible outcomes.

Incomplete information provided by a combination of PSA tests and TRUS biopsy often leads to inappropriate treatment recommendations. Men with cancers that can be safely monitored often receive radical treatment. They may suffer undesirable side effects of treatment, such as incontinence and impotence, when they didn't require treatment at all.

USPSTF Recommendations for Screening

By using incomplete data provided by PSA testing to indeterminately recommend men for biopsy, doctors are doing their patients a disservice. This unnecessarily places men at risk for complications from biopsy and has subjected many men to the side effects of unnecessary treatment. It also led the U.S. Preventive Services Task Force (USPSTF) to recommend against PSA-based prostate cancer screening in a 2012 decision.

"Prostate cancer is a serious health problem that affects thousands of men and their families," read a statement from USPSTF

co-chair Michael LeFevre, MD, issued at the same time as prostate cancer screening guidelines. "But before getting a PSA test, all men deserve to know what science tells us about PSA screening: there is a very small potential benefit and significant potential harms."

To the USPSTF, saving lives is a "very small potential benefit" of screening men with the PSA. While there are significant potential harms, it is irresponsible to recommend against screening when lives can be saved. Rather than denying access to screening, the medical community should adopt a strategy to recommend screening while communicating both the potential harms and the potential benefits to patients. Patients with high-grade, aggressive cancers should not be denied the chance for treatment or a cure.

Fortunately, advocates for prostate cancer screening can point to advancements in prostate cancer treatment and in new diagnostic tools to make their case. Over the past several years, multiparametric MRI has emerged as an effective way to detect prostate cancer, triage men for biopsy and guide treatment recommendations.

What is Multiparametric MRI & How Does it Work?
Researchers have experimented with MRI of the prostate since the 1980s. However, recent technological advancements and the development of specific imaging techniques have allowed MRI to emerge as an effective way to visualize the prostate gland that can aid in prostate cancer detection. Multiparametric MRI provides detailed anatomical and functional information unavailable from grey scale ultrasound.

Multiparametric MRI Sequences
Radiologists can use multiparametric MRI to measure the extent of a tumor, identify the location or locations of a tumor, estimate the Gleason score of a tumor and determine whether a tumor has spread beyond the prostate gland. A multiparametric MRI exam consists of three separate imaging techniques ('parameters'): T2-weighted imaging, diffusion-weighted imaging and dynamic contrast-enhanced imaging.

T2-Weighted Imaging
A T2-weighted imaging sequence provides anatomic information about the prostate gland. It offers detailed visualizations of the prostate gland and its distinct zones. T2-weighted imaging has applications in the detection, localization and staging of prostate cancers.

On T2-weighted images, cancers in the peripheral zone of the prostate typically appear as areas of enhancement or bright spots against a dark background. Cancers in the transition zone are more difficult to detect. They appear as smudged charcoal against a grey background.

T2-weighted imaging also provides opportunity to evaluate seminal vesicles and the bladder wall to determine if a tumor has spread beyond the prostate. Other prostate conditions can be mistaken for cancer on T2-weighted images.

Diffusion-Weighted Imaging
Diffusion-weighted imaging (DWI) measures the motion of water molecules within the prostate to provide useful functional data about cancers. This sequence produces an ADC value for different areas of the prostate gland. ADC values measure the degree of motion through different tissues. Lower ADC values appear in cancerous tissue than healthy tissue. ADC values also correlate with Gleason scores, with lower ADC values indicating a higher Gleason score.

Dynamic Contrast-Enhanced Imaging
During dynamic contrast-enhanced (DCE) imaging, a contrast agent (gandolinium) is used to evaluate blood flow through the prostate. Cancerous tissue absorbs the contrast agent more quickly than healthy tissue, which is apparent on DCE images. The role of DCE imaging is secondary to T2-Weighted Imaging and DWI, but it can help to detect small, yet significant cancers missed by the other two sequences.

Multiparametric MRI Interpretation
Multiparametric MRI exams are interpreted according to the Prostate Imaging Reporting and Data System (PI-RADS). This is a classification system that uses a 5-point scale to standardize assessment of exams. A PI-RADS assessment indicates the likelihood of intermediate- and high-risk cancers based on findings from the three multiparametric MRI sequences.

- **PI-RADS 1 –** Highly unlikely that clinically significant cancer is present.
- **PI-RADS 2 –** Unlikely that clinically significant cancer is present.
- **PI-RADS 3 –** Uncertain whether clinically significant cancer is present.
- **PI-RADS 4 –** Likely that clinically significant cancer is present.
- **PI-RADS 5 –** Highly likely that clinically significant cancer is present.

For results of PI-RADS 4 or 5, patients should be recommended for biopsy. For results of PI-RADS 1 or 2, a recommendation

for biopsy is likely inappropriate, but other factors should be considered. For results of PI-RADS 3, biopsy may be appropriate depending on patient history, local preferences and preferred standard of care.

Targeted Biopsy

Another benefit of multiparametric MRI is that it enables targeted biopsy. Biopsy needles can be guided using real-time MRI images or multiparametric MRI images can be fused with real-time ultrasound images to guide biopsy needles. These procedures are respectively referred to as MRI-guided biopsy and MRI-TRUS fusion biopsy.

When PI-RADS results are used to triage men for biopsy, both MRI-guided and MRI-TRUS fusion biopsy offer improved higher diagnostic yields with fewer needles over TRUS biopsy. However, MRI-TRUS fusion biopsy is less costly.

Patient Considerations

Physicians referring patients for multiparametric MRI and patients thinking about multiparametric MRI should consider the technology used by different radiology facilities. They should also consider the experience of radiologists interpreting exams. Evidence suggests that multiparametric MRI is ideally performed with 3T MRI and results interpreted by radiologists with significant experience reading multiparametric MRI exams.

Magnet Field Strength

Different MRI machines utilize magnets of different field strengths, with a 3T magnet offering higher field strength than a 1.5T magnet. Multiparametric MRI can be adequately performed with either 1.5T or 3T MRI. However, multiparametric MRI with a 3T magnet benefits from higher signal-to-noise ratio, which produces images of higher quality than those produced by 1.5T MRI.

Endorectal Coil

An endorectal coil may be inserted into the rectum during multiparametric MRI to improve image quality, essentially acting as an antenna. Multiparametric MRI can often produce quality results without the use of an endorectal coil. An endorectal coil is more likely to be used during multiparametric MRI performed with a 1.5T magnet.

Multiparametric MRI as an Aid to Prostate Cancer Screening & Management?

Dr. LeFevre of the USPSTF was correct to call prostate cancer a 'serious health problem.' According to American Cancer Society estimates, more than 220,000 new cases will be diagnosed in 2015 and more than 27,500 will die from prostate cancer. Around 1 man in 7 will be diagnosed in his lifetime. However, many men have been led to fear prostate cancer screening more than they fear the disease.

This assertion and these statistics do not suggest that prostate cancer screening is unimportant. The European Randomized Study of Screening for Prostate Cancer shows that a screening program can decrease prostate cancer mortality by 20 percent or more. Additional research shows that men who forego screening often present with late-stage, often incurable, prostate cancer. While harms of screening should be taken seriously, they should not outweigh the potential to save lives. These numbers show that men deserve a more effective screening program that reduces harms and still saves lives.

A PSA-based prostate cancer screening program that incorporates multiparametric MRI could improve screening for and management of prostate cancer in several ways.

- Reduce total number of biopsies and total number of biopsy needles used, limiting complications associated with biopsy.
- Improve diagnostic accuracy for intermediate- and high-risk prostate cancers.
- Reduce detection of low-risk, indolent prostate cancers.
- More confidently recommend active surveillance when appropriate rather than radical treatment.

MRI-Guided Biopsy vs TRUS Biopsy

Researchers led by Morgan Pokorny, MD, published results July 2014 in *European Urology* that show how multiparametric MRI could improve the process for triaging patients for biopsy. Their study investigated multiparametric MRI in 233 men with elevated PSA and no prior prostate biopsy. Each patient received multiparametric MRI that was subsequently interpreted according to PI-RADS.

If MRI results showed no suspicious findings, patients received conventional TRUS biopsy. If results returned PI-RADS score of 4 or 5, patient received targeted, MRI-guided biopsy. Patients who received targeted biopsy also received subsequent TRUS biopsy. A strategy that referred men with PI-RADS 4 or 5 results for targeted biopsy produced desirable results.

- **36 % reduction in number of biopsies compared with TRUS.**
- **84 % reduction in number of needles used.**
- **87 % reduction in detection of low-risk, indolent cancer.**
- **18 % increase in detection of intermediate- and high-risk cancer.**

By using multiparametric MRI in asymptomatic men with elevated PSA to selectively guide biopsy decisions, rather than indiscriminately ordering TRUS biopsy, researchers showed an ability to reduce the need for biopsy while improving overall detection of intermediate- and high-risk cancers.

MRI-TRUS Fusion Biopsy vs TRUS Biopsy

Researchers led by Mohummad Minhaj Siddiqui, MD, performed a similar study, except they compared MRI-TRUS fusion biopsy rather than MRI-guided biopsy with TRUS biopsy. MRI-TRUS fusion offers several benefits over MRI-guided biopsy. While both offer high accuracy, MRI-TRUS fusion biopsy is more cost-effective and keeps biopsies in the realm of urologists rather than radiologists.

Siddiqui and his colleagues studied more than 1,000 men with elevated PSA or suspicious digital rectal exam results. Each

patient received multiparametric MRI followed by concurrent MRI-TRUS fusion biopsy and conventional TRUS biopsy. Targeted MRI-TRUS fusion biopsy was able to detect 30 percent more high-risk cancers than conventional TRUS biopsy. Additionally, MRI-TRUS fusion biopsy detected 17 percent fewer low-risk cancers.

Researchers concluded that MRI-TRUS fusion biopsy was associated with increased detection of high-risk prostate cancers and decreased detection of low-risk prostate cancers.

Applications for Multiparametric MRI Beyond Biopsy

Researchers have produced convincing evidence that multiparametric MRI could aid prostate cancer screening and diagnosis, with the most prominent benefit being higher diagnostic yields with fewer needles. This reduces harms associated with biopsy, decreased chance of identifying low-risk and increased detection of intermediate- and high-risk cancers. Once a diagnosis of prostate cancer has been confirmed, multiparametric MRI can continue to play a role in patient management.

Detailed anatomic and functional information provided by multiparametric MRI can help to guide treatment decisions. For instance, multiparametric MRI can effectively identify seminal vesicle invasion, extracapsular extension and pelvic lymph node involvement. For patients requiring surgery, this can help to determine surgical approach and whether a nerve-sparing procedure is possible.

In addition to predicting risk pathology of lesions, multiparametric MRI provides details about lesion location, volume and relation to the urethra, neurovascular bundle and rectum. This can help patients and physicians to determine whether focal therapy would be a safe and appropriate treatment option. Guidelines for focal therapy treatments are beginning to call for the use of multiparametric MRI to guide these decisions. MRI is also increasingly used during focal therapy. For instance, real-time MRI is often used to guide high-intensity focused ultrasound and laser induced thermal therapy. Innovative MRI-TRUS fusion platforms are also emerging as effective tools for the guidance of focal therapy.

One of the greatest benefits of multiparametric MRI is its ability to help men more confidently choose active surveillance as a management strategy rather than radical therapy. Monitoring men in active surveillance was previously accomplished using a combination of PSA tests and blind biopsy. With multiparametric MRI and targeted biopsy, doctors are able to better differentiate patients with low-risk, indolent disease from those with intermediate- and high-risk disease. This approach allows men with low-risk disease to delay therapy and their side effects, potentially indefinitely, until there is evidence of disease progression.

Multiparametric MRI Will Improve Prostate Cancer Care

For many years, prostate cancer patients and their doctors have sought diagnostic tools that provide accurate information about the disease. The conventional model for prostate cancer screening requires men to receive routine PSA testing and, if PSA levels are elevated, subsequent TRUS biopsy. There are problems with this model. PSA levels are a useful biomarker, but they provide incomplete information about prostate health. Additionally, the diagnostic accuracy of TRUS biopsy does not allow us to differentiate men with low-risk, indolent disease from those with intermediate- and high-risk disease.

TRUS biopsy does not detect cancer in approximately two-thirds of men with elevated PSA levels. PSA levels can fluctuate due to numerous factors and a group of men with normal PSA levels still develop prostate cancer. **The inability of grey-scale ultrasound to identify suspicious lesions means many cancers are missed and many more are under-graded.** This often results in inappropriate disease management strategy and this process, as well as the potential for harms, has led the USPSTF to recommend against prostate cancer screening.

Prostate cancer is a tale of two diseases. Many men with prostate cancer have low-risk, indolent tumors that are unlikely to grow or cause problems *(is there a word missing here?...)* for a long time, if ever. Other men have high-risk tumors that can quickly become lethal if they are not detected and treated as early as possible. Because the combination of PSA testing and TRUS biopsy provides incomplete assessment of the prostate gland, many men with low-risk, indolent disease elect to receive radical treatment that could be more harmful than it is beneficial. Numerous men unnecessarily suffer from complications like impotence and incontinence, even with the introduction of robotic prostatectomy.

USPSTF recommendations against screening and uncertainty surrounding prostate cancer diagnoses have led many men to fear screening more than they fear the disease itself. Prostate cancer kills more men than any other cancer besides lung cancer. With more than one million biopsies performed each year, men deserve a screening model that can better identify those who would benefit from biopsy and offer high diagnostic accuracy. The emergence of multiparametric MRI as an adjunct to PSA allows us to better identify candidates for biopsy, as well as differentiate those who require treatment from those who can be safely monitored.

High-quality anatomic and functional data provided by multiparametric MRI can identify suspicious prostate nodules and enables targeted biopsy. A screening model that adds multiparametric MRI to PSA testing would require fewer biopsies while improving detection of intermediate- and high-risk cancers. This model would allow men to avoid complications associated with biopsy and to more confidently adopt a disease management strategy appropriate for their disease.

Discouraging men from screening is a misguided approach to a serious health problem like prostate cancer. Prostate cancer screening has been proven to save lives. By working together and implementing a screening model that utilizes multiparametric MRI, we can achieve higher diagnostic yields with fewer biopsy needles.

YOUR APPROACH AND YOUR MEDICAL TEAM

Lonnie Silva
Hayward Support Group Facilitator
Publisher of Prostate World

If this is your first time being diagnosed with prostate cancer, it's best to set-up a plan of action from the onset of your diagnosis. Once you have received your diagnosis, I highly recommend conducting your own Internet research using reputable sites to gather as much information and resource tools as possible. There are many reputable prostate cancer patient information sites on the Internet like Mayo Clinic, Johns Hopkins University, UCSF, Stanford University, University of Michigan Health System (a top-ranked medical school), PAACT, PCRI, Health Alert and US-TOO to name a few to jump start your research. Arming yourself with as much knowledge, information, and resources, immediately after your diagnosis will help you make better & more informed decisions, as well as help you to understand the various medical terms that will be thrown at you at future appointments. You need to gain an idea and perspective for this new area of your life that you are entering.

First and most important, you will need a back-up plan that includes bringing someone with you to your initial appointment such as your spouse or significant other. When you are first informed that you have prostate cancer, it will hit you like a brick, to put it mildly. Half the things that you're going to be told at your diagnosis appointment you won't remember due to the imminent news you will receive, which is why I strongly recommend bringing a trusted companion along. That person can play a significant role at your meeting by just being there for support, but also asking questions and taking notes to help gather important information. In some medical establishments, you may be allowed to record the appointment via a Smart phone or recording device (provided you get advanced permission). Recording your conversation with your physician can serve as a meaningful tool that will enable you, your family & significant others in your life, to hear what was discussed and shared at your initial appointment in case you are unable to relay the information to them. An audio file can be sent to them via text or Email by you at any time after the appointment. This is also a good resource tool for you to have if you opt to see a physician outside your medical group or have a need to relay this first appointment to a specialist. This audio tool particularly works well when significant others or relatives live far away and can't be there in person with you.

Establishing your medical team will consist of: 1) Your primary physician; 2) Your urologist; 3) Your medical radiologist; and 4) Your medical oncologist. I would suggest very strongly that you get opinions from ALL of these specialists in order to come to a conclusion and decision of what course you want to take and how you are going to proceed. And above all, YOU must be the one who makes the final decision, because YOU are the person that will pay for it in body damage, that is damage from the side effects from any treatment, procedure, surgery, or medication you choose to undergo. You only have one body and one time to make the most informed decision you can with the facts given to you by your physician. There is no redo or do over when it comes to your physical health. You need to remain in the driver's seat by being proactive with doing your research, understanding your disease, and finding out the latest, innovative procedures available. Support groups are a great opportunity to talk to other men (and significant others as well) who have undergone similar procedures, or chose not to undergo treatment and why. The positive side about doing research, as well as talking to other prostate cancer patients, will show that medical procedures and technology have greatly advanced in the last one to two decades that now promote less down time, quicker healing, and advancing your physical life to its fullest potential.

The most important thing is to minimize what you will have to endure. It's ideal to undergo a one-time treatment, but unfortunately, this does not exist. This is the reason it is so important for you to gain knowledge and to understand the various procedures and side effects, which you most likely will have to endure the rest of your life. A small amount of information will help you in the long run to make the best medical decision about treatment options available to you.

Always remember this is your life. You are not in it alone - you have the medical community, support groups, and your family and friends along with you on this journey. You may ignore prostate cancer, but it WILL not ignore you so LEARN and LIVE. And, don't give into prostate cancer without RESEARCHING, LEARNING, and LIVING.

We've Got Mail!

Mr. Profit,

I am a prostate cancer patient who was diagnosed in 2012. Your Prostate Cancer Communication quarterly publication is a very helpful source to men with this disease.

I found your information package that was sent to me in 2012 to be a welcome source of information on making decisions in my care.

The booklet on blood tests was lent to a man on active surveillance and he was unable to find it to return it to me. I would appreciate another copy being sent to me.

Enclosed is a check for $55 and thank you for providing this important information.

Very truly yours,
FG

I have lost track of time, but I got to talk to Lloyd, Sr. a year or two before he passed. Hope you can keep going.
DL

Keep up the good work!!!
PK age 85
18 year survivor thanks to Dr. Michael Dattoli.

To PAACT,
A little help from me, 88+, almost 22 years free from PC & prostatectomy.
Moyad is amusing and informative.
HH

Mr. Profit,
Please find the enclosed check for $100.
Continue the good work.
Happy Holidays,
AS

Your newsletter and information is extremely valuable to me.
GN

Your newsletter has helped us so much. Thank you very much. Hope you can continue.
DG

Mr. Profit,

How time flies. In reviewing my check register, I find it is in excess of a year and a half since I last contributed to PAACT. I suggest you institute some type of "dues notice" with an option to opt out for those unable to pay. I for one would hate for PAACT to go defunct. Your publication has been a great source of comfort and information to me.

Regards,
BM

Thanks for helping me PAACT,

When things get a little tight and you have a little over 9 years to reach your goal of 100 years old, it's more than a little difficult to express your innermost feelings of gratitude. And to say that 2008 & the stock market bent me a little is a gross understatement! Please use enclosed check for $100 as you see fit.

Anyway – Thanks Guys!!
BB

Mr. Profit,

Thanks so much, you were more than kind. People like you aren't easy to find! Thanks again for your time and wonderful help talking to me. I always feel good when I talk to you, you take care.

Your friend,
LM

About the year 2004, we were informed of my prostate cancer and I was given 6 months to a year to live. Same year we were informed of the Prostate Cancer Communication newsletter. GOD heard our prayer – still alive! Age 89!

AS

Dear Sir,

I am sorry to hear of your financial plight. I take this opportunity of enclosing a check of $100. Many thanks to you & the men and women who have helped bring to us your very informative articles.

Every success,
JC

Please inform Dr. Moyad that the enclosed check could have been more except for the rising cost of the annual victory celebration by the Ohio State University over the team up north!

JB
OSU '61

Mr. Profit,

Enclosed is a donation to "PAACT" for use to defray general expenses as you deem necessary.

Very truly yours,
JR

Rick,

Sorry to read about the status of things. You have done a superb job of carrying on after Lloyd Ney!!

NV

Dear Molly,

Thank you for all you do.

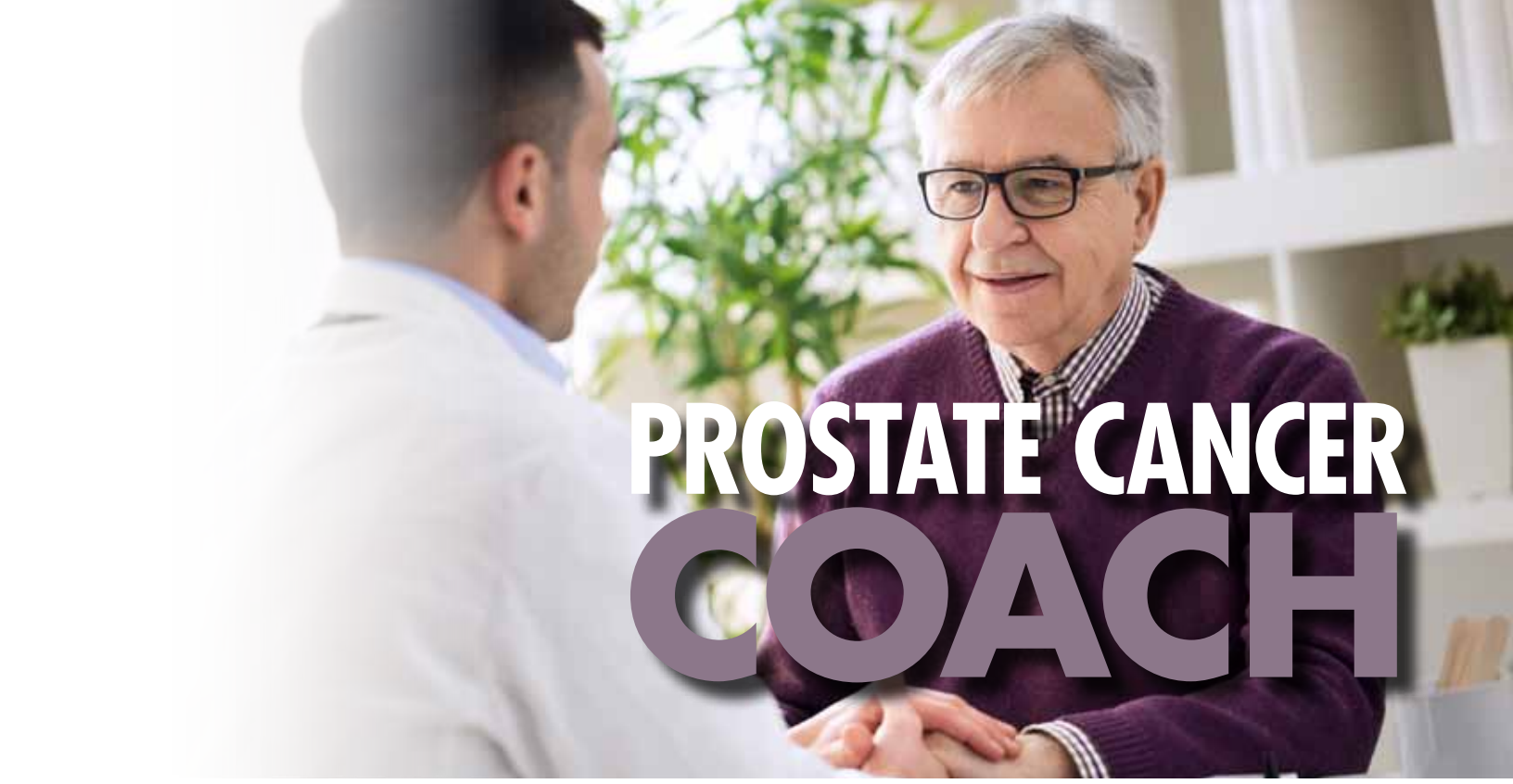
Best regards,
DB

Thank you for all you do. I will support your good work on a yearly basis.

Best regards,
DB

Your good work very much appreciated.

A survivor



PROSTATE CANCER COACH

Growing up, your parents raised you, your teachers educated you, but your Coach inspired you. They all helped make you the adult you are. When you got prostate cancer, you had to quickly gather a support team around you. First, you probably wanted to cushion the blow of hearing, "Your biopsy was positive for prostate cancer." You told your family; they comforted you. You found an US Too support group where others shared their experiences and gave you survivorship pointers. You found doctors to educate you on the current, accepted medical options for treatment. But did you look for a prostate cancer Coach?

Some of you are asking, "What's a prostate cancer Coach? Never heard of one." That's not surprising, since there aren't a lot of us. A prostate cancer Coach functions a lot like the Coach you had in high school or college. He drills you at practices, pushes you to succeed, shows you the value of teamwork, and brings you to a level of excellence as a player. What a Coach teaches you has value both on and off the field, both in and out of the field of medicine.

A prostate cancer Coach knows you well, really well, as a player and as a person, as a family man, as a professional. He knows your strengths and weaknesses, your flaws and talents, your virtues and vices. He cheers you on your good days and carries you through your bad days. A prostate cancer Coach cares about you beyond your cancer.

Today's average prostate cancer patient is more educated than ever before. Everyone should strive to become an educated patient, one who's gotten opinions from different doctors, checked the internet and other resources, and learned as much as he can on his own. Today's prostate cancer patient is driving on an information highway, at high speed, with more and more information being added every day.

Teaming with a Coach will help you balance all the medical opinions you've received against the info on the internet. It can be tricky to sort out. A prostate cancer Coach can be a liaison between all the info you've gathered and what you really want to do. He can help you prioritize treatment options according to your preferences.

What qualities should you look for in a prostate cancer Coach?

1. Optimism is definitely a quality you want in a Coach. Hope doesn't have to be dashed by statistics. Your Coach has to believe that you have what it takes to be a successful player. He should make you feel confident that you can use much of the wisdom and judgement you have acquired in life and now apply it to managing prostate cancer.

2. Being unbiased is critical. Your Coach should not push one treatment over another just because that is how he makes his living. Your Coach should not be your surgeon, your oncologist or your radiologist. Being unbiased means he is really able to weigh one treatment over another without prejudice.

3. Your Coach should be seasoned. He should have a broad range of experience in all stages of prostate cancer and in all types of treatment. He should be an expert in the field.

4. I know and respect those individuals who come out of the ranks of being patients themselves and are helping others. They are A+, self-educated students of prostate cancer, and you will find them doing a great job at support groups and, running conferences. But when we talk about prostate cancer and the decisions you will have to make, you need a professional Coach at some point. Ideally, your prostate cancer Coach should be a retired physician whose career was devoted to prostate cancer. There aren't a lot of us, but we are here.

5. Your Coach should have a philosophy of life, and a message for living a fulfilling life. He should help go beyond being a prostate cancer patient; you need to get back to living. He will teach you how to move from being an average educated patient to being in the driver's seat. My driving coach taught me much more than the mechanics of when to put my foot on the brake and when to put my foot on the gas. He taught me much more than the rules of the road, when to yield, when to pass. He taught me that my attitude matters, that driving requires respect towards other drivers. He taught me that when I get there isn't as important as getting there safely. Your prostate cancer Coach will teach you much more than the data points of disease; he will teach you the wisdom of "minimum intervention, but maximum surveillance."

6. Availability is another key. Every doctor in clinical practice sees 20-30 patients a day. A prostate cancer Coach might be on the phone or internet with one patient a day. You have his attention and his full focus.

7. Accessibility. In the age of information technology, I am not confined to a brick and mortar office. I talk with people via web meetings, smart phone programs, emails, the Cloud. There are so many ways to have a meeting. I have done coaching with people all over the U.S. and all over the world. A Coach can talk to you, face to face, anywhere, anytime. We have even developed a web based program, the Medical Smart Chart, to access your medical records anywhere, anytime. We can bring any specific lab report that we want to discuss up on the screen and highlight the text we want to focus on. We record our coaching calls and send you an audio email to listen to again, just as major league coaches film their games and practices to analyze details of the plays and the players. Find a Coach who is technology proficient; it makes a difference.

When do you need to add a prostate cancer Coach to your team?

Certainly, when you are <u>newly diagnosed</u>. You need to educate yourself in the language of prostate cancer. You need to form your own philosophy of treatment. Do you want a cure or disease containment? Are you risk averse or willing to gamble? Is maintaining quality of life a high priority or a low priority? A Coach for a newly diagnosed individual will tutor you and bring you up to speed very quickly.

The initial diagnosis period is the time to leave no stone unturned in your diagnostic, risk-assessment phase. Before you go to war, you need to know every little bit of information about the enemy, where he is camped, what weapons he has, how strong his numbers are, who his commanders are. The same holds true for prostate cancer. First, you scout and gather intelligence, then you fight.

Another time to huddle with a Coach is <u>when there is a change in your medical situation</u>, for example, a rise in PSA, a change in a bone scan or MRI, a conflicting opinion between two physicians. It's easier to make small adjustments, small changes as you go along than to make a huge turn-around after you're lost deep in the woods.

There are times when you want <u>a fresh set of eyes to look at your situation and make suggestions, or think outside the box</u>. Sure, when you drive, any GPS will give you directions, but every GPS gives the same directions, regardless of who the driver is. In much the same way, the medical establishment gives a standard set of options to every cancer patient. Having a Coach at your side will personalize your GPS instructions and make the driving easier.

There are times <u>when you want to push the envelope</u> of standard care; you want to know what clinical trials or new treatments there are. That's also the role of a Coach; he will be well versed on non-standard treatments and on clinical trials.

There are times when you want a fresh set of eyes to look at your situation and make suggestions, or think outside the box.

There are times when you want to validate some information you found on the internet. <u>A Coach can help you sort out information from misinformation.</u> The internet is an information highway, but sometimes, the hardest part is figuring out where to exit and where to merge or which turn to take. It's easy to get lost.

And yes, there are times <u>when you simply need reassurance</u>. Are you are on the right track, are you are in a danger zone, has the window of opportunity to pick a definitive treatment closed? This is especially true for patients on Active Surveillance. The less you do in terms of treatment, the more you need to monitor your landmarks to be sure you're still on the road and not headed for a ditch. Don't dismiss the human need for reassurance; we all need and deserve it, and that especially applies when you have cancer.

When the moment comes and you are <u>ready to decide on a definitive treatment</u>, call a Coach before you finalize the decision. So many times, I have said, "I wish you had called me <u>before</u> you decided to do this or that." When you buy a car, you take it to a mechanic to make sure it's not about to fall apart. When you buy a house, you get an appraiser and you do a thorough home inspection. Choosing a cancer treatment is much more important than a car or a house; it will have an impact on the rest of your life. Yet the majority of people haven't asked an unbiased expert to review and approve their treatment decision.

Talk to your family, your friends, your support group fellows, your internist, your surgeon, your radiologist, and your specialists. But after you see all the doctors and get all opinions, before you make your final decision, get a Coach.

For more information on a prostate cancer coach, please contact Israel Barken, MD at 619-906-4700 or write him at info@pcref.org.

Note from PAACT: *This is an ideal scenario/relationship for patients to have with their treating medical physician, although this is not always possible to receive because of a medical physician's schedule or by you financially. Dr. Barken fills a void from a doctor's perspective. PAACT and other non-profits are similar, but focus their attention primarily on the patient, treatments available and physician's and centers of excellence for patients, all at no cost, voluntary donations only.

JUDY BRYANT

Aunt of President Richard H Profit, Jr.

Baby Sister of Co-Founder Janet Ney

Judith "Judy" Eileen Bryant, age 72, of Kentwood peacefully went home to be with Jesus on Monday, February 27, 2017, surrounded by her sons. She was preceded in death by her husband, Robert D. Bryant. She will be lovingly remembered by her sons, Dale (Sheila) Bryant, Randall (Sonya) Bryant; dear, long-time friend, John Johnson; grandchildren, Jessica, Emily, Joshua, Maria, David, Noah, Alexxa, Kylla, Owenn; sisters, Janet Ney, Rae Hensel, Marilyn Perez; special nephew and niece, Rick and Becky Profit; dear friends, Beth and Herre Komdeur; "adopted daughter", Cheryl Lloyd; and many other cousins, nieces, nephews and good friends.

Please don't grieve for me,
as this is a celebration, you see.
The Lord my Savior has called me home,
and now I'm free.

I stayed as long as I could stay.
I enjoyed my time to laugh, to love,
my late night dance party, and all my years of play;
the overwhelming joy and peace
the evening of my last day.
Oh, and I know Wayne Newton, by the way...

If my parting has left a void,
fill it with remembered joys.
Please don't be burdened with sorrow,
let the sunshine which I loved fill you with tomorrow.

And know that I have no more pain;
I'm in paradise dancing with my Bob,
and yes, we're listening o Wayne.

My life's been full and I savored so much.
Now I'm your angel, so be looking for my special touch.
My life was blessed with an amazing grace,
and although you may think it was brief,
please don't lengthen it with undue grief.

Lift up your hearts and let's celebrate;
I'm in heaven with JESUS now,
and there's nothing more great.

Written by son Randall Bryant

ACKNOWLEDGEMENTS OF CONTRIBUTIONS

July 1, 2016 through December 31, 2016

*(YOUR NAME WILL APPEAR BELOW IF WE DEPOSITED YOUR DONATION BETWEEN THE **ABOVE DATES**)*

MEMORIAL CONTRIBUTIONS

In Loving Memory of ***Lloyd J Ney, Sr.,***
Founder of PAACT, INC.,
Grand Rapids, MI

In Loving Memory of ***Lloyd***

Dr. Duke Bahn
George C Montgomery, Jr.
Ronald Hankins
Leonard Stevens

In Loving Memory of Dr. Fred Lee
Harold Horneffer

In Loving Memory of Harold Abramson
Gloria Abramson

In Loving Memory of My Late Husband, Don Zank
Lynne Zank

In Loving Memory of Rev. Paul Soukup
Sandra Soukup

In Loving Memory of Walter Plegel
Maureen Plegel

In Loving Memory of My Late Husband, Jan Zlotnick
Jeanette Lebell

In Loving Memory of Israel Fisher
Ted Fisher

In Loving Memory of My Dad, Loren Johnson
Christine Smith

In Loving Memory of My Father
Jeremy D Michaels, Esq

In Loving Memory of John P Pavacic
Carol Dubin

In Loving Memory of David Neimark and Anne Steim
Sheridan & Dana Neimark

In Loving Memory of Lee Crawford
Informed Prostate Cancer Support Group, Inc

In Loving Memory of Dave Lageschulte
Ed & Marsha Droste

In Loving Honor of Steven Fleming
Phyllis J Edmundson

Contributions
($1,000 and Above)
Hayden, Jerry
Julian Braun Charitable Trust
Mabry, Fred
Mackey, Robert
Michael & Ina Korek Foundation
Ryan, William
US-TOO PC Support Group, Coram, NY

Contributions
($500 to $999)
Albrecht, Ted
Freuler, Anthony
Gunnin, John
Hudspeth, Jack
Leibowitz, Dr. Bob
Montgomery, Allen
Riederer, Richard
Swindell, Murray
Villars, Ashton
Vogler, John

Contributions
($100 to $499)
Anonymous
Ayer, Donald
Baker, Charlie
Bartholomew, Anthony
Barton, William
Beizer, Lance
Berg, Henry
Berger, Richard
Bialek, Fred
Black, William
Borer, Paul
Bothwell, Bruce
Boundy, Bruce
Bowen, James
Brecht, Marshal
Bucy, M Peyton
Buhl, Frank
Burkey, Gary
Byrne, Donald
Carlstedt, Richard
Cataldo, John
Cline, Robert
Cohen, Irwin
Copeland, William
Davies, Ronald
Davis, George
Degouff, John
Derris, David
Ern, Gary
Evans, Cynthia
Ford, Ralph
Fuchs, David
Gaudioso, Robert
Geissinger, Lloyd
Goodson, James
Grassano, Alan
Green, Ronald
Greenblatt, Elias
Gunderson, James
Harris, John
Hawvermale, Herbert
Heffron, Charles
Jackson, George
Jezek, Ray
Juday, Bernard
Kenworthy, David
Kimura, Kei
Korstanje, John
Lacour, Lucien
Lair, Richard
Larson, Mary
Lawrence, Virgil
LeBlanc, Michael
Lewis, Fred
Lilley, Richard
Magee, Edward
Majka, Joseph
Mather, Hal
McGovern, Robert
McKenny, Louis
Men to Men – Poughkeepsie, NY
Murphy, Edward
Nero, Morrie
Oklahoma City Community Foundation
Pavlick, Doug
Pepe, Richard
Petronko, Ronald
Purdy, Peter
Rea, Thomas
Richards, James

Richardson, Charles
Robb, Walter
Robisch, Victor
Royston, Charles
Rubinstein, Jack
Rumford, Jim
Sarna, Walter
Schlicksup, Edward
Schmitt, Richard
Shaline, John
Shimer, Alan
Shollin, Thomas
Silva, Lonnie
Slipher, Earl
Smyers, William
Snyder, William
Stone, Jeremy
Strickland, John
Sullivan, Neil J
Targ, Russell
Teets, Jeff
Trueblood, Harry
Truist
Underwood, A.J.
Wahtera, Edward
Ward, T.A.
Weatherly, Ted
West, Stuart
Williamson, Lee
Wrubel, Irwin
Zaboji, George
Zayon, Seymour

PAACT Membership ($50 to $99)

Aaronson, David
Agresti, Louis
Altiere, Elmer
Anderson, D.C.
Anonymous
Bailey, Theodore
Baker, Eugene
Batista, Richard
Bayless, Gary
Blake, Charles
Block, Louis
Brabner, Richard
Bubel, Bob
Busch, Michael
Carlson, Edward
Clyma, Frank
Coles, Tom
Cummings, Merlyn
Davis, Dennis
Degnan, Patrick
Denney, James
Dohse, Gunther
Donnellan, Lloyd
Eldridge, David
Farmer, Thomas
Fernicola, William
Fletcher, Herbert
Geier, Frank
Gifford, Steven
Gluck, Sidney
Green, Gerald
Greilsamer, Calvin
Gritter, John
Hannum, Terry
Hastie, John
Hegyi, Dennis
Heintz, Jeffrey
Higdon, Mark
Hobbs, Leonard
Hone, John
Hoppe, Lee
Horylev, Walter
Hutchinson, Roy
Hyatt, Stuart
Ibarria, Frank
Jacobson, James
Jobsky, Richard
Kalos, Peter
Kavanagh, Donald
Keck, Robert
Kim, Gary
Kortebein, Stu
Kusnirik, Robert
Labuzeta, James
Largman, Ted
Leath, James
Linde, Ronald
Lolicata, Paul
Lott, Adriano
Magic, Michael
Mark, Robert
Martin, Troy
Maxwell, Joseph
McKelvey, Wesley
McNaught, Richard
Merkt, Jerome
Merrill, Richard
Mikkelson, Daniel
Miller, Donald
Morris, Charles
Morrison, James
Neuner, Louis
Nixon, Robert
Noteware, Gary
Olmstead, Stewart
Ott, David
Patterson, Brent
Pausig, Ronald
Phillips, Bundy
Pontius, Jack
Powley, Carl
Reinhard, Guido
Robertson, Gary
Rowe, Robert
Schmidt, Richard
Schoenfeld, Jay
Secrist, C Robert
Sherwood, Roger
Slagle, John
Smith, David
Smith, Jack
Snyder, William
Spriggs, Mordecai
Staly, Tom
Stewart, John
Steyer, Joseph
Strathy, Robert
Stump, Pat
Suhr, James
Swisher, Robert
Thompson, Paul
Thompson, Richard
Tiller, John
Unice, Robert
Vanecek, Michael
Vardaro, Christina
Veale, Donald
Wakely, William
Warner, Edward
Wissmer, John
Yaffe, Gerald
Youmans, Joseph
Young, Joseph
Young, Robert
Zigler, Vernon
Zimmerman, Ned

Miscellaneous Contributions (less than $50)

Abbott, Steve
Allshouse, Gary
Anonymous
Betancourt, Joe
Ciavolella, Antonio
Cohen, Martin
Criley, David
Davis, Robert
Derbabian, George
Dreier, John
Eason, Francis
Filippello, Vincent
Ganas, Steven
Hays, Henry
Hofstatter, Alfred
Hummel, Richard
Jacobson, Jerome
Jewell, Walter
Johnson, H Mark
Kapso, Howard
Keniry, John
Koenig, Jack
Korff, Marvin
Kubecka, Paul
Kuhn, Edwin
Kurland, Leonard
Lee, Jeff
Loos, Jack
Mackey, Stanley
Manarite, Jan
Maples, R Wayne
Markowski, Gary
Mazurek, Robert
McCann, Alfred
McCarthy, Michael
McElroy, James
Middleton, Byron
Parker, Ted
Piersiak, Robert
Pitt, John
Rand, Leonard
Ruble, Robert
Sandstrom, Carl
Sizer, John
Solazzo, Dominic
Swiggart, Hurst
Vance, Norman
Vickers, Earl
Warren, Carl
Wihlen, John
Woosnam, Thomas

Contributions by State

Alabama 1
Alaska 0
Arizona.....15
Arkansas.....1
California 54
Colorado.....14
Connecticut 8
Delaware 0
Florida.....31
Georgia.....4
Hawaii 2
Idaho 0
Illinois 7
Indiana.....2
Iowa.....0
Kansas 0
Kentucky 1
Louisiana.....0
Maine 0
Maryland 8
Massachusetts 2
Michigan 38
Minnesota.....1
Mississippi 1
Missouri 2
Montana 1
Nebraska 0
Nevada 4
New Hampshire 5
New Jersey 14
New Mexico.....0
New York 24
N Carolina.....7
N Dakota 0
Ohio.....9
Oklahoma.....3
Oregon.....4
Pennsylvania 9
Rhode Island 0
S Carolina.....2
S Dakota.....0
Tennessee 3
Texas 2
Utah.....0
Vermont.....2
Virginia.....4
Washington.....13
West Virginia.....1
Wisconsin.....7
Wyoming.....1
Washington DC 1
Virgin Islands 0

Foreign Patrons

Australia
Bulgaria
Canada
Cayman Islands
China
Costa Rica
Denmark
England
France
Germany
Grand Cayman Islands
India
Indonesia
Isle of Man
Israel
Luxembourg
Mexico
Netherlands
New Zealand
Portugal
Saudi Arabia
Scotland
Slovenia
Rep of South Africa
Spain
Sudan
Uganda
United Kingdom

FINANCIAL SUMMARY REPORT

January 1, 2016 through December 31, 2016

	GENERAL FUND
REVENUES RECEIVED -	
Membership Contributions	51,434.83
Memorial Income	4,198.00
Trusts & Bequests	9,588.00
Grant Money	80,000.00
Goodsearch Earnings	0.00
Stipend	600.00
Investment Income	5,913.92
Miscellaneous Incomew	275.00
Total Revenues	**152,009.75**
EXPENDITURES-	
Loss/Disposal of Fixed Asset	3,996.05
Depreciation Expense	196.34
Employee Wages	159,464.29
Payroll Taxes	12,593.22
Insurance (Health, House, Workman's Compensation)	40,853.46
Outside Services, Labor	2,415.00
Rent	13,200.00
Meals, Motel, and Transportation	13,787.34
Auto Expense	3,396.67
Printing	33,003.20
Postage and Delivery	21,301.53
Telephone	6,271.08
Service Plans/Licenses & Permits	6,937.27
Computers - Tech Support	4,300.21
Program Expense-Conference Exhibit Fees	2,770.19
Office and Computer Supplies	2,041.55
Utilities - Refuse	400.80
Repairs (Building, Equipment)	1,436.94
Miscellaneous	5,277.38
Total Expenditures	**333,642.52**
Assets:	
Checking Account	22,125.70
Petty Cash	50.00
Savings Account	29.63
Certificates of Deposit, Stocks, and Bonds	222,161.10
Equipment	3,958.13
Net Assets:	**248,324.56**
Clinical Research Endowment/Money Market Funds	**240,101.01**

PAACT INC
Patient Advocates for Advanced Cancer Treatments
11555 Jadon Ct NE, Sparta, MI 49345-8155
PO Box 45 • Sparta, MI 49345
Phone: (844) PAACT4U • (616) 453-1477
Fax: (616) 453-1846
paact@paactusa.org
www.paactusa.org or
www.paact.help

SPRING 2017

CHANGE SERVICE REQUESTED

NONPROFIT ORG
U.S. POSTAGE
PAID
GRAND RAPIDS, MI
PERMIT NO. 875

Join Us on Facebook!

PAACT MEMBERSHIP FORM

Name: _____ Birthdate: / / _____

Address: _____

City: _____ St/Province: _____ Postal Code: _____

Telephone HM: _____ WK: _____ Fax: _____

E-Mail: _____

Other: _____

ANNUAL MEMBERSHIP CLASSIFICATION

- ☐ Patient $55
- ☐ Advocate $55
- ☐ Professional $100
- ☐ Other ..... $_____
- ☐ Donor $500
- ☐ Sponsor $1000
- ☐ Corporate $5000
- ☐ Anonymous ..... $_____
- ☐ Include me as a PAACT member, although I currently cannot contribute_____

Tribute gifts support the daily operations of PAACT, Inc., by furnishing PC patients, doctors and advocates with the latest information available on the methods of detection, diagnostic procedures, evaluation and treatments for prostate cancer. We also participate in matching gift programs and United Way. For more information contact us at (844) PAACT4U • (616) 453-1477.

☐ **Check Enclosed** ☐ **Charge to my credit card (below):** ☐ **MC** ☐ **VISA** ☐ **Discover** ☐ **American Express**

Enclosed is $ _____, In memory of Lloyd J. Ney, Sr.
Enclosed is $ _____, for PAACT's general operation expenses.
Enclosed is $ _____, I wish to remain anonymous.
In Memory of _____

Please send acknowledgement card to:
Name _____

Address _____

City _____ **State** _____ **Zip** _____

Account Number: _____ 3 digit CVV/ Security Code ☐☐☐ **Amount $** _____

Signature: _____ **Expiration Date:** _____