

**Medical Advisors**

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*Thanks!*

*Thought of The Day*

“Our very survival depends on our ability to stay awake, to adjust to new ideas, to remain vigilant and to face the challenge of change.”

– Martin Luther King Jr.

***April Meeting:***

**Date:** Wednesday, 15 April, 2020

**CANCELLED**

\* Due to Covid-19 crisis all public meetings of MPCSG are suspended until further notice.



The Manitoba Prostate Cancer Support Group offers support to prostate cancer patients but does not recommend any particular treatment modalities, medications or physicians ; such decisions should be made in consultation with your doctor.

**MPCSG – active since 1992.**

## Mpmri Before Biopsy – A Step Change In Prostate Cancer Diagnosis For Men

### What is mpMRI?

A multi-parametric magnetic resonance imaging (mpMRI) scan is a special type of scan that creates more detailed pictures of your prostate than a standard MRI scan. It does this by combining four different types of image. These images give your doctor information about whether or not there is any cancer inside your prostate.

Before having an mpMRI scan, you will be injected with a Gadolinium-based contrast agent which is an essential part of this type of imaging. It allows for a clearer picture of the prostate. The gadolinium (a metal ion) in these dynamic contrast

agents has been chemically adapted to make it safe to use as part of an mpMRI scan. Part of the quality control for mpMRI involves using the lowest possible effective dose of the contrast agent. There is not yet any clinical evidence that gadolinium causes any harm when used as a contrast agent for mpMRI, however, we will continue to monitor the situation carefully.



### Why mpMRI is better than previous diagnostic methods

Until recently, the only way to investigate suspected localised prostate cancer and determine whether or not it needs treating was based on the results of a TRUS (trans-rectal ultrasound) biopsy. This involves needles inserted into sample tissue across the prostate, to see whether or not it contains any cancerous cells.

On occasions, the needle can miss significant cancer if the section of the prostate where its located isn't sampled. Although biopsies are a key part of diagnosis, they can be invasive for men and come with a risk of serious infection. Finding a way to improve the number of significant prostate cancers that get caught in time, whilst reducing the number of men who have biopsies

unnecessarily, is really important.

In 2017, the results of a new study called PROMIS were published. The study involved hundreds of men and examined whether mpMRI before biopsy can provide a more accurate diagnosis for men with suspected prostate cancer and can rule some men out of unnecessary biopsy. The study has shown that mpMRI:

- is significantly better at identifying clinically significant prostate cancer compared to TRUS biopsy
- reduces the number of men having biopsies unnecessarily by a quarter (27%) because the scan will only pick up cancers which could cause men harm and need further tests
- helps improve the accuracy when taking biopsy samples, targeting directly any suspicious areas seen on the MRI

Source: <https://prostatecanceruk.org/about-us/projects-and-policies/mpmri>

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## Multiparametric MRI

With improvements in equipment, the introduction of new imaging sequences and studies involving thousands of men with prostate cancer, dedicated MRI has been shown to be a valuable tool in the diagnosis, treatment choice and treatment planning algorithms for prostate cancer. Multiparametric (mp) MRI with anatomic (T1 and T2 Weighted) and functional ((T2 and Diffusion Weighted/DWI, Dynamic Contrast Enhanced/DCE) imaging sequences enables tumor localization

and characterization with great accuracy. Information from a mpMRI of the prostate improves the predictive staging accuracy generated from clinical information and transrectal ultrasound (TRUS) guided biopsy findings used in the PRIAS, D'Amico and Epstein Criteria, CAPRA score and other algorithms. The review article authored by David C. Johnson and Robert Reiter in the June 2017 issue of Translational Andrology & Urology neatly summarizes the multifaceted role

of mpMRI in the diagnosis and management of nonmetastatic prostate cancer.

Multiparametric MRI of the prostate has been shown to be useful in the following:

The patient with clinical suspicion of cancer, but a negative TRUS (transrectal ultrasound-guided) biopsy or clinical findings suspicious for higher grade tumor than indicated by

*(Continued on page 3)*

(Continued from page 2)

TRUS biopsy pathology: In these patients, mpMRI may show a primary tumor in the anterior prostate that is “out of the range” of the standard TRUS biopsy needle or may detect a tumor that was undersampled by the TRUS needle (explainable since most prostate cancers are undetectable on the ultrasound images used to guide the TRUS biopsy). It is likely that the patient will be re-biopsied if mpMRI detects a tumor that was not or was possibly inadequately sampled on the TRUS biopsy. An accurate re-biopsy may be directed to the MRI detected lesion in one of several ways: a) by cognitive fusion, in which the urologist reviews the MRI images and directs the biopsy needle to the area shown on the images, b) electronic fusion of MRI images with real time TRUS or transperineal biopsy images at the time of re-biopsy and c) real time MRI biopsy with the patient in the scanner utilizing special MRI compatible biopsy devices.

Candidates for active surveillance (AS): Incorporating mpMRI into the evaluation of patients with newly diagnosed prostate cancer can separate those patients who are candidates for AS from those may be candidates by clinical criteria, but have significant lesions not detected on initial TRUS biopsy and thus require definitive treatment. The high negative predictive value of a negative mpMRI makes it highly unlikely that the patient who is an AS candidate by clinical criteria harbors clinically significant cancer. In addition, studies suggest that periodic mpMRI monitoring of patients on AS may decrease the number of re-

biopsies currently recommended for patients on AS, thus decreasing the possible morbidity and negative impact on quality of life that can be associated with multiple re-biopsies such as pain, infection and bleeding. Although men with stable MRI findings have a low likelihood of pathologic progression, the recognized limitations of mpMRI in detecting small, multifocal tumors, including small high grade lesions, suggest that serial monitoring with mpMRI cannot completely replace periodic standard TRUS or transperineal biopsy in following AS patients.

Multiparametric MRI as an adjunct in clinical staging and treatment planning:



MRI directly visualizes the prostatic capsule, seminal vesicles and neurovascular bundles and differentiates malignant from benign tissue. Optimal accuracy in clinical staging as well as both radiation and surgical treatment planning is achieved by combining clinical data with mpMRI findings. From a surgical standpoint, evidence of tumor outside the prostate on mpMRI would help the urologist advise against surgery, or at

least inform the patient that he will need further therapy such as radiation and/or hormone treatments after surgery. From a radiation standpoint, mpMRI would help the radiation oncologist plan the external beam radiation fields in order to cover any tumor that is found outside the prostate. In addition, mpMRI can help determine if the patient is a good candidate for brachytherapy. Similar to surgery, extensive cancer outside the prostate may make the patient a less than ideal candidate for brachytherapy, or at least help the radiation oncologist advise the patient that more aggressive or additional treatment may be needed. Finally, it is also important to note that the equipment used and the experience of the radiologists are key to a good

prostate mpMRI program. Several studies included in the review article by Johnson and Reiter show the improved performance of mpMRI done with 3.0 vs. 1.5 Tesla magnets and emphasize the importance of having radiologists who specialize in the interpretation of prostate mpMRI interpreting the examinations.

by, Dr. James W. Borrow

Dr. James W Borrow is a Diagnostic Radiology

Specialist in Seattle, Washington. He graduated with honors from University Of Washington School Of Medicine in 1971. Having more than 46 years of diverse experiences, especially in DIAGNOSTIC RADIOLOGY, Dr. James W Borrow affiliates with no hospital, and cooperates with other doctors and specialists without joining any medical groups.

Source: <https://prostatecancerfree.org/multiparametric-mri/>

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## Exercise May Improve Outcomes for Patients with Prostate Cancer Beginning ADT

A short-term study, published in *BJU International*, of supervised exercise in patients with prostate cancer beginning androgen-deprivation therapy (ADT) resulted in sustained improvements in quality of life (QoL) and cardiovascular events risk profile.<sup>1</sup>

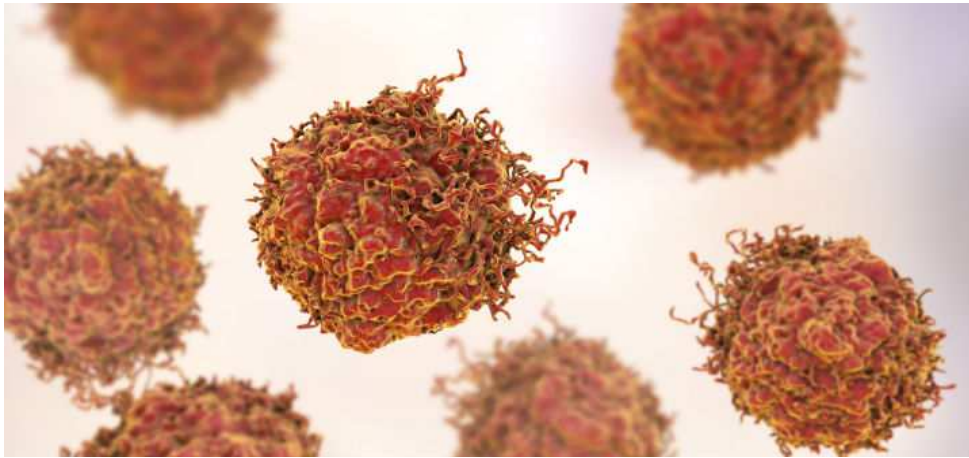
These data suggest that clinicians should prescribe a short-term exercise program at the beginning of ADT to try and assuage these important treatment-related side-effects.

“The problem is ADT has several side-effects, including increased body fat, decreased cardiopulmonary fitness and increased fatigue,” Anthony S. Leicht, associate professor in the College of Healthcare Sciences at James Cook University in Australia, said in a press release.<sup>2</sup> “These can increase the risk of a cardiovascular event and reduce health-related quality of life.”

In a cohort of 50 patients with prostate cancer scheduled for ADT, 24 were randomized to an exercise group and 26 to a control group. The exercise group did 3 months of supervised aerobic and resistance exercise training twice a week for 60 minutes, followed by 3 months of self-directed exercise. Researchers assessed the outcomes at baseline, 3, and 6 months.

The primary outcome for the study was difference in fat mass at 3-months. Secondary outcomes included fat-free mass, cardiopulmonary exercise testing variables, QRISK2 (ClinRisk Ltd, Leeds, UK) score, anthropometry,

blood-borne biomarkers, fatigue, and QoL.



At 3-months, exercise training prevented adverse changes in peak O<sub>2</sub> uptake (1.9 mL/kg/min; P = 0.038), ventilatory threshold (1.7 mL/kg/min; P = 0.013), O<sub>2</sub> uptake efficiency slope (0.21, P = 0.005), and fatigue (between-group difference in Functional Assessment of Chronic Illness Therapy-Fatigue score of 4.5 points; P = 0.024) compared with controls. After withdrawing the supervised exercise though, the differences in cardiopulmonary fitness and fatigue were not sustained, but the exercise group did demonstrate significantly better QoL (Functional Assessment of Cancer Therapy-Prostate difference of 8.5 points; P = 0.034) and a reduced QRISK2 score (-2.9%; P = 0.041) compared to controls.

“What was important, and different from most other studies, was that the patients started the exercise program before the ADT treatment began,” Leicht said. “Other studies have examined patients already undergoing treatment.”

However, lack of time, financial costs, and transport difficulties are common barriers to exercise cited by patients with cancer and older adults in general.

Additionally, using self-report questionnaires may have exposed the study to subjective bias, though anecdotal evidence helped confirm whether or not the patients maintained the exercise. Researchers suggested that future studies should seek to better understand how to improve participation within this patient group in exercise training programs.

“In older people we often see reductions in strength and physical function just 3 months after halting supervised exercise. They may stop exercising because of cost or other reasons,” said Leicht. “A more pragmatic approach such as home-based exercise or a shorter period of supervision with follow-on remote support could help get around these restrictions and provide measurable benefits to prostate cancer sufferers.”

### References:

1. Ndjavera W, Orange ST, O’Doherty AF, et al. Exercise-induced attenuation of treatment side-effects in patients with newly diagnosed prostate cancer beginning androgen-deprivation therapy: a randomized controlled trial. *BJU International*. doi:10.1111/bju.14922.
2. Exercise works for those beginning cancer treatment [news release]. Australia. Published March 12, 2020. [jcu.edu.au/news/releases/2020/march/exercise-works-for-those-beginning-cancer-treatment](http://jcu.edu.au/news/releases/2020/march/exercise-works-for-those-beginning-cancer-treatment). Accessed March 18, 2020.

Hannah Slater March 20, 2020

<https://www.cancernetwork.com/prostate-cancer/exercise-may-improve-outcomes-patients-prostate-cancer-beginning-adt>

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## New Test Distinguishes between Aggressive and Less Harmful Forms of Prostate Cancer

Scientists at the University of East Anglia (UEA) say they have discovered why some prostate cancers are more aggressive, spread to different parts of the body, and ultimately cause death. The team, which published its study, “A novel stratification framework for predicting outcome in patients with prostate cancer”<sup>1</sup> in the *British Journal of Cancer*, hopes its findings will help transform patient treatment.

“Unsupervised learning methods, such as Hierarchical Cluster Analysis, are commonly used for the analysis of genomic platform data. Unfortunately, such approaches ignore the well-documented heterogeneous composition of prostate cancer samples. Our aim is to use more sophisticated analytical approaches to deconvolute the structure of prostate cancer transcriptome data, providing novel clinically actionable information for this disease. We apply an unsupervised model called Latent Process Decomposition (LPD), which can handle heterogeneity within individual cancer samples, to genome-wide expression data from eight prostate cancer clinical series, including 1,785 malignant samples with the clinical endpoints of PSA failure and metastasis,” write the investigators.

“We show that PSA failure is correlated with the level of an expression signature called DESNT (HR = 1.52, 95% CI = [1.36, 1.7], P =  $9.0 \times 10^{-14}$ , Cox model), and that patients with a majority DESNT signature have an increased metastatic risk (X2 test, P = 0.0017, and P = 0.0019). In addition, we develop a stratification framework that incorporates DESNT and identifies three novel molecular subtypes of prostate cancer. These results highlight the importance of using more complex approaches for the analysis of genomic

data, may assist drug targeting, and have allowed the construction of a nomogram combining DESNT with other clinical factors for use in clinical management.” The findings come after the same team developed a test that distinguishes between aggressive and less harmful forms of prostate cancer, helping to avoid sometimes-damaging unnecessary treatment. The new study shows how the number of aggressive cells in a tumor sample defines how quickly the disease will progress and spread. The study also reveals three new subtypes of prostate cancer that could be used to stratify patients for different treatments.

Lead researcher Colin Cooper, PhD, from UEA’s Norwich Medical School, said: “Prostate cancer is the most common cancer in men in the U.K. It usually develops slowly, and the majority of cancers will not require treatment in a man’s lifetime. However, doctors struggle to predict which tumors will become aggressive, making it hard to decide on treatment for many men. This means that many thousands of men are treated unnecessarily, increasing the risk of damaging side effects, including impotence from surgery.



The team developed a test to distinguish aggressive prostate cancers from less threatening forms of the disease, by applying complex math known as Latent Process Decomposition.

A collaborator, Vincent Moulton, PhD, from UEA’s School of Computing Sciences, added “By applying the Latent Process Decomposition process and analyzing global prostate cancer datasets, we discovered an aggressive form of prostate cancer known as DESNT, which has the worst clinical outcomes for patients.”

In the latest study, published today, the team studied gene expression levels in 1,785 tumor samples. They found that the amount of DESNT subtype cells in a sample is linked with the likelihood of disease progression, the more DESNT cells, the quicker the patient is likely to progress.

Co-lead researcher Daniel Brewer, PhD, noted: “If you have a tumor that is majority DESNT you are more likely to get metastatic disease, in other words it is more likely to spread to other parts of your body. This is a much better indication of aggressive disease. We also identified three more molecular subtypes of prostate cancer that could help doctors decide on different treatment options for patients. This research highlights the importance of using more complex approaches for the analysis of genomic data.”

March 20, 2020

Source: University of East Anglia

<sup>1</sup> [www.nature.com/articles/s41416-020-0799-5](http://www.nature.com/articles/s41416-020-0799-5)

Source: [www.genengnews.com/news/new-test-distinguishes-between-aggressive-and-less-harmful-forms-of-prostate-cancer/](http://www.genengnews.com/news/new-test-distinguishes-between-aggressive-and-less-harmful-forms-of-prostate-cancer/)

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## Younger Men With Prostate Cancer Benefit From More Aggressive Treatment

For younger men diagnosed with prostate cancer, a "wait-and-see" approach is often recommended - sometimes delaying treatment until the disease, and its symptoms, worsen.

However, the findings of a new study published Thursday by JAMA Network Open indicate that these men may actually benefit from more aggressive therapy.

Researchers noted that those who received so-called "non-definitive therapy" - either systemic therapy or no initial therapy - were more than twice as likely to die from the disease than those who underwent more aggressive treatment, including surgical removal of the prostate or radiotherapy.

"Younger men with prostate cancer should not be complacent," study co-author Dr. Chad Tang, a radiation oncologist at MD Anderson Cancer Center in Houston, told UPI. "With more aggressive forms of prostate cancer, (they) should seek surgery or radiation."

Prostate cancer is the second most common form of cancer in men in the United States, after skin cancer, according to statistics from the American Society of Clinical Oncology. Roughly 200,000 American males will be diagnosed with the disease this year, 60 percent of them 65 years of age and older.

The average age at time of diagnosis is 66, per ASCO.

For their study, Tang and his colleagues looked at data for 72,036 men between 30 and 70 years old, with median age of 63, who had high-risk prostate cancer without regional lymph node or distant metastatic disease. Of these, 5,252, or 7.3 percent, initially received non-definitive therapy - either systemic hormone-based androgen-deprivation therapy or chemotherapy or active surveillance, known as "watchful waiting."

The others underwent more aggressive treatment, such as radical prostatectomy, or surgical removal of the prostate; external beam radiation therapy; or brachytherapy-based radiation therapy, perhaps in combination with androgen-deprivation therapy.

In addition to the differences in overall survival between the two groups, the authors noted that men without health insurance, as well as those on Medicaid or Medicare, were more likely to receive systemic therapy or no treatment initially than those with private health insurance. There were also racial disparities in care, with black and Hispanic men more likely than white men to be administered systemic therapy or no treatment initially.

Between 2004 and 2014, men without insurance or who were enrolled in Medicaid had lost nearly twice as many years of life due to the disease compared with those on private insurance.

"Hopefully urologists and those at the front lines of prostate cancer treatment will take this study to suggest that aggressive pursuit of definitive therapy is warranted in younger men with more aggressive forms of prostate cancer," Tang said. "That may mean working with them to obtain insurance coverage or being more willing to accept less desirable forms of reimbursement. These men should not be treated with non-definitive treatment strategies indefinitely."

Added co-author Dr. Alex Bagley, a resident surgeon at MD Anderson, "Interventions aimed at providing greater definitive local therapy for younger patients with high-risk prostate cancer, such as expanding access to health insurance, may have a survival benefit in this population."

March 19, 2020 UPI

By Brian P. Dunleavy

Source: [https://www.upi.com/Health\\_News/2020/03/19/Younger-men-with-prostate-cancer-benefit-from-more-aggressive-treatment/1801584627655/](https://www.upi.com/Health_News/2020/03/19/Younger-men-with-prostate-cancer-benefit-from-more-aggressive-treatment/1801584627655/)

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## Novel Technique Outperforms Traditional Imaging For High-Risk Prostate Cancer

A novel molecular imaging technique demonstrated higher diagnostic accuracy than conventional imaging among a cohort of men with high-risk prostate cancer, according to results of a randomized phase 3 study published in The Lancet.

"Taken together, our findings indicate

that prostate-specific membrane antigen PET-CT scans offer greater accuracy than conventional imaging and can better inform treatment decisions. We recommend that clinical guidelines should be updated to include prostate-specific membrane antigen PET/CT as part of the diagnostic pathway for men with high-risk

prostate cancer," Michael S. Hofman, MBBS, FRACP, FAANMS, professor of nuclear medicine at Peter McCallum Cancer Centre in Melbourne, Australia, said in a press release.

Standard-of-care imaging with CT

*(Continued on page 7)*

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and bone scan has insufficient sensitivity and specificity for detection of nonlocalized prostate cancer, researchers wrote.

In the multicenter, two-arm, prospective proPSMA study, Hofman and colleagues assessed whether gallium-68 prostate specific-membrane antigen (PSMA)-11 PET-CT — an imaging technique that delivers detailed body scans of patients as it detects prostate cancer cells — could improve accuracy and affect treatment management.

The researchers randomly assigned 300 men (median age, 69 years; interquartile range [IQR], 63-73.5) with biopsy-proven prostate cancer and high-risk features across 10 hospitals in Australia to conventional imaging (n = 152) or PSMA-11 PET-CT (n = 148).



Accuracy of first-line imaging for identifying either pelvic nodal or distant metastatic disease, defined by the receiver operating curve using a predefined reference standard including histopathology, imaging and biochemistry at 6-month follow-up, served as primary outcome.

Men underwent first-line imaging within 21 days after randomization and crossed over to the alternate imaging group unless three or more distant metastases were found. Five men dropped out of the study or did not have follow-up data available.

All study participants received a second round of medical imaging at 6-month follow-up. Researchers used results of scans, biopsies and changes in blood tests to confirm tumor spread.

Eighty-seven men (30%) had pelvic nodal or distant metastatic disease.

Researchers observed greater accuracy with the novel imaging technique compared with conventional imaging (92% vs. 65%;  $P < .0001$ ). In addition, PSMA-11 PET-CT was associated with greater sensitivity (85% vs. 38%) and specificity (98% vs. 91%).

Results of subgroup analyses showed superiority of PSMA-11 PET-CT vs. conventional imaging among men with pelvic nodal metastases (area under the curve, 91% vs. 59%) and men with distant metastases (AUC, 95% vs. 74%).

Hofman MS, et al. *Lancet*. 2020; doi:10.1016/S0140-6736(20)30314-7.  
Moore C. *Lancet*. 2020;doi:10.1016/S0140-6736(20)30527-4.

March 23, 2020

Source: <https://www.healio.com/hematology-oncology/prostate-cancer/news/online/7B1a3a7768-ab6b-41e2-a889-ad9ff866faf9%7D/novel-technique-outperforms-traditional-imaging-for-high-risk-prostate-cancer>

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### ***Notice to recipients of the printed version of this newsletter:***

*We are exploring ways to reduce costs while continuing to meet the information needs of our readership. To do this we are testing the effectiveness of providing meeting information for two months in one printed issue. That's why there are two meetings listed on the front page of this issue. There will not be a printed version of our newsletter in the months of April and June.*

*Information about our speakers for these months will be published in the previous month's issue .*

*We welcome feedback from our readers and anticipate getting back to our regular monthly print schedule beginning in July. The electronic version will still be available each month and can easily be accessed on our website (manpros.org). We urge you to convert to email receipt of our newsletter if at all possible.*

*Thank you.*

*The Board*

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**FUTURE MEETINGS 2020**

*Watch this space for speakers for future meetings which will resume once the Covid-19 crisis passes*

All meetings (except September) will be held at :  
 The First Unitarian Universalist Church of Winnipeg, 603 Wellington Crescent

All meetings are 7 – 9 pm.  
 (First hour for general discussion;  
 second hour for expert guest speaker)

Everyone Welcome Plenty of free parking

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Irek Iskat — membership

For general information please contact Jos Borsa at number listed above



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