PCCN Markham

Newsletter

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PEER SUPPORT MEETING

Tuesday, December 10, 2019 - 7:30PM

St. Andrews Presbyterian Church – Main St Markham

Rose Room - Downstairs

(Free Parking & Room access off George Street)

Peer Support Session

Meetings provide an opportunity for you to talk in complete confidence with prostate cancer survivors.
There's usually someone at a meeting who has had the treatment you are considering and this gives you an opportunity to talk directly to men who've been through the various treatments.
Group provides an opportunity to talk with others about managing life with prostate cancer.
Note: ***we cannot give medical advice, but can share our knowledge of treatments and experiences.***

ALL WELCOME!!

IN THIS ISSUE …

Thanks to Dr. Boudakian for his support and informative talk in November!

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High-risk men 'should get prostate cancer checks'

5 November 2019

Men born at high risk of developing prostate cancer should have extra checks every year from the age of 40, experts say.

Men with certain mutations in their DNA, their genetic code, are more likely to develop prostate cancer.

Scientists at the Institute of Cancer Research (ICR) said an annual blood test could help spot tumours early, when they were easier to treat.

Prostate Cancer UK said any decisions needed to be made carefully.

The ICR researchers said about one in 300 men in the UK had mutations in Brca2, which increases their risk.

However, most will not know whether they carry the mutation in their DNA as it is not routinely tested for.

Brca2 mutations are the same genetic errors that increase the risk of breast and ovarian cancer in women - and men will have been tested for it only if such cancers run in the family.

Screening

Prostate-specific antigen (PSA) is a protein made only by the prostate gland.

PSA levels go up with prostate cancer but it is not a sufficiently reliable measure to justify screening all men for the disease.

Prof Ros Eeles said: "Our research shows very clearly that men with the Brca2 gene fault are at increased risk of aggressive prostate cancer and that regular PSA testing could go some way to improving early diagnosis and treatment.

She has been making the case at the National Cancer Research Institute Cancer Conference, in Glasgow.

She said men or anyone with a prostate and Brca2 mutations were nearly twice as likely to have a severe cancer that needed treatment rather than simple monitoring.

Dr Matthew Hobbs, from the charity Prostate Cancer UK, said: "[We are] funding a project to model the long-term effectiveness of a range of potential screening strategies, including defining whether there are certain high-risk groups for whom the benefits of regular screening greatly outweighs the potential for overtreatment.

"It may be that screening all men with a Brca2 mutation could be one of the answers, so we will look carefully at the results of this study."

https://www.bbc.com/news/health-50291318

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Wait-and-see approaches to prostate cancer

Active surveillance and watchful waiting are the most conservative — and increasingly popular — approaches to prostate cancer management. Is one of these right for you?

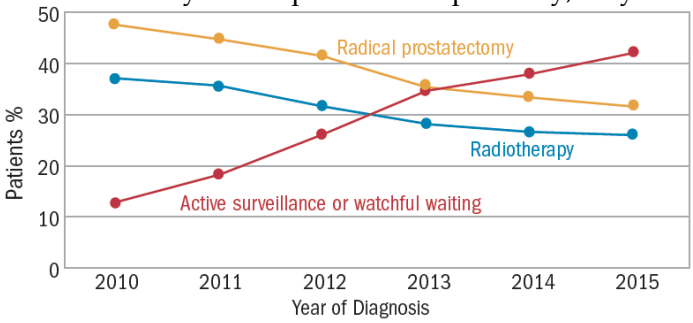
Published: November, 2019*Harvard Men's Health Watch*

Over the years, the outcome for prostate cancer has turned out to be better than expected for many men. While prostate cancer is quite common, the risk of dying from the disease is low, even without treatment. In fact, most diagnosed men will die from something else, like heart disease. Even so, prostate cancer remains the second leading cause of cancer deaths (after lung cancer) in men, according to the American Cancer Society.

"Men still need to treat prostate cancer as a serious ailment and be aware of the many options available," says Dr. Frank McGovern, a urologist with Harvard-affiliated Massachusetts General Hospital.

Two of the more popular options for prostate cancer now are active surveillance and watchful waiting. They are the most often recommended ways to manage low-risk prostate cancer, in which the cancer is confined to the prostate gland and unlikely to grow quickly or spread. In both, you don't begin any treatment right away.

"Active surveillance and watchful waiting help men take a step back and analyze their situation before jumping straight into invasive procedures and treatments, which can lead to side effects that diminish quality of life and may not improve life expectancy," says Dr. McGovern.



Get active about surveillance

While the terms active surveillance and watchful waiting often are used interchangeably, the approaches are quite different. Active surveillance involves monitoring your prostate-specific antigen (PSA) levels for changes and having regular digital rectal exams. A PSA test measures the blood level of PSA, a protein produced by both cancerous and noncancerous tissue in the prostate. The results are reported as nanograms of PSA per milliliter of blood (ng/ml). In general, the higher a man's PSA level, the greater likelihood he has

prostate cancer. Also, a continuous rise in PSA levels over time may be a sign of cancer. (See "PSA by the numbers.")

In a digital rectal exam, your doctor inserts a lubricated, gloved finger into your rectum and feels for abnormal areas on your prostate that may indicate possible cancer.

During active surveillance, you have a PSA test and a digital rectal exam every six months. If your PSA level rises or if a new or enlarging growth is detected by a rectal examination, your doctor will likely recommend a prostate biopsy to see if the cancer has become more aggressive.

A traditional biopsy takes 12 samples from different parts of the prostate. Even if your PSA does not rise, your doctor may still recommend periodic biopsies as part of active surveillance.

If a biopsy shows any changes, you and your doctor may decide to continue with active surveillance, or to move ahead to treatment with surgery, radiation, or hormonal therapy.

Active surveillance is not a passive option, Dr. McGovern points out. "You follow a firm schedule of regular PSA testing and follow-ups, so you are constantly monitoring your condition," he says. "Active surveillance is like a highway that you get on, but if anything unusual happens, you get off and likely get on the treatment road."

Pros: The main benefit with active surveillance is that you avoid treatment that you don't necessarily need and its potential side effects like erectile dysfunction and urinary problems.

Cons: One issue with active surveillance is that it hinges primarily on PSA tests, with or without biopsies. PSA tests are not definitive, and an abnormal result could push a man toward treatment that was never going to change his life span.

Yet, the main downside to active surveillance is psychological — the constant worry that something could be wrong. "Just because you qualify for active surveillance, you don't have to do it," says Dr. McGovern. "If wait-and-see is too stressful, you can always go straight to treatment."

PSA by the numbers

There is no "normal" level of PSA, but there are general guidelines for detecting possible prostate cancer:

- 0 to 2.5 ng/ml is considered safe, but men can still have cancer with a PSA this low.
- 2.6 to 4 ng/ml is normal, but talk with your doctor about other risk factors.
- 4 to 10 ng/ml suggests the possibility of cancer, but more often is due to an enlarged prostate (benign prostatic hyperplasia).
- Higher than 10 ng/ml often means the presence of cancer, but an inflamed prostate gland (prostatitis) can also cause high levels.

Watch and wait

Watchful waiting is different from active surveillance, and most often a consideration for men ages 70 and older, especially if life expectancy is fewer than 10 years. With watchful waiting, there are no scheduled PSA tests or rectal exams.

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"The idea is to avoid treatment unless you get symptoms — like extreme fatigue, weight loss, bone pain, or urinary retention — that can interfere with quality of life," says Dr. McGovern.

Similar to active surveillance, a man who has originally chosen watchful waiting can change his mind and have closer monitoring or a repeat biopsy.

Pros: If you are in your 70s or 80s, you may not wish to pursue treatment because most often the potential side effects outweigh any benefits. "Plus, if you are dealing with other health issues, you may not want to put yourself through the added stress of prostate cancer treatments," says Dr. McGovern.

Cons: Watchful waiting is not as proactive as active surveillance. By waiting until symptoms occur, you may miss a chance for earlier treatment. "Also, if you do wait longer before starting treatment, the procedures can be more difficult to endure, with a longer recovery period compared with when you were younger," says Dr. McGovern.

https://www.health.harvard.edu/mens-health/wait-and-see-approaches-to-prostate-cancer

Why Hasn't Immunotherapy Been Working For Prostate Cancer? Bone Tumors May Be The Answer

Nov 16, 2019, 12:21pm Victoria Forster Contributor Healthcare

Researchers from MD Anderson in Texas have uncovered new clues as to why immunotherapy may fail in ... [+] Getty

Immunotherapy drugs called immune checkpoint inhibitors have revolutionized therapy for several types of cancer. However, so far these drugs have been mostly ineffective for one of the most common types, prostate cancer.

New work from researchers at MD Anderson Cancer Center in Texas has revealed a major new clue as to why immunotherapy has been largely unsuccessful so far in these patients.

The research published this week in the journal *Cell*, describes how the metastatic prostate tumors destroy bone, unleashing a protein called TGF-Beta (β), which disrupts tumor-busting immune cells. They show that T-cells which would normally be stimulated to attack the tumor after treatment with immune checkpoint inhibitors are blocked by TGF-β.

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Prostate cancer is a common cancer in men and often becomes significantly more serious for the patient after spreading to other sites in the body such as the bones. In 60-70% of men, the cancer spreads to the bones and is then even more difficult to effectively treat.

Previous work by the researchers treated men with prostate cancer with a combination of checkpoint inhibitor therapies targeting PD-1 and CTLA-4, finding that individuals with metastatic bone tumors were resistant to the therapies. The researchers theorized that perhaps, these bone metastases were directly producing something to disrupt this immune response.

"Our studies indicated high Th17 cells, as opposed to high Th1 cells, in bone marrow of patients with metastatic castration-resistant prostate cancer involving the bone," said Padmanee Sharma, M.D., PhD, professor of genitourinary medical oncology and immunology at MD Anderson and senior author on the paper. "Additional studies demonstrated that these patients also had high TGF-β levels in the bone marrow," she added.

Security Means Understanding Assets, Adversaries, And Threats

These Th17 and Th1 cells, types of T-cells, are part of an orchestra of multiple, complex parts which if perfectly conducted can mount an immune response against tumors. TGF-β in this case is a protein called a growth factor, which causes an overproduction of Th17 cells rather than Th1, meaning that the correct cells to trigger an immune response after immune checkpoint therapies are simply not present in the bone tumors.

The researchers next used a mouse model of prostate cancer, giving them a drug to inhibit TGF-β alongside immune checkpoint therapy, finding that this combination stifled growth of bone metastases in the mice.

"We need to be more thoughtful about the immune microenvironment in different areas of metastasis to take into account different immune responses in those microenvironments when we develop treatments," said Sharma.

To test the hypothesis in humans, the researchers compared TGF-β levels in the bone marrow of healthy donors and prostate cancer patients with and without bone metastases. There was no difference in TGF-β levels between healthy controls and patients without bone metastases, while patients with bone tumors had very high levels of TGF-β in their bones.

The researchers next hope to see whether the approach of inhibiting TGF-β alongside immune checkpoint inhibitors will work in people with prostate cancer with bone metastases and believe that the work may also be applicable to other types of tumor that have spread to the bones.

"We're working to develop a combination clinical trial of anti-CTLA-4 and anti- TGF-β for metastatic prostate cancer. This mechanism may be at play in other tumor microenvironments and needs to be studied further," said Sharma.

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Why Treat Prostate Cancer Metastases with Ablative Radiation?

Rationale for Metastasis-Directed Therapy (MDT) in Prostate Cancer

Traditionally, the management of metastatic cancer has been chiefly through systemic treatments (excellent summary guidelines for systemic management are available[1,2]) while local therapies such as radiation have been used primarily for palliation of symptomatic lesions. Prostate cancer commonly spreads to the bones, causing pain and potentially leading to fractures at weight-bearing sites such as the femoral neck, acetabulum, or vertebral bodies. Radiation is highly effective at reducing pain caused by osseous metastases and can be delivered in one or multiple fractions of external beam radiotherapy (EBRT) or with the systemic radiopharmaceutical radium-223.[3,4]

Beyond palliation, radiation may also impact the course of metastatic disease. Three decades ago, Soloway and colleagues[5] correlated 2-year survival rates with extent of metastatic disease as determined by radionuclide bone scans in men with prostate cancer receiving androgen deprivation therapy (ADT). Most notably, those men with fewer than 6 lesions had a 2-year overall survival of 94%. Just 2 years later, in a retrospective study of 136 men with prostate cancer who received pelvic radiation, Kaplan and colleagues[6] observed that coincidental irradiation of 30-50 Gy to the lumbar spine was associated with a significantly decreased incidence of subsequent lumbar spine metastases. While the mechanism for this apparent protective effect of moderate-dose radiotherapy is not fully understood, hypotheses at the time included treatment of occult micrometastatic disease or alteration of the local microenvironment. These observations led to the notion that aggressive treatment of metastatic deposits with metastasis-directed therapy (MDT) using radiation may alter the natural history of metastatic disease and/or potentially be curative by limiting disease burden and preventing further spread.

The Clinical Argument for MDT in Oligometastatic Prostate Cancer

In their editorial "Oligometastases," Hellman and Weichselbaum[7] discuss the opposing hypotheses of cancer metastasis as well-ordered and predictable based on knowable anatomic and physiologic data or, alternatively, as the manifestation of cancer as a systemic disease with widespread, initially undetectable micrometastases present at the time of diagnosis but maturing to clinical relevance over time; ultimately they propose that our understanding of cancer behavior is most consistent with a continuum spanning these extremes and with many intermediate states. Their formulation of a "clinical significant state of oligometastases" describes a point on this continuum where metastatic disease is present but potentially curable through consolidation of both the primary tumor and all metastases with local therapies (see **Fig 1**). The oligometastatic state in prostate cancer includes de novo hormone naïve metastatic disease present at initial diagnosis, oligorecurrent disease following definitive primary treatment with surgery and/or radiation, and isolated areas of treatment-resistant or oligoprogressive disease which persist after otherwise successful systemic therapy such as in castration-resistant prostate cancer (CRPC) (see **Figure 2**).

The Radiobiologic Argument for Ablative Radiation

Many factors go into the choice of total dose and fractionation during the radiation planning process. Radiology best practices dictate that one of the most important aspects is assessing tissue radiosensitivity with respect to optimizing tumor control while minimizing toxicity to normal tissues. This is often done through the $\alpha/ß$ constant, a component of the linear-quadratic model which describes cell kill in response to radiation therapy, both for tumor control and for normal tissue complications. Typically, cells with lower $\alpha/ß$ ratios become dramatically more sensitive to radiation as the dose per fraction increases. In contrast, cells with higher $\alpha/ß$ ratios exhibit a much more muted response to radiation and have a less steep slope on the cell survival curve as dose per fraction increases. The implication of this assumption is that if particular cancer cells have a low $\alpha/ß$, then treating with higher dose per fraction should yield the highest therapeutic ratio by optimizing tumor cell kill and minimizing normal tissue complications. Indeed, for prostate cancer there is good evidence that it has a very low $\alpha/ß$, lower than most surrounding normal tissues[8], and therefore a therapeutic advantage may exist for the use of moderately hypofractionated or intensely hypofractionated stereotactic ablative radiation therapy (SABR) regimens. While extrapolating the linear quadratic equation in these circumstances is fraught with inaccuracies, it is currently the best available model. Thus far, clinical data of SABR in the definitive treatment of prostate cancer have shown promising clinical results.

SABR as MDT Is Well-Tolerated and Clinically Effective

To date, prospective and retrospective trials[9-23] have been performed describing the safety and efficacy of SABR as MDT in oligometastatic prostate cancer (OMPC), including one randomized controlled trial[13] (**Table 1**). While the definitions, detection methods, and use of concurrent ADT vary across these studies, there is agreement across studies that SABR is well tolerated, with grade 3 toxicity occurring in few patients reported in the aforementioned studies and no grade 4 or 5 toxicity. Similarly, these studies consistently show lesion control rates of 97-100% at 1 year and 93-100% at 2 years.

SABR May Facilitate Delay of ADT Initiation

Controversially, the favorable safety profile and durable lesion control afforded by SABR has led to interest in using this approach to forestall initiation of ADT, in so called oligorecurrent men, in order to avoid unpleasant side effects including hot flashes, fatigue, and sexual dysfunction. The shining example of this approach is the STOMP trial, which randomized men with 3 or fewer extracranial prostate cancer metastases to surveillance alone or SABR to all detectable foci of disease.[13] With a median follow-up of 36 months they observed that median ADT-free survival in men receiving SABR was 21 months vs 13 months with surveillance alone. The clinical relevance of this finding remains a point of active disagreement amongst experts.[24] Those in favor of early ADT initiation may cite the TOAD trial [25], which showed an overall survival benefit (unadjusted hazard ratio [HR], 0.55; $P = .05$) with immediate initiation of ADT as compared to a recommended 2 year delay. Those opposed may cite the overall lack of impact on development of metastases with early ADT in the analysis of US Department of Defense patients by Moul et al.[26] and the results of EORTC 30891[27], which showed similar prostate cancer-specific survival in men not suitable for local treatment receiving early vs delayed ADT. Despite the controversy, an ADT backbone is the standard of

care in men with metastatic disease and other novel approaches including MDT are still best evaluated under the auspices of a clinical trial.

When to Treat Prostate Cancer Metastases with Ablative Radiation?

Selecting Patients for Metastasis Directed Therapy - Definitions of Oligometastatic Prostate Cancer

Quantitative cutoffs based on the number of metastatic foci are often used to define the oligometastatic state for simplicity as well as association with disease outcome.[5, 28] Nine prospective clinical trials have numerically defined the oligometastatic state in prostate cancer; three allowed up to three metastases, two up to four, three up to five, and one up to 10. The literature of other published retrospective reviews generally included five or fewer metastatic foci.[9,17,19]

A critical limitation of any numerical definition for the oligometastatic state is its reliance on detection methods which are not absolutely sensitive nor specific and which may provide conflicting information when compared with complementary modalities. While computed tomography (CT), magnetic resonance imaging, and ^{99m}Tc scintigraphy remain the backbone of prostate cancer staging, the diagnostic toolbox is expanding rapidly and include ^{18}F-NaF, ^{11}C-choline, ^{18}F-fluorocholine, ^{18}F-fluciclovine, and a variety of prostate-specific membrane antigen (PSMA)-targeted radiotracers including ^{18}F-DCFBC, ^{18}F-DCFPyL, ^{68}Ga-PSMA-HBED-CC, and ^{177}Lu-PSMA several recent reviews have detailed the evidence for and unanswered questions surrounding the use of these agents.[24,29-31] It should be noted that a major challenge in defining the role of targeted imaging in the diagnosis and management of oligometastatic prostate cancer are the limited data correlating radiologic findings with gold standard surgical pathology, especially regarding distant metastases which may not be amenable to resection.

As detection methods continue to evolve, technological differences between studies must be taken into consideration when evaluating outcomes of MDT; patients with five or fewer lesions detectable with leading-edge methods may represent a population with a lower disease burden than those identified using conventional imaging alone.

While numerical definitions remain the best approach to defining the oligometastatic state, there is significant interest in defining the biology that differentiates men whose disease may yet be arrested with local consolidation from those with as yet undetectable, but nevertheless widespread disease who would be best served by systemic therapy.[32, 33] While such definitions have not yet been identified for prostate cancer, the recent description of a molecular phenotype associated with a 94% 10-year overall survival in patients with de novo oligometastatic colon cancer who undergo resection of liver metastases[34] provides evidence that these biological descriptions are feasible.

Location Of Metastases

Studies of MDT for OMPC have primarily addressed nodal or skeletal metastases. Visceral metastases, while rare, portend a worse prognosis and relatively poor response to systemic therapies.[35] Sites may include liver and lung, which are potentially amenable to SABR, but it is unclear whether these lesions represent individual deposits that may benefit from MDT or inherently unfavorable biology best approached systemically. It is also

important to consider surgical resection as an alternative approach to MDT in the treatment of OMPC. Several studies have included patients who underwent surgical resection, albeit representing a small number compared to SABR.[13,17] The recent STOMP trial[13] included six patients who underwent surgery, five of which were salvage pelvic lymph node dissections and one a lung metastectomy. Surgical resection may be the preferred intervention based on tumor location with, for example, central lung lesions where SABR would result in high toxicity[36], large brain metastases where radiosurgery alone would result in lower rates of local control[37], or spine metastases threatening cord compression.

How Is MDT Using Ablative Radiotherapy Delivered?

Target Volumes, Dose, and Fractionation

Optimal ablative dosing is contingent on multiple factors including radiobiological properties of prostate cancer cells and dosimetric constraints of adjacent organs at risk. Studies reporting on the use of SABR for the definitive treatment of prostate cancer have utilized regimens with biological effective doses (BED) (see **Box 1**) ranging from 168 to 407 Gy[38-45] with some evidence suggesting BED of 200 Gy (either for SABR or conventionally fractionated RT) is associated with better disease control.[46]

STOMP, the only published prospective randomized trial of MDT in oligometastatic prostate cancer, utilized a dose of 30 Gy in 3 fractions.[13] Other retrospective and observational studies of MDT in oligometastatic prostate cancer utilized doses ranging from 16 to 50 Gy in 1 to 10 fractions (**Table 2** with some suggestion that a BED higher than 100 Gy is associated with superior local control.[10, 11,17-19]

Toxicity from SABR is generally mild across several lesion locations. Every other day scheduling is often used as it has shown reduced toxicity compared to daily treatments in definitive treatment of the prostate[41], however even with daily treatments toxicity rates remain low (**Table 1**).

Specific Considerations by Treatment Site

Gross tumor volumes (GTV) (see Box 2) generally include all tumor seen on imaging. Clinical target volumes (CTV), such as with spinal or vertebral metastases, are typically based on consensus contour guidelines.[47] Planning target volumes (PTV) vary by institution based on set up uncertainties, but generally are on the order of 3-5 mm when daily image guidance is used (**Table 2**). Dose constraints for organs at risk (OAR) are based on American Association of Physicists in Medicine Task Group 101 recommendations or other SABR-based clinical trials and delineation of specific OARs are guided by established guidelines and atlases.[48,49] All patients should be custom fitted with immobilization devices created at the time of simulation. Motion management is necessary for rib lesions and (the less common) pulmonary metastasis using either 4-dimentional CT or an active breath coordinator.

Concurrent ADT and Other Systemic Therapies

One goal of MDT in OMPC is to avoid systemic therapy and its associated side effects. However, a more aggressive approach may involve intensification aimed at simultaneously eradicating sites of microscopic metastatic disease in addition to local consolidation with SABR through the use of concurrent ADT, non-castrating antiandrogens such as enzalutamide, chemotherapies such as docetaxel, and even complimentary

forms of systemic radiation such as radium-223. No level 1 evidence exists for this treatment paradigm, however retrospective data[19] suggests a possible improvement in distant progression-free survival with the concurrent use of ADT and SABR. Therefore, prospective studies are on-going to address this question.

Follow-Up After MDT

Guidelines following biochemical failure typically recommend follow up, with physical exam and prostate-specific antigen (PSA), every 3-6 months with imaging as indicated for symptoms. However, individuals treated with local rather than systemic therapies warrant closer follow-up for several reasons. First, though studies of MDT in oligometastatic disease have shown promising results, these patients have known systemic disease and therefore are still at risk for disease progression. For instance, 30% of patients in STOMP treated with MDT progressed to polymetastatic disease within one year.[13] Additionally, patients who develop oligometastatic recurrence can be successfully treated with additional SABR. For example, 25% of patients in Decaestecker et al[17] who developed oligometastatic recurrence and were subsequently treated with additional SABR remained progression-free at last follow-up. Finally, while PSA monitoring is the current standard to assess treatment response, there is great potential in the future to use circulating tumor cells or circulating tumor DNA as an alternative or complementary method.

Ongoing Studies and Future Directions

As investigation into the curative potential of MDT in OMPC continues, several major questions remain unanswered. Can MDT alone produce durable clinical benefits and, if so, how can patients be most appropriately selected? Does MDT provide additive benefit when combined with ADT and other systemic therapies? Does MDT have clinical benefit in oligoprogressive CRPC? Can MDT be combined with immunotherapy to encourage a systemic antitumor response?

Multiple prospective randomized clinical trials are ongoing to answer these first two questions. Similar to STOMP, the Baltimore ORIOLE trial (NCT02680587)[50] is evaluating progression, ADT-free survival, and immunologic correlates in men with OMPC randomized to receive observation or SABR. PCS IX (NCT02685397) is investigating the clinical benefit of adding SABR to systemic treatment with ADT and enzalutamide in patients with CRPC. CORE (NCT02759783) and STEREO-OS (NCT03143322) are randomizing patients with prostate, breast, or lung cancers with 1-3 oligometastases to standard of care systemic therapy with or without SABR. STORM (NCT03569241) is randomizing patients with oligorecurrent prostate cancer confined to the lymph nodes to MDT (salvage lymph node dissection or SABR) with six months of ADT ± whole pelvic radiotherapy. Finally, the Movember GAP6 international initiative is pooling tissue samples from clinical trials such as these in order to promote collaborative efforts to facilitate further biologic understanding of the oligometastatic state in prostate cancer.[51]

There are encouraging but still preliminary data with oligoprogressive CRPC that MDT can have a role in advanced disease but more clinical experimentation is needed (reviewed in ref 52).

The last of these questions remains a subject primarily for preclinical evaluation, with only a single phase III randomized trial to date showing a trend towards improved progression-free survival and PSA response rate

in patients with metastatic CRPC treated with ipilimumab after a single 8 Gy radiation treatment.[53] There is still significant work to be done, preclinically and in smaller phase I/II trials, with respect to optimizing the sequencing and dosing of radiotherapy in conjunction with immunotherapy before large trials will be feasible.

Conclusion

In summary, SABR is a well-tolerated approach to MDT in prostate cancer with proven palliative benefits and promising data to support continued investigation into its ability to provide durable disease control either alone or in combination with systemic therapies. At present, the strongest indication for this approach would be pain relief for symptomatic lesions. The randomized phase II STOMP trial and an increasingly compelling volume of retrospective series and phase I/II trials suggest that SABR may also be a valuable tool in the definitive management of OMPC. Patients should be educated on the proposed benefits and ongoing clinical trial opportunities.

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https://www.cancernetwork.com/article/metastasis-directed-therapy-prostate-cancer-why-when-and-how

Prostate cancer: Investigating the impact of diet

A recent review searches for links between dietary choices and prostate cancer. The authors conclude that there may be an association between plant based diets and a decreased risk of prostate cancer, as well as a link between dairy intake and increased risk.

The relationship between diet and disease will not give up its secrets easily.

According to the National Cancer Institute, there will be an estimated 174,650 new cases of prostate cancer in the United States this year.

In the U.S., about 11.6% of men will receive a diagnosis of prostate cancer at some point during their lifetime.

As with other types of cancer, scientists are still uncovering the full range of risk factors for prostate cancer.

Some scientists have turned to nutrition, but — for various reasons — measuring the effect of the diet on disease is notoriously difficult. As one example, food intake can fluctuate wildly from day to day, month to month, and year to year.

Also, certain dietary habits tend to tie in with lifestyle factors that influence health. For instance, someone who exercises regularly is also generally more likely to eat healthfully. These associations make it difficult to unpick whether it is lifestyle, diet, or both that have a protective effect.

For these reasons and many more, studies investigating the links between prostate cancer and diet have produced conflicting results.

Recently, researchers from Mayo Clinic in Rochester, MN, carried out an extensive literature review in an effort to cut through the noise. They published their findings in *The Journal of the American Osteopathic Assoc*.

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A clearer picture?

According to the authors of the latest study, there is some circumstantial evidence that diet might influence prostate cancer risk.

They note that Western countries have much higher levels of prostate cancer than Asian countries, where people consume much lower levels of dairy.

Also, they explain that "decreasing mortality rates in the U.S. for several common cancers, including [prostate cancer], coincides with decreased meat and dairy intake and increased plant based food consumption."

Of course, these correlations do not prove that dietary choices can influence prostate cancer risk. As the authors explain, the decrease in the mortality rates of cancer might be, at least partly, thanks to improved cancer screening and treatment. However, they believe that these correlations merit further scrutiny.

To investigate, they carried out a review of relevant studies that researchers published between 2006 and 2017. In all, they examined 47 studies, which included more than 1 million participants. The authors outline their overall findings:

"**Most studies showed that plant based foods are associated with either decreased or unchanged risk of [prostate cancer], whereas animal based foods, particularly dairy products, are associated with either increased or unchanged risk of [prostate cancer].**"

The authors found neither an increase nor a decrease in prostate cancer risk in studies that assessed red meat, white meat, processed meat, or fish intake.

In short, even with access to an impressive quantity of data, uncovering solid links between diet and cancer is still challenging.

With that said, the authors believe that the potential increase in risk relating to dairy is worth investigating further.

"Our review highlighted a cause for concern with high consumption of dairy products. The findings also support a growing body of evidence on the potential benefits of plant based diets."

Lead author Dr. John Shin

https://www.medicalnewstoday.com/articles/326762.php#4

What foods should I eat or avoid if I have prostate cancer?

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You may have heard of certain foods or dietary supplements that might help slow the growth of prostate cancer or lower the risk of it coming back after treatment. Or that some foods could be harmful for men with prostate cancer.

This page has information on some of these foods. But there isn't strong evidence for any of them, as different studies have had different results. This means we can't say for sure whether any of these foods are likely to be helpful or harmful if you've been diagnosed with prostate cancer.

Many men want to know if any foods, or a particular diet, can help or even cure prostate cancer. But until there's more evidence that any individual food has an effect, it's best to have a balanced diet, including lots of fruit and vegetables and a wide range of other healthy foods.

Can any foods help with my prostate cancer?

Some studies suggest that certain foods could help slow down the growth of prostate cancer or lower the chance of it coming back after treatment. We describe some of these foods below. With all of these foods, the evidence isn't very strong and other studies haven't shown any effect. This means we can't say for sure whether any of these foods can help.

Soya beans and other pulses

Soya beans belong to a group of plants called pulses or legumes. Some of the chemicals in soya beans are also found in other pulses, such as kidney beans, chickpeas and lentils.

We don't know whether pulses have an effect on prostate cancer, but they are a good source of protein and other nutrients that are important for general health. Three heaped tablespoons of cooked pulses can count as one of your five daily portions of vegetables.

Soya beans are available in some supermarkets in the frozen foods or dried snacks sections. If you decide to eat more soya beans, you could try products such as soya milk and yoghurts, tofu, soya bread, miso and tempeh. Try to avoid products with added salt and sugar.

Green tea

Some studies suggest that chemicals in green tea might protect against prostate cancer growth and advanced prostate cancer. But we can't say for certain about the effects of green tea, as other studies haven't seen the same benefits.

If you decide to drink green tea, you'll need to brew it for five minutes to make sure plenty of nutrients are released, making the flavour quite strong. You might want to choose a decaffeinated variety, especially if you have urinary problems, as caffeine can irritate the bladder.

Tomatoes and lycopene

Tomatoes contain a plant chemical called lycopene. Some studies have suggested that eating tomatoes could help to protect against prostate cancer growth and aggressive prostate cancer. But experts recently looked at all of the studies on lycopene and only found limited evidence of any benefit for men with prostate cancer. So we don't know if it's helpful.

Cooked and processed tomatoes, such as tomato sauces, soups, purees and pastes, are a better source of lycopene than fresh tomatoes. This is because the body finds it easier to absorb lycopene from tomatoes that have been cooked or processed, particularly with a little oil. Try to choose low-salt and low-sugar options as some products, such as ketchup, have added salt and sugar.

Lycopene is also found in watermelons, pink grapefruits, guava and papaya. As lycopene isn't stored inside the body for very long, you need to eat foods containing lycopene regularly to keep some in your body. You may need to avoid grapefruit if you take certain medicines, including some drugs to lower cholesterol or blood pressure, drugs to treat erection problems, and warfarin to thin your blood. Ask your doctor or pharmacist if you're unsure.

Cruciferous vegetables

These include broccoli, cauliflower, cabbage, Brussels sprouts, bok choy, spinach and kale. Some studies suggest that cruciferous vegetables may help slow down the growth of prostate cancer and reduce the risk of advanced prostate cancer. But we need more research into the effects of cruciferous vegetables, as other studies haven't found this.

Pomegranate

Some studies suggest that pomegranate juice may be good for men with prostate cancer. But we don't yet know if this is the case. If you want to try pomegranate juice, choose a variety with no added sugar. You may need to avoid pomegranate if you use certain prescription drugs. Ask your pharmacist for advice.

Are there any foods I should eat less of?

There is some evidence that eating a lot of certain foods may be harmful for men with prostate cancer. We describe some of these foods below. There's no need to cut any of these foods out of your diet completely. We need more research to fully understand their effect on prostate cancer, but you can still eat most of them in moderate amounts as part of a healthy, balanced diet.

Dairy foods and calcium

Dairy foods are high in calcium. Calcium is important for strong bones and your overall health, so you need some calcium in your diet – around 700mg a day, or 1200-1500mg a day if you're on hormone therapy. Normal amounts of calcium and dairy foods won't increase your risk of advanced prostate cancer. But some studies suggest that eating a lot of calcium might increase the risk of your prostate cancer growing and spreading. Others have found no link, but it may be an idea to avoid eating more than 2000mg of calcium – the amount in about 1.6 litres of milk – a day.

Meat

The effect of red and processed meat on men with prostate cancer isn't clear. Some research suggests that eating too much may raise your risk of aggressive and advanced prostate cancer, while other research hasn't found any effect. Some studies have also suggested that a diet that is low in meat but high in fruit and vegetables may help to slow the growth of prostate cancer.

Red meat includes beef, pork and lamb. Try to eat no more than 500g of cooked red meat (700 to 750g before cooking) a week. Processed meat is meat that has been preserved by smoking, curing or salting, or with preservatives. It includes ham, bacon and some sausages, such as salami. It's best to avoid processed meat.
Large amounts of meat that have been cooked at very high temperatures or are very well done, such as barbecued, grilled or fried meat, may also increase your risk of advanced cancer. This may be caused by chemicals that are made when meat burns, as they can damage cells. So try to avoid eating lots of meat cooked at very high temperatures.

Fat

You need to eat some fat for your body to work properly. But eating too much fat can make you put on weight, which raises your risk of being diagnosed with aggressive or advanced prostate cancer.
There are different types of fat. Replacing animal fats with vegetable oils may help men with prostate cancer to live for longer. There is also some research that suggests eating lots of saturated fat might be linked with an increased risk of prostate cancer coming back after surgery, and of developing advanced prostate cancer. But we need more research to know for sure whether this is the case, as other studies haven't found a link.

Should I use supplements or herbal remedies?

Some people like to use dietary supplements or herbal remedies, but there's little evidence that they're helpful for men with prostate cancer. Some may even be harmful.

Dietary supplements

There's little evidence that supplements are helpful for men with prostate cancer. Some supplements may also interfere with your treatment for prostate cancer, so let your doctor, nurse or dietitian know if you're taking any.
Most people should be able to get all vitamins, minerals and other nutrients they need by eating a balanced diet, without taking supplements. If you do choose to take supplements, speak to your doctor first and don't take more than the recommended daily allowance (RDA).
Some men may need to take specific supplements. For example, if you're on hormone therapy, your doctor might recommend calcium and vitamin D supplements.

Herbal remedies

Some men like to take herbal medicines to help manage their prostate cancer or the side effects of treatment. For example, some men drink sage tea to help with hot flushes, which are a common side effect of hormone therapy. But there is very little evidence that herbal remedies can help to treat prostate cancer or reduce side effects.
It's important to tell your doctor about any complementary therapies you are using, including herbal remedies. Some herbal remedies may interfere with your cancer treatment and some may affect your prostate specific antigen (PSA) level, making the PSA test unreliable.
Not all herbal remedies in the UK are licensed and the quality varies a lot. Be very careful when buying herbal remedies over the internet. Many are made outside the UK and may not be high-quality. Many companies

make claims that are not based on proper research. There may be no real evidence that their products work and some may even be harmful. Remember that even if a product is 'natural', this doesn't mean it is safe. For more information about using herbal remedies safely, visit the Medicines and Healthcare products Regulatory Agency (MHRA) website.

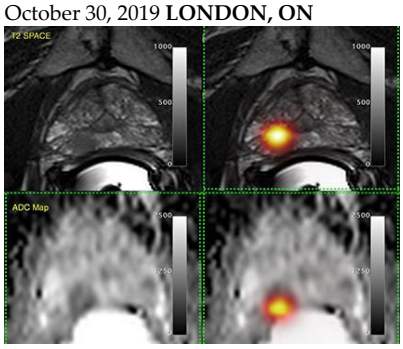
Herbal supplements being tested

Recently researchers have been looking at supplements containing a number of things such as pomegranate, green tea, broccoli, turmeric, soya and lycopene, to see whether they have an effect on prostate cancer.
There have been mixed results, with some studies suggesting they may be helpful and others suggesting they don't help. These studies have all been small and run for a short time, so we need larger studies lasting for several years to find out whether any supplements actually help.
https://prostatecanceruk.org/prostate-information/living-with-prostate-cancer/your-diet-and-physical-activity/foods-to-eat-or-avoid

NOTABLE

Study gives Ontario men access to advanced prostate cancer imaging

October 30, 2019 **LONDON, ON**



Led by researchers at Lawson Health Research Institute, a multi-centre registry trial is testing the use of a new imaging tracer, called a PSMA tracer, for early detection of recurrent prostate cancer. The registry gives patients access to a new type of imaging and will assess the impact on patient care.
PSMA tracers are used in positron emission tomography (PET) scans to target a protein found in prostate cancer cells called prostate specific membrane antigen (PSMA). Supported by Cancer Care Ontario and McMaster University's Centre for Probe Development and Commercialization (CPDC), the goal of the registry trial is to capture detailed PET images to guide treatment decisions made by patients and their care teams.
The trial is providing valuable insights to research participants like Wayne Smith, a 71-year-old man from Ingersoll, Ontario. When he was diagnosed with prostate cancer in 2013, Wayne made the decision to have his prostate removed. After some time, his prostate specific antigen (PSA) levels began to rise and his doctors were concerned that the cancer was coming back.

A challenge of the standard PSA blood test is that it can indicate a cancer is returning before the location of the tumour can be detected by a bone scan or computed tomography (CT) scan.

"I was told a PET scan was available through research and that it could help locate the disease," says Wayne. He went for the scan earlier this year at St. Joseph's Hospital, part of St. Joseph's Health Care London.

"Nothing showed up on the scan, but that was good news; it meant the cancer was microscopically small." Wayne and his doctors decided on hormone therapy and radiation therapy to eradicate any cancerous cells. He was treated at London Health Sciences Centre's (LHSC) London Regional Cancer Program.

"Early evidence suggests that a clear PET scan despite rising PSA levels is likely associated with persistent cancer at the original site," explains Dr. Glenn Bauman, Lawson Scientist and Radiation Oncologist at LHSC. "Based on the scan, Wayne was able to do a much shorter round of hormone therapy – six months rather than being on hormone therapy indefinitely."

Wayne is one of 1,500 Ontario men who will participate in the PSMA-PET Registry Trial. Eligible participants are those with suspected prostate cancer that cannot be detected in conventional bone and CT scans. Participants have a PET scan using a specific PSMA tracer called 18F-DCFPyL. The tracer is injected and spreads out in the body to find spots of cancer which are then visible on the scan.

"With this trial, men in Ontario can access a promising test that could impact their treatment outcomes," says Dr. Bauman. "The PSMA tracer may be able to locate prostate cancer that was once undiscoverable."

Led by Dr. Bauman along with Drs. Ur Metser and Tony Finelli at University Health Network (UHN), the trial is currently available across five sites in Ontario: London Health Sciences Centre; St. Joseph's Health Care Hamilton; Sunnybrook Health Sciences Centre; Princess Margaret Cancer Centre (UHN); and Thunder Bay Regional Health Sciences Centre. The trial is also expected to open at The Ottawa Hospital this year.

The PSMA tracer is considered an investigational agent in Canada and is currently only available through clinical trials. After studying the accuracy of the tracer in detecting early cancer recurrence, the research team hopes to have enough data to recommend when it could be used in the clinic.

In 2016, Lawson researchers were the first in Canada to use the 18F-DCFPyL PSMA tracer to capture PET images with a patient at St. Joseph's Hospital. The tracer is provided by CanProbe, a joint venture between CPDC and UHN located in Toronto, and was set up with funding from the Movember Foundation.

"We conducted an initial trial that included 20 men with prostate cancer who were having their prostate removed. The goal was to determine how effective the PSMA probe was in detecting disease at the time of initial treatment," explains Dr. Bauman. "We found the PET scan was able to detect spots of cancer in almost all participants, which corresponded to spots of cancer identified in the prostate after it was removed and examined under the microscope."

ntario men with recurrent prostate cancer who are interested in participating in the PSMA-PET Registry Trial are asked to contact one of the participating sites. Contact information can be found on www.clinicaltrials.gov. For more information on PET scanning in Ontario, including referral forms, visit www.petscansontario.ca.

PCCN Markham

Prostate Cancer Canada Network

Newsletter

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ABOUT LAWSON HEALTH RESEARCH INSTITUTE

As the research institute of London Health Sciences Centre and St. Joseph's Health Care London, and working in partnership with Western University, Lawson Health Research Institute is committed to furthering scientific knowledge to advance health care around the world.

FOR MORE INFORMATION, PLEASE CONTACT:

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QUOTABLE

Christmas Quotes

"Christmas, here again. Let us raise a loving cup; Peace on earth, goodwill to men, and make them do the washing up." Wendy Cope

"Christmas waves a magic wand over this world, and behold, everything is softer and more beautiful." - Norman Vincent Peale

"The only real blind person at Christmas-time is he who has no Christmas in his heart." *~Helen Keller*

"People really act weird at Christmas time! What other time of year do you sit in front of a dead tree in the living room and eat nuts and sweets out of your socks?" -Author Unknown

Whatever you may celebrate in December we wish everyone Happy Holidays, Happy New Year and a very Merry Christmas!

PCCN Markham

Newsletter

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PCCN Markham

Prostate Cancer Support Group

Meets the 2nd Tuesday
Every month
September – June
St. Andrew's Presbyterian Church
143 Main St Markham

The Markham PCCN Prostate Support Group is generously supported by Dr. John DiCostanzo, Astellas Pharma, St. Andrews Presbyterian Church, PCCN, and the Canadian Cancer Society.

The group is open to all; survivors, wives, partners, relatives and those in our community who are interested in knowing about prostate health. Drop by St Andrews Presbyterian Church 143 Main Street Markham at 7:30PM, the 2nd Tuesday every month from September to June. The information and opinions expressed in this publication are not endorsements or recommendations for any medical treatment, product, service or course of action by PCCN Markham its officers, advisors or editors of this newsletter.

Treatment should not be done in the place of standard, accepted treatment without the knowledge of the treating physician.

The majority of information in this newsletter was taken from various web sites with minimum editing. We have recognized the web sites and authors where possible.

PCCN Markham does not recommend treatment, modalities, medications or physicians. All information is, however, freely shared.

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We look forward to your feedback and thoughts. Please email suggestions to markhampccn@gmail.com

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