REMINDER

ANNUAL PHCSG MEMBERSHIP $20

Join our Monthly meetings on the third Tuesday (Feb – Dec) 10am – 12:30pm

EFT Payments to:
Prostate Heidelberg CSG
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Prostate Heidelberg

February 2021 Issue 203

For Education, Information and Support

Meeting Hall: Ivanhoe Uniting Church 19 Seddon Street, Ivanhoe
POB 241 Ivanhoe Victoria 3079
Email: prostateheidelberg@gmail.com
Website: www.prostateheidelberg.info

Next PHCSG Meeting – Tues 16 Feb (via Zoom)

10am – 12:30pm

Join Zoom Meeting

Copy link and paste into your browser

https://us02web.zoom.us/j/83637266935?pwd=eGhnY3lFV0l1eTZVSjl5S2lFNjQ3QT09

Meeting ID: 836 3726 6935
Passcode: 475818

Prostate Heidelberg Cancer Support Group

PHCSG provides information, education and support for those affected by Prostate Cancer. At our meetings we are committed to:

- showing respect to members, speakers and guests
- allowing members to speak without interruption
- respecting confidentiality

PHCSG's First Meeting for 2021

We intend to recommence face-to-face meetings in March but also hope to continue to invite members and guest speakers via Zoom. This month's meeting will be a Zoom catchup with members.

A timely reminder that the 2021 PHCSG Membership Fees are due and many thanks to those of you who have already paid.

In this month's newsletter we highlight:

- 2 Austin Health's 1000 min Challenge & the advantages of Coffee
- 3 Our Biological Clock
- 4 Statins Tied to Better Outcomes
- 5 What's New in Inflammation
- 6 New PC Management Techniques
- 7 About the Patch Trial
- 8 Eating a Colourful Diet
- 9 Dose Painting
- 10 Advancement in Focal Therapy
- 11 & 12 Trials

Photographs this month by Clare Waller. *Silo Art Trail, Victoria*.

If there is anything you want to talk through in relation to your treatment or wellbeing please don't hesitate to ring:

Max Shub	0413 777 342
Mike Waller	0438 616 240
Michael Meszaros	0407 837 538

Improving the health of our community, together

1 – 31 March 2021

Walk, run, ride, roll, swim…choose an activity you enjoy that gets your heart beating faster and muscles working harder for just over 30 minutes a day. Track your activity on our website and be rewarded along the way!
Austin Health's 1000 Minute Challenge is the best way to show support for your healthcare heroes. By raising funds for additional medical equipment, we can do more for you and your loved ones, plus you'll be improving your own health and fitness. It's a win-win!

YOU COULD WIN SOME GREAT PRIZES TOO!

You could win a prize simply by signing up before 14 February! We have loads of prizes and incentives up for grabs and if you're lucky, you could win more than one! https://1000minutechallenge.org.au

Coffee Consumption Tied to Reduced Prostate Cancer Risk, Study Shows

Nick Brown | January 12, 2021

Coffee consumption may be linked to lower risk of developing prostate cancer, according to a review of 16 different studies involving more than 1 million men.

The study also suggested that the more coffee men consume, the lower their risk of developing prostate cancer, noting a "relative risk" reduction of about 1% per each additional daily cup.

Conducted by researchers in China, the review explored results from studies that were originally carried out in North America (7), Europe (7) and Japan (2) up to September 2020. Each of the studies noted coffee consumption as well as various health outcomes among the cohorts. Of the 1.08 million men from which data was gathered, more than 57,000 developed prostate cancer.

Within those studies, researchers identified the highest and lowest coffee consumption categories, with the highest ranging from "two or more" to "nine or more" cups per day. When those highest consumption categories were viewed collectively, they showed a 9% reduction in the development of colon cancer, with 1% attributed to additional cups.

Applying the analysis to different grades of prostate cancer, the highest consumption category resulted in a 7% lower risk of localized prostate cancer, and a 12-16% lower risk for advanced and fatal prostate cancer.

While noting that the design of the original studies may skew such pooled risk estimates, and that the variables of coffee consumption reporting such as drink type or brewing method were not consistent study to study, the paper's authors did suggest that coffee's potential to mitigate prostate cancer risk may have some biological explanations, including the drink's anti-inflammatory and antioxidant properties.

"This study suggests that increased coffee consumption may be associated with a reduced risk of prostate cancer," they wrote. "Further research is still warranted to explore the underlying mechanisms and active compounds in coffee."

The research follows a years-long period of generally good news for coffee as it relates to certain types of cancers in humans. In 2017, a landmark study found that coffee may cut liver cancer risk by as much as half. Late last year, research funded by the National Cancer Institute (U.S.) found that coffee consumption has been linked to improved outcomes for colon cancer patients.

After a nearly decade-long legal battle, a California court in 2019 officially exempted coffee from the list of products requiring Prop 65 cancer warnings; and the American Cancer Society's latest dietary guidelines — used as a resource by physicians — noted coffee's effectiveness in preventing certain types of cancers.

The complete study on coffee and prostate cancer was published yesterday in BMJ.

An unexpected, and novel, target for prostate cancer: Our biological clock

Researchers find that CRY-1, a regulator of circadian rhythms, promotes tumor progression by altering DNA repair

Source: https://www.sciencedaily.com/releases/2021/01/210115091354.html

Our biological or circadian clock synchronizes all our bodily processes to the natural rhythms of light and dark. It's no wonder then that disrupting the clock can wreak havoc on our body. In fact, studies have shown that when circadian rhythms are disturbed through sleep deprivation, jet lag, or shift work, there is an increased incidence of some cancers including prostate cancer, which is the second leading cause of cancer death for men in the U.S. With an urgent need to develop novel therapeutic targets for prostate cancer, researchers at the Sidney Kimmel Cancer -- Jefferson Health (SKCC) explored the circadian clock and found an unexpected role for the clock gene CRY-1 in cancer progression. The study was published on January 15th in *Nature Communications*.

"When we analyzed human cancer data, the circadian factor CRY-1 was found to increase in late stage prostate cancers, and is strongly associated with poor outcomes," explains Karen Knudsen, MBA PhD, executive vice president of oncology services for Jefferson Health and enterprise director of SKCC, and senior author of the study. "However, the role CRY-1 in human cancers has not been explored."

A common therapy for prostate cancer involves suppressing the male hormone androgen and/or the androgen receptor, as prostate tumors require androgens to develop and progress to advanced disease. With their collaborators in the U.S. and Europe, the researchers found that CRY-1 is induced by the androgen receptor in prostate tumor tissue obtained from patients, thus explaining in part the high levels of CRY-1 observed in human disease.

"This was a clear indication of CRY-1's link to prostate cancer," says Ayesha Shafi, PhD, a postdoctoral researcher in Dr. Knudsen's lab and first author of the study. "As we looked further into the role of CRY1, we unexpectedly found that the circadian factor was altering the way that cancer cells repair DNA."

Cancer treatments aim to damage the DNA in cancer cells and cause defects in repair mechanisms; eventually the cells self-destruct when the damage is severe. The researchers probed CRY-1's possible role in DNA repair in cultured cells, animal models and tissue harvested from prostate cancer patients. They first induced DNA damage by exposing cancer cells to radiation and found that CRY-1 levels became elevated, indicating that it was responding to this type of damage. They also found that CRY-1 directly regulates the availability of factors essential for the DNA repair process, and alters the means by which cancer cells respond to DNA damage. The findings suggest that CRY-1 may offer a protective effect against damaging therapies.

"The fact that CRY-1 is elevated in late-stage prostate cancer may explain why androgen-targeting treatments become ineffective at those later stages," says Dr. Shafi. "It also tells us that if a tumor has high levels of CRY-1, DNA repair targeting treatments may be less effective for them."

"Not only have we outlined a role for CRY-1 outside of its canonical function in circadian rhythms, Dr. Shafi's findings are the first to reveal the means by which CRY1 contributes to aggressive disease," adds Dr. Knudsen. "It's notable that the pro-tumor functions of CRY1 may be viable targets to treat prostate cancer, and this is a direction that Dr. Shafi's future work will explore."

Looking ahead, the team plans to explore how best to target and block CRY-1 and what other existing therapies may work synergistically to hinder DNA repair in prostate cancer cells. They also plan to study more circadian rhythm genes and determine how circadian disruption may affect cancer treatment.

"It's been shown that circadian disruptions can affect efficacy of treatment, but also that aligning treatment with the body's natural rhythms or giving therapy at certain times of the day can be beneficial," explains Dr. Knudsen. "Our findings open up a multitude of important research questions exploring the link between the circadian clock and cancer."

This work was supported by a Young Investigator Award and Challenge Award from the Prostate Cancer Foundation to Dr. Shafi and Dr. Knudsen respectively, NCI grant F99CA212225, NCI R01-CA182569, The KWF Dutch Cancer Society, SKCC Support Grant (5P30CA056036). Drs. Shafi and Knudsen thank lead collaborators and their research groups -- Dr. Felix Feng, Dr. Michael Brunner, and Dr. Wilbert Zwart. The authors report no conflict of interest.

Materials provided by Thomas Jefferson University. Original written by Karuna Meda. *Note: Content may be edited for style and length.*

Statins Tied to Better Outcomes in Men With Prostate Cancer Starting Androgen Deprivation

Source:
Reuters Health 11 January 2021

Statin therapy is associated with improved outcomes in men initiating androgen-deprivation therapy (ADT) for prostate cancer (PCa), new research suggests.

“Interest in statins as a potential chemopreventive agent has grown, and there exist biological rationale, and laboratory and clinical data supporting our findings,” the study team writes in a manuscript published online in European Urology. Observational studies examining statin use and PCa risk have shown a modest but statistically significant overall risk reduction and a more clinically meaningful reduction in advanced or high-grade disease. Whether statin use at the time of primary treatment is associated with improved outcomes is unclear.

To evaluate the association between statin use and outcomes, Dr. Robert Hamilton with Princess Margaret Cancer Center in Toronto, Canada, and colleagues did a post hoc secondary analysis of a randomized controlled trial of men initiating intermittent androgen deprivation (IAD) versus continuous ADT.

The 1,364 men in the trial had PSA levels >3 ng/mL more than one year after primary/salvage radiotherapy (RT). The 585 (43%) statin users were younger than non-statin users (72.7 vs. 73.8 years, P=0.001) and were less likely to have PSA >15 ng/ mL (20 vs. 25%, P=0.04, a statistically significant difference). After adjusting for potential confounders, statin therapy was associated with a 36% reduction in risk of death (hazard ratio [HR], 0.64; 95% confidence interval [CI], 0.53-0.78) and a 35% reduction in risk of PCa-specific death (HR, 0.65; 95% CI, 0.48-0.87, P=0.004, a statistically significant difference).

As an exploratory endpoint, the researchers examined whether statin use was associated with time off ADT among 681 men in the IAD group. They found that statin users in the IAD group had longer time off treatment (P=0.06, not a statistically significant difference).

The authors say limitations of their study include the potential for residual confounding between statin users and nonusers, and confounding by indication. They conclude, “This study supports the benefit of statins in men on ADT. A prospective trial is warranted.”

PLEASE NOTE:
Treatments may vary in Australia. Please ensure you discuss your diagnosis and treatment options with your consulting specialist

What's New in Inflammation & Prostate Cancer?

Source: https://www.pcf.org/c/whats-new-in-inflammation-and-prostate-cancer/
Janet Farrar Worthington

Anti-Inflammatory Drugs

If inflammation can lead to prostate cancer, could anti-inflammatory agents help protect against its? Johns Hopkins epidemiologist and friend to PCF Elizabeth Platz, Sc.D., has been intrigued by this possibility for many years. She is senior author of a new study on the use of aspirin and statins, published in *Cancer Prevention Research*.

The study, of men in the placebo arm of the Prostate Cancer Prevention Trial, doesn't answer this question once and for all – but adds more weight to the idea that, for lowering the risk of developing potentially fatal prostate cancer, fighting inflammation is a good thing.

Evidence from observational studies has suggested that when taken regularly over time, aspirin may lower the risk of prostate cancer. These drugs block enzymes that play a key role in the body's inflammatory response. Other studies have linked long-term use of statins, prescription drugs that are used to lower cholesterol but that also are anti-inflammatory, to a lower risk of advanced and metastatic prostate cancer.

In this most recent study, the investigators looked for inflammation markers in benign prostate tissue samples. "We compared the use aspirin and statins with the presence and extent of inflammation in the prostate tissue," says Platz. They also looked at prostate biopsy slides for the presence of certain immune cells that are involved in inflammation.

"Of 357 men, 61 percent reported aspirin use, and 32 percent reported statin use," Platz continues. "Aspirin users were more likely to have low FoxP3, a T regulatory cell marker, and statin users were more likely to have a low CD68, a macrophage marker." "Our results suggest these medications may alter the immune environment of the prostate. A next step is to determine whether these immune alterations may underlie the epidemiologic observations that taking an aspirin or statin may protect against getting advanced prostate cancer, and dying from it."

Prostate Cancer Loves Fats

Here's some more recent research out of Johns Hopkins, a neat bit of basic science that may help explain the findings of Platz's recent study. "Our work is mechanistic," says investigator Marikki Laiho, M.D., Ph.D., director of the Division of Molecular Radiation Sciences, "and provides insight into how the tumor microenvironment senses the excess load of lipids (fats). Diet and statins obviously relate to the amount and regulation of the lipids, and have shown those clear correlations to prostate cancer. However, we need to understand *why* to be able to correct the problem. Our work provides at least one explanation how the lipids fuel cancer." One step "was just to feed the prostate cancer cells with cholesterol, which made them more invasive."

It turns out that even on a cellular level, prostate cancer gravitates to its own kind of junk food – the tiny version of deep-fried Oreos with a side of chili cheese fries. Laiho and colleagues have just figured out *how* the body enables prostate cancer's terrible diet.

The key is a lipid-regulating protein called CAVIN1, the scientists reported in the journal, *Molecular Cancer Research*. In lab studies, when CAVIN1 was removed from cells in and around the prostate tumor, the fatty acid that was in those cells spilled into the tumor's microenvironment. The effect on prostate cancer cells was dramatic: the cancer cells soaked up the lipids, which then acted as turbo fuel to make the cancer spread more aggressively.

"In every prostate cancer cell line we tested," says research fellow Jin-Yih Low, Ph.D., the study's first author, "tumor cells universally had an appetite for the lipids, using them to strengthen the protective membrane around the cell, synthesize proteins and make testosterone to support and fuel the cancer's growth. The tumor cells then behaved more aggressively, exhibiting invasive and metastatic behavior. Just having access to the lipids gave the tumor cells more power; the tumor's behavior changed."

But wait! There's more: nearby cells changed, too. Deprived of their regular type of lipids, normal stromal cells started to churn out inflammatory molecules, adding fuel of their own to the fire.

Laiho's team then confirmed their findings in mouse models, comparing tumors with and without CAVIN1 in the stromal cells. In the mice, Laiho says, "although the presence or absence of CAVIN1 did not affect the speed of tumor growth, lack of CAVIN1 definitely caused the cancer to spread. All of the mice with tumors that lacked CAVIN1 had a twofold to fivefold increase in metastasis. The tumors also had a fortyfold to hundredfold increase in lipids and inflammatory cells."

The investigators were surprised at these results, Laiho adds. "We suspected CAVIN1 was important, but we didn't realize how important. The tumor's microenvironment matters, and the amount of lipids matters a lot." Just changing the level of lipids "created a situation of rampant metastasis."

What could come from this research? One possibility is development of a new biomarker: a loss of CAVIN1 in local or locally advanced cancer, for example, could signal a higher risk of metastasis. The next step is to understand more about the inflammatory process in the tumor's microenvironment. "We want to understand why the inflammation brings in macrophages, immune cells that further exacerbate the inflammatory process, instead of T cells, which should attack the cancer."

New Prostate Cancer Management Techniques

Source:
Forward (Abstract) from Professor Mark Emberton, M.D., FRCS (Urol) University College London Hospital:

Despite high-profile technical developments that have undoubtedly refined the process of surgery and radio- therapy as treatments for prostate cancer, the underlying principles of care have not really changed since the two approaches to treatment were first developed. Both aim to eradicate all prostate tissue – one by complete removal, the other by exposure to ionizing radiation. Indeed, a recent randomized trial of robotic assisted versus traditional prostatectomy demonstrated that the two approaches to care resulted in very similar outcomes. While principles of care have not changed, the advent of modern imaging and genomic technologies has opened the door to an era of precision diagnosis, ultimately enabling a paradigm shift to individualized and personalized treatments.

Switching our therapeutic target from the host organ to the cancer within it represents the first real departure from standard care since Hugh Hampton-Young undertook the first prostatectomy at Johns Hopkins over 100 years ago. It is this advancement in modern imaging enabling a transition from traditional whole organ treatment to a targeted one based on the clinical significance of the diagnosis and that aims to preserve healthy tissue and patient quality of life that is the subject of this white paper. The timing of this white paper is important. It comes very soon after the publication of a landmark study demonstrating that our traditional risk-stratification methods – prostate biopsy that is blind to tumor location – are wanting and that modern magnetic resonance imaging (MRI) doubles the accuracy of diagnosis. MRI provides the ability to 'see' prostate cancer and therefore derive its volume and location – two attributes that have so far evaded us – and thus permitted the departure from the conventional whole gland therapies. It is important to indicate why this departure from our traditional approach to therapy is needed. There are two principal reasons.

First, is the need to reduce the harms associated with treatments. The discovery that treatments preserving at least 50% of the prostate tissue as part of a prostate cancer treatment have hardly any measurable impact on genito-urinary function has been one of the big discoveries of the last decade.

Second, is the need to reduce the burden on the already stretched modern health services. These focally applied tissue-preserving approaches tend to be done as day-case procedures as a 'one-off', sometimes outside the traditional surgical operating theater.

These aspects contribute to mitigating the future economic burden of prostate cancer care as the population of men ages and therefore become more at risk. It is important to note that these tissue-preserving approaches cannot and will not be delivered in isolation. Because they are all predicated on state-of-the-art imaging they will need to be delivered as part of a multi- disciplinary care team comprising urologists, oncologist, radiologist, and application specialists. Moreover, it should be noted that despite the novelty and potential benefit that should result from implementing this new system of care, traditional approaches to treatment – active surveillance for low risk disease – and multi-modality treatment (surgery, radiotherapy, systemic agents) for higher risk disease will still be needed. Finding the exact place for each of these approaches will take us some time, but will be simplified now that the accuracy of risk-stratification has improved by the introduction of MR imaging.

Link to white paper:
http://profoundmedical.com/wp-content/uploads/2017/12/ProstateCa...

Professor Neal Kassell (University of Virginia School of Medicine) hosts a very interesting discussion on using Ultrasound to Cure Cancer.
https://youtu.be/VbDZzBcMd5E

Link to Johns Hopkins experience with new prostate cancer management techniques

https://www.inspire.com/groups/us-too-prostate-cancer/discussion...

About the Patch Trial

Source:

https://www.ctu.mrc.ac.uk/studies/all-studies/p/patch-pr09/

About the study

Prostate cancer needs the male hormone testosterone to grow. Hormone therapy is usually used to lower the level of testosterone, which helps to control the growth of the cancer. LHRH agonists (luteinizing hormone-releasing hormone agonists) are the most common type of injection or implant. The pituitary gland in the brain makes a hormone called luteinising hormone (LH), and LHRH agonists work by interfering with this action and stop the testicles making testosterone. There are several available that all work in the same way, including:

- goserelin (Zoladex®)
- leuprorelin acetate (Prostap®)
- triptorelin (Decapeptyl®)

Unfortunately, standard hormone treatment with injections or implants can cause a range of long-term side effects. They may cause bones to thin which might lead to them becoming fragile (osteoporosis) and more likely to break. They might also increase the chance of developing diabetes or heart disease.

An alternative way of giving hormone therapy is through the use of hormone patches. These patches, referred to as transdermal oestradiol, allow oestradiol (a type of hormone) to pass through the skin. Giving hormone therapy this way might be able to treat the cancer in a similar way as standard hormone therapy without causing some of these side effects.

The PATCH trial has already shown transdermal oestradiol can suppress testosterone as effectively as standard hormone therapy, while having a number of other potential benefits:

- It does not cause the bone to thin.
- Men treated with transdermal oestradiol generally reported better quality-of-life than those on hormone injections.
- Cholesterol and glucose levels increased in men on hormone injections but decreased in those on transdermal oestradiol.

The PATCH trial has been extended in order to look at whether transdermal oestradiol patches can control prostate cancer as well as standard hormone injections.

PLEASE NOTE:
Treatments may vary in Australia. Please ensure you discuss your diagnosis and treatment options with your consulting specialist

Your Best PC Diet is Colourful

Source: https://www.pcf.org/c/the-best-of-the-best-food-science-and-prostate-cancer/
Janet Farrar Worthington
21 January 2021

Janet Farrar Worthington asks Harvard epidemiologist and PCF-funded scientist Lorelei Mucci, M.P.H., Sc.D., for her expert opinion on some of the top foods for prostate cancer. Here's the rundown, in no particular order:

Your best diet is colorful: a rainbow of plant-based foods, low in sugar, and moderate in animal protein.

Extra virgin olive oil (EVOO): Yes! More than 2 tablespoons a day. Among other things, EVOO contains hydroxytyrosol, which scientists now recognize as a natural means of cancer chemoprevention. It is a powerful antioxidant, and it has been shown to protect against cancer by slowing proliferation of tumor cells and increasing apoptosis – "suicide" – of cancer cells.

Tomatoes: Yes! Especially when cooked in or drizzled with olive oil, which helps you absorb a key component of tomatoes, lycopene. "The prostate accumulates a lot of things," including cholesterol. "It accumulates lycopene. When a man eats a diet high in lycopene, for some reason, lycopene levels in the prostate go up. Lycopene makes sense biologically, because it does accumulate in the prostate. It is an antioxidant. This is one of the individual dietary components that seems pretty promising."

Don't like tomatoes? Good news: Lycopene is in watermelon and grapefruit, too!

Coffee: Yes. "Coffee is looking more and more promising. There are now a number of studies that suggest drinking coffee regularly, one to two cups a day, can help prevent aggressive forms of prostate cancer. Some studies say three to four cups offer even more of a benefit, but there's an initial benefit with one to two cups. Coffee may also lower the risk of diabetes, liver cancer, and Parkinson's disease."

Tea: Sure, what the heck. There are far fewer studies on tea than on coffee, but tea has antioxidants. People in Asia, which has less prostate cancer than the U.S., drink a lot of green tea. "Tea lowers inflammation, but has not been shown to have an effect on insulin levels." However, and this is important: it doesn't seem to *raise* your risk of getting prostate cancer.

Note: If you go to a fancy coffee shop and get a 1,500-calorie coffee with not only cream but whipped cream, and loads of sugar, or if you drink a super-sweet tea loaded with sugar or high fructose corn syrup, the effects on insulin resistance and risk of weight gain will probably cancel out the antioxidants.

Fish: Yes. "We published a meta-analysis of epidemiologic studies that looked at fish and prostate cancer death, and there was a pretty good benefit with regular consumption of fish." Particularly "dark-meat" fish rich in omega-3 fatty acids, like salmon and red snapper.

Devil's advocate: Are men healthier because they eat fish, or because if they choose fish, they're not eating a big old ribeye steak cooked in butter? Talk amongst yourselves, but *fish is not nearly as pro-inflammatory as red meat*.

Nuts: Sure. "There's not much evidence one way or another with prostate cancer death, but they really seem to lower the risk of cardiovascular disease and overall mortality." Also, if you're eating a handful of nuts as a snack, maybe you won't be eating a bag of chips. "In one of our studies, we observed that substituting 10 percent of calories from carbohydrates for calories from healthy, plant-based fat (nuts) was associated with a 29-percent lower risk of prostate cancer death, and a 26-percent lower risk of all-cause death," says Chan.

Pasta: In moderation. However, non-traditional pastas, made from cauliflower or chick peas, are another way to sneak in vegetables. They may also help you manage your weight. "Excess body weight, particularly the visceral fat around the abdomen, is associated with worst outcomes from prostate cancer. Anything men can do to help reduce their weight – limiting bread and pasta, and increasing things like cauliflower pasta and vegetable intake overall – is beneficial."

Charred meat: Try to limit it. When meat is charred, it makes a chemical compound called PhIP, that is a known carcinogen. Even worse: those beautiful grill marks combined with a pro-inflammatory food, like red or processed meat.

Soy: sure. "Consumption of soy is much higher in Asia, where the incidence of prostate cancer death is lower. Soy is probably part of a strategy for maintaining healthy weight, and it's a way of replacing red meat. Does it lower prostate cancer death? I don't know that we have that evidence." Another complicating factor: "Men who eat more healthy diets tend to get screened for prostate cancer. If you get regular PSA testing, you're five times more likely to get diagnosed with prostate cancer."

And, if you get diagnosed early, you are more likely to get early treatment while the disease is confined to the prostate. It's like the children's book, *If You Give a Mouse a Cookie,* a domino effect.

Vitamin D: Yes. "There's really promising data on vitamin D and prostate cancer mortality." One randomized trial, the VITAL study, "if you look at prostate cancer mortality, specifically in black men who have low levels of vitamin D, there's a reduction in prostate cancer mortality. Evidence from many studies suggests that this makes sense; there's a lot of genetic data on inherited vitamin D pathways; this pathway seems to be very important for prostate cancer." Vitamin D is found in some foods such as fatty fish and egg yolks, and the body produces vitamin D through sunlight. Most men do not get sufficient vitamin D, however, and the best strategy is to take a vitamin D supplement.

Source:
Posted: 28 Jan 2021 02:20 PM PST
https://prostatecancerinfolink.net/2021/01/29/dose-painting-simultaneous-integrated-boost-to-the-dominant-intraprostatic-lesion/

Dose Painting: simultaneous integrated boost (SIB) to the dominant intraprostatic lesion (DIL)

Two technologies have come together to allow for a new kind of radiation treatment known as *simultaneous integrated boost (SIB)*, or, more informally, "dose painting." The two technologies are:

- improved imaging by multiparametric MRIs that can more precisely locate tumors within the prostate, and
- improved external beam technology that can deliver doses with submillimeter accuracy.

Dose painting can be achieved with brachytherapy as well. But just because it *can* be done, doesn't mean it *should* be done. That is, the following two questions must be answered:

1 Is there any benefit in terms of oncological outcomes?
2 Is there any increase in treatment toxicity attributable to it?

The arguments *for* dose painting include:

- There is often a *dominant intraprostatic lesion (DIL)* or *index tumor*. There is some evidence that cancer spreads via clones from it. Because such tumors are often large and high grade, some think that the index tumor may be relatively radioresistant, perhaps because of hypoxia or cancer stem cells. Therefore, a higher dose of radiation may be necessary to kill its cancer cells.
- By concentrating the radiation's killing power at the DIL, it may be possible to reduce the radiation dose where it is less needed, and thus spare organs at risk (e.g., bladder and rectum).

The arguments *against* dose painting include:

- The index tumor hypothesis is far from proven. In fact, prostate cancer is multifocal in about 80% of men. Reducing the dose elsewhere is risky because cancer cells may survive and propagate.
- If the dose needed to kill the cancer cells is inadequate, why not increase the dose throughout the prostate to a dose that is adequate? With today's pinpoint technology, the clinical target volume (the prostate) can be defined with sub-millimeter accuracy and near-perfect shaping.
- Using mpMRI to precisely delineate the DIL may miss much of it. In fact, a study at UCLA found that tumors delineated by mpMRI missed 80% of the tumor's actual volume.
- While mpMRI is good at finding large high-grade tumors, sometimes the highest grade tumor is not large, and mpMRI cannot locate it.
- Intense foci of radiation may increase the probability of normal tissue complications, including damage to the urethra, bladder neck, sphincter, rectum and bowel.

With all these pros and cons in mind, the FLAME randomized clinical trial was instituted to determine whether dose painting is effective and safe in real-world application. Kerkmeijer et al. reported the results of 571 patients treated at 4 institutions in Belgium and the Netherlands from 2009 to 2015. Patients were:

- Predominantly (85%) high risk
- Adjuvant ADT was given to 65% for a median of 18 months.
- Received hypofractionated radiation to the prostate: 77 Gy in 35 treatments, which is biologically equivalent to 82 Gy in 41 treatments.
- Half received a SIB to the DIL as well: 95 Gy in 35 treatments, which is biologically equivalent to 116 Gy in 58 treatments.
- The boost dose was reduced sometimes to meet very tight dose constraints on organs at risk.

After 6 years of follow-up:

- 5-year biochemical disease-free survival (bDFS) was 92% for those that received the SIB and 85% for those who didn't, a significant difference.
- Both biochemical failures and clinical recurrences were cut in half by the SIB
- In the limited follow-up period, there weren't enough distant metastases or deaths to detect a significant difference.
- There were no significant differences in Grade 2 or Grade 3 urinary or rectal toxicity,
- As previously reported, late-term Grade 2 or greater toxicity was 10% for rectal, 27% for urinary with no significant differences.
- There was no late-term Grade 3 rectal toxicity, and minimal late-term Grade 3 urinary toxicity in either arm.
- There were no significant differences in patient-reported quality of life for urinary, rectal or sexual outcomes.

Because oncological results were as good as brachy boost therapy, the current gold standard for treating high-risk patients, and late-term urinary toxicity was minimal, hypofractionated IMRT with SIB is poised to become the new standard of care for high-risk patients. Longer follow-up will determine whether the results hold up.

There are some opportunities for improving results for patients even further.

- SBRT with SIB: As we've seen extreme hypofractionation *may* provide more lasting results with equally good toxicity. Whole gland treatment with as high as 47.5 Gy in 5 fractions did not incur any excess toxicity in trials (see this link).
- Tumor detection and delineation with PSMA PET/CT scan: a small comparative study showed that PSMA PET/CT had superior sensitivity and positive predictive value compared to mpMRI. More importantly, it can eliminate patients who would not benefit from localized treatment because of occult metastases.
- Genomics to detect radio-resistant tumors and radiation sensitivity
- Imaging to detect hypoxic tumors (e.g., BOLD MRI, FAZA PET, or MISO PET)

Focal therapy offers advanced treatment options for prostate cancer

Source: https://www.uclahealth.org/vitalsigns/focal-therapy-offers-advanced-treatment-options-for-prostate-cancer

Advances in imaging technology have dramatically improved the ability of physicians and their patients to take a more conservative approach to treating prostate cancer. Because physicians can more accurately biopsy the prostate, many men with tumors that are unlikely to be lethal now opt for "active surveillance" — closely monitoring rather than treating the cancer and thereby avoiding the side effects associated with the two mainstays of prostate cancer treatment, surgery and radiation. Now, a multidisciplinary team headed by UCLA urologist Leonard S. Marks, MD, is pursuing a new frontier in prostate cancer treatment — focal therapy, which uses various approaches to target the cancer in ways that are far less invasive than traditional treatments, resulting in fewer side effects.

What is driving the effort to develop focal therapies for prostate cancer?

The rationale behind focal therapies is to destroy the tumor while leaving the normal tissue alone. This dramatically reduces adverse side effects such as incontinence and erectile dysfunction that are associated with radical prostatectomy (traditional prostate cancer surgery) and radiation. The analogy is the lumpectomy for breast cancer. It used to be that the only approach to surgical treatment of breast cancer was radical mastectomy; then studies showed that when breast-conserving surgery was appropriate, survival was equal. The same has been true for other cancers such as thyroid, colon and lung, for which partial removal can be effective. Now we are beginning to see this approach ramped up for certain prostate cancers.

What is making these therapies possible?

It is the advent of sophisticated MRI. When we were using transrectal ultrasound, we couldn't actually see the cancer. Instead, we relied on the PSA [prostate-specific antigen] test. When a patient's PSA was elevated, we would do a biopsy. Even though it was guided by ultrasound to show where the prostate was, since we were not able to see the cancer, if we found something, we were likely to remove or radiate the entire prostate. Within the last decade, for the first time we can see cancer in the prostate gland, put a biopsy needle specifically into that spot, characterize how aggressive it might be and, for low-risk patients who choose active surveillance over treatment, track it through repeat biopsies. This ability to see the cancer also has opened the door to focal therapy approaches to treating it more precisely.

Is this a middle ground between active surveillance and traditional surgery or radiation?

Exactly. Active surveillance is the most rapidly growing management strategy for prostate cancer. Many men with low-risk tumors who would have gotten surgery 10 or 20 years ago now are choosing active surveillance, thanks to our ability to view and follow the cancer to make sure it doesn't become a threat. But there's a large group of men who fall into the intermediate-risk category, where the cancer is not immediately life-threatening but is too risky to follow in active surveillance.

What are the focal therapy approaches currently available or under investigation?

The first form of focal therapy for prostate cancer was cryotherapy, which involves removing part of the prostate by freezing it. This technology has been around for a while, but the delivery systems have improved, and we currently offer it through a clinical trial. High-intensity focused ultrasound, or HIFU, uses powerful ultrasonic energy to destroy the tumor. We have been performing HIFU at UCLA since 2010 and have an Food and Drug Administration-approved HIFU device for the noninvasive treatment of prostate cancer, though this treatment is not yet covered by insurance. At UCLA, we are studying laser focal ablation. Using the same technology as for our targeted prostate biopsy to pinpoint the cancer, we insert a laser fiber to deliver energy to heat and destroy the tumor while keeping the surrounding tissue intact. We have a $3.1 million grant from the National Cancer Institute to develop and commercialize this treatment. For the sake of full disclosure, I am the co-founder of a company that is collaborating with UCLA to do so.

Who would be a candidate for focal treatment?

This is for men with intermediate-risk prostate cancer, in which the tumor is confined to one identifiable part of the prostate, and the prostate gland is not too large. It's important to note that although we think the time is right to move forward with this treatment, because we are still early in its use, every man who gets a focal therapy treatment at UCLA undergoes a follow-up MRI-guided biopsy six months later, just to make sure that we did what we set out to do. Based on our cryotherapy experience, which is the best documented of the focal therapy treatments here, about 80 percent of the men getting those follow-ups have had no cancer in the tissues.

Leonard Marks, MD

New Prostate Cancer Trials

ENZA-p

Enzalutamide is a potent hormone therapy that prevents testosterone from reaching prostate cancer cells, thereby stopping cancer growth. It is already widely used in men with prostate cancer that has stopped responding to standard hormone treatments (castration-resistant prostate cancer). However, most cancers become resistant to enzalutamide over time, with almost 1 in 4 being resistant from the start of treatment.

Many prostate cancers, in particular those that have spread or become resistant to hormonal therapies, have a substance on their cell surface called prostate specific membrane antigen (PSMA). Lutetium-177 PSMA (Lu-PSMA for short) is a new treatment in advanced prostate cancer. Lu-PSMA is a radioactive molecule that attaches to the surface of prostate cancer cells throughout the body. This drug is given as an injection through the vein and allows targeted radiation to be delivered directly to prostate cancer cells.

Smaller pre-clinical studies have demonstrated synergistic effects by combining Lu-PSMA with enzalutamide. It is possible that Lu-PSMA can prevent early resistance to enzalutamide, extending the time that men benefit from treatment.

The ENZA-p clinical trial aims to compare the effectiveness of enzalutamide in combination with Lu-PSMA, versus enzalutamide alone for the treatment of prostate cancer. This is a randomised study, so half the men in this trial will be randomly allocated to receive Lu-PSMA and enzalutamide, and the other half will be randomly allocated to receive enzalutamide alone. We plan to enroll 160 participants across Australia.

The trial is open and recruiting.

Interested in this trial? Print off the ENZA-p trial details from the Australia New Zealand Clinical Trials Registry and take it to your GP.

DASL-HiCaP Trial

The purpose of this study is to see if a new tablet drug, darolutamide, combined with the current best treatments, can improve outcomes for men with high risk prostate cancer that has not spread beyond the prostate area. Previous studies have shown promising results for darolutamide preventing disease progression and improving survival for men with advanced prostate cancer. This is a randomised controlled trial, which means that, in addition to best standard treatments, half the participants on the study will receive darolutamide, and the other half will receive placebo. The trial is being led from Australia by ANZUP in collaboration with the NHMRC Clinical Trials Centre. We plan to enrol 1,100 men from Australia, New Zealand, Canada, the US, Ireland, and the UK.
The trial is open and recruiting.

Interested in this trial? Print off the DASL-HiCaP trial details from the Australia New Zealand Clinical Trials Registry and take it to your GP.

New randomized clinical trial of Lu-177-PSMA-617 for men who are still hormone sensitive

Novartis announced a new international Phase 3 clinical trial slated to begin 3/5/21 for men with metastatic hormone-sensitive PC. There will be a crossover after SOC failure, so everyone will get the drug. They haven't announced the sites yet, but with a sample size of 1126, I expect it will be the same as the VISION trial.

clinicaltrials.gov/ct2/show...

They are really trying to get newly diagnosed patients. They are trying to prove that Lu-177-PSMA-617 is as good as a first therapy as chemo, Zytiga, Xtandi or Erleada. Once they can prove that, it would take its place as a new standard of care.

Learn to be your own researcher to make the best treatment decisions, by being proactive and an advocate for your own health

New Prostate Cancer Trials

A Study of Adding Apalutamide to Radiotherapy and LHRH Agonist in High-Risk Patients With Prostate-Specific Membrane Antigen-Positron Emission Tomography (PSMA-PET) Positive Hormone- Sensitive Prostate Cancer Participants (PRIMORDIUM)

The hypothesis of study is addition of apalutamide to RT+ LHRHa provides superior efficacy in terms of PSMA-PET metastatic progression-free survival-ppMPFS. Apalutamide is a non-steroidal androgen receptor (AR) antagonist being developed for the treatment of prostate cancer. RT+LHRHa is a combination therapy, when administered concomitantly, in high-risk patients with BCR (biochemical recurrence) relapsing after RP, potentially leads to relevant delay in the metastatic progression of prostate cancer at an early stage of the disease, or even cure in some cases. Study consists of 2 cohorts (intervention and observational cohort). At screening, eligible participants will undergo prostate-specific membrane antigen-positron emission tomography (PSMA-PET), whole-body Tc-bone scan, computed tomography (CT). Interventional Cohort, consisting of PSMA-PET positive participants, will undergo 3 phases: Treatment Phase, a Post-treatment Phase and a Post-PSMA-PET Progression Phase. After 6-month Treatment Phase, participants will be prospectively assessed in Post-treatment Phase until PSMA-PET-positive metastatic progression is confirmed. Observational cohort will run parallel to interventional cohort. PSMA-PET negative, participants will be observed until time-point when number of events required for analysis of primary endpoint is reached in Interventional Cohort. This cohort provides an approach to document the selection of treatments and observation of interventions in a real-life clinical practice setting. The duration of the study is estimated to be approximately 7 years.

Trial ID

NCT04557059

Phase of Trial

Phase 3

Recruitment Dates

Anticipated start date
12/11/2020

International Locations including Australia.

In Victoria: Epworth, Richmond & St Vincent's, Fitzroy.

Prostate Heidelberg Cancer Support Group Meetings

While we are having to distance ourselves and are unable to hold face-to-face group meetings we are engaging speakers via video conferencing.

We are planning to recommence our regular monthly meetings at Ivanhoe Uniting Church. When this happens we will also try to continue to provide for attendance via Zoom for those who cannot attend in person.

Internet Resources

Members have found the following websites useful

Prostate Cancer Foundation of Australia for guides & help
https://www.pcfa.org.au
https://onlinecommunity.pcfa.org.au/

Australian Cancer Trials Information on clinical trials
https://www.australiancancertrials.gov.au

USA Prostate Cancer Foundation (Guide) PDF guide for men newly diagnosed with PC
https://www.pcf.org/guide/

Us TOO International PCa Education (USA) USA PC support groups' information & newsletter
https://www.ustoo.org

Cancer Council Victoria for general support services
https://www.cancervic.org.au

ExMed Cancer Program Melbourne based 'best practice' exercise medicine program
https://www.exmedcancer.org.au

ProstMate (PCFA) A companion to record PC results

Beyond Blue for help with depression and anxiety
HELPLINE 1300 22 4636

Continence Foundation of Australia for assistance with incontinence aids
HELPLINE 1800 33 0066

PCRI Prostate Digest (USA) Prostate Cancer Research Institute supporting research and disseminating information to educate and empower patients, families and the medical community
https://pcri.org/insights-newsletter

PAACT Newsletter (USA) Patient Advocates for Advanced Cancer Treatments
http://paact.help/newsletter-signup/

A Touchy Subject
https://www.youtube.com/channel/UCdyuxGuAuCWJbe-kZvwVSzQ

The internet is a good source for research but it should not be trusted to give you answers for your personal care. Always speak to your doctor to clarify any medical advice.

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PHCSG Correspondence

Mike Waller Convener
Max Shub Co-Facilitator
Peter Anderson Treasurer
Spiros Haldas Library
David Bellair Web Site
Michael Meszaros Welfare Officer
Sue Lawes Secretary/Newsletter

PHCSG Meetings 2021 10am – 12:30pm

Tues 16 Feb
Tues 16 March
Tues 20 April
Tues 18 May
Tues 15 June
Tues 20 July
Tues 17 August
Tues 21 September
Tues 19 October
Tues 16 November
Tues 14 December (including Xmas lunch)

Please note that all face-to-face meetings have been cancelled until further notice. Please check your email regularly for updates from the PHSCG Committee.

2021 PHCSG Articles

If you have any feedback or wish to include articles on specific aspects of Prostate Cancer please contact Sue at:

prostateheidelberg@gmail.com

January 2021

- Exercise Infographic
- Sexual Dysfunction & Shared Decision Making
- FDA Approves first Oral Hormone Therapy
- Prolonged ADT Reduces Cardio Fitness
- Reducing the Burden of Out-of-Pocket Expenses
- BAT Sensitizes CRPCa to Subsequent Therapy
- Targeting Bone Mets with Radiation in Oligorecurrent Men

Prostate Cancer Trials

- PEACE V:STORM
- UpFront PSMA Phase II
- NINJA

February 2021

- Advantages of Coffee
- Our Biological Clock
- Statins tied to Better Outcomes
- IWhat's New in Inflammation
- New PC Management Techniques
- About the Patch Trial
- Eating a Colourful Diet
- Dose Painting
- Advancement in Focal Therapy

Prostate Cancer Trials

- Enza-P
- DASL-HiCaP Trial
- Lu-177-PSMA-617
- Adding Apalutamide to Radiotherapy & LHRH Agonist

2020 PHCSG Articles

If you have any feedback or wish to include articles on specific aspects of Prostate Cancer please contact Sue at:

prostateheidelberg@gmail.com

March 2020
- PCFA Consumer Advisory- Coronavirus and Cancer

April 2020
- Telehealth & Delayed Hospital Treatments due to COVID-19
- Fexapotide Triflutate (FT) injection – a new kind of focal treatment to extend time on active surveillance

Prostate Cancer Trials
- DASL-HiCaP Trial
- Evaluation of a mainstream model of genetic testing for men with prostate cancer

May 2020
- ADT May Offer Some Protection From COVID-19 in Men with Prostate Cancer
- TULSA – Novel MRI-guided ultrasound treatment destroys prostate cancer
- Whack-a-Mole A Treatment of Oligometastasis
- Long-term adjuvant ADT improves results of brachy boost therapy in unfavorable-risk prostate cancer patients
- Harnessing the immune system to control prostate cancer spread to the bone

Prostate Cancer Trials
- A study to see whether PET scans using a chemical called Exendin can detect metastatic PC
- Evaluation of a mainstream model of genetic testing for men with prostate cancer

June 2020
- Evaluating the Outcomes of AS in Gleason Grade 2 Prostate Cancer
- Advancing precision medicine for metastatic prostate cancer
- Impact of Primary Prostate Cancer Treatment with Subsequent Metastatic Disease
- Comparative Analysis & Survival Outcomes in a Real-World Practice Setting
- Fexapotide Triflutate (FT) injection – a new kind of focal treatment to extend time on AS

Prostate Cancer Trials
- Impact of 18F-DCFPyL PET scanning in patients undergoing post-prostatectomy Radiotherapy

July 2020
- Testosterone Therapy does not Increase the Risks of PCR or Death after Definitive Treatment for Localised Disease
- Association of Pre-Salvage Radiotherapy PSA Levels after Prostatectomy with Outcomes of Long-term Antiandrogen Therapy in Men with Prostate Cancer
- Testosterone Replacement in the treatment of Advanced Prostate Cancer
- Memorial Sloan Kettering Cancer Center PCa nomograms Prediction Tools

August 2020
- Advanced Prostate Cancer Algorithm
- Blood Test Predicts Response to PC Treatment (liquid biopsy)
- The Perils and Pitfalls of Treating PSA in PCa
- Reprogramming Immune Cells could Switch Defence into Attack in PCa
- Maintenance of Sexual Activity Following ADT

September 2020
- ProtecT Trial showing patient outcomes after AM, RP & EBRT
- Changes in Penile Length after RP
- Active Surveillance for PC – is it right for you?
- The final part of The Perils and Pitfalls of "Treating PSA" in Advanced Prostate Cancer
- Managing Erectile Dysfunction – A Patient Guide

Prostate Cancer Trials
- Efficacy and Safety of Pembrolizumab (MK-3475) Plus Enzalutamide Plus Androgen Deprivation Therapy (ADT) Versus Placebo Plus Enzalutamide Plus ADT in Participants with (mHSPC)
- Navigate: An online treatment decision aid

October 2020
- World Osteoporosis Day
- Lifestyle Factors and Chronic Disease
- Hormone Therapy for PC
- Early ADT for Recurrent PC Challenged
- Unexpected aPC weakness can be targeted by drugs
- Hijacking an Epigenetic Program
- New PC Research: Immunotherapy; Gut Microbiome
- Veyonda New Research on Survival Rates

Prostate Cancer Trials
- MIndonline - mindfulness

November 2020
- Life insurance & Genetic Testing
- World First Surgery in NZ
- Melatonin increases survival
- SBRT disease control
- Public vs Private Hospitals
- Early ADT for Recurrent PC challenged
- Enzamet trial results

Prostate Cancer Trials
- Randomised Phase 2 of sequential 177Lu-PSMA & Docetaxel
- Exercise for Heart Health

December 2020
- ACTA Trial Award
- Rethinking Metastasis
- ESMO Phase 1 AMG160
- Five Ways to Get it Right
- Immunotherapy Offers Hope
- SBRT Doubles Pain Response
- Elevated Streess Hormone Levels

Prostate Cancer Trials