FROST & SULLIVAN

PROSTATE CANCER CARE

Addressing Unmet Needs to Transform Diagnosis and Treatment

Technology has played multifaceted roles in transforming prostate cancer care. One of the most interesting amalgamations of technology and human behavioural science is the emergence of social media, which is playing a pivotal role in spreading awareness about prostate cancer. Movember is an example that showcases the power of combining technology and society led innovation in transforming healthcare products and services and delivering value for patients.

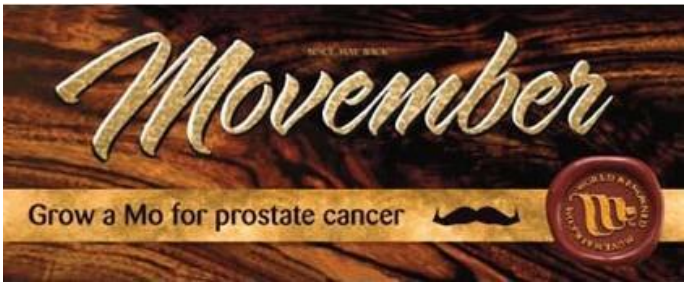


Image source: The Movember Foundation

What started in 2003 as a small event in a bar, supported by 30 people adamant to bring back the ‘70s moustache fashion back, has transformed into a massive movement. Supported by over five million people in 21 countries, the organisation, Movember, has since raised over €700 million and funded over 1,200 projects focused on finding cures for prostate cancer, testicular cancer, and other issues on men’s health. This is resulting in enhanced physician-patient relationships and new care delivery models.

One of the most promising projects launched by the organisation that is reinventing patient support programs is the TrueNTH program. It has brought together over 300 health experts, across six countries, to assist prostate cancer patients throughout their cancer care journey. It uses various tools such as online portals, community care group discussions, and six weeks of focused training programs for participating survivors to assist new patients track their progress, seek support, and discuss any challenges.

Image source: The Movember Foundation

Another unique program by Movember that has dissolved geographical barriers and brought together researchers globally is the Global Action Plan (GAP). The program accelerates research through collaboration and knowledge sharing amongst researchers. Currently, the program is working on several projects, the most promising of which is the GAP1 Global Prostate Cancer Exosome Biomarker initiative.

This project has resulted in the development of a prototype device that enables diagnosis of prostate cancer from a urine or blood sample. If this is available for routine use, it can save men from having invasive biopsy procedures. The project is also focused on developing a test that can differentiate between aggressive and low-risk forms of the disease based on urine and blood-based biomarkers. Treatment will only be provided when an aggressive form of cancer is detected. This will help in avoiding side effects such as urinary incontinence and sexual dysfunction in men with low-risk disease, thereby enhancing their quality of life.

The organisation's efforts have been lauded by policymakers globally. Several UK MPs have donned moustaches showcasing their solidarity with Movember. Former Prime Minister of UK, David Cameron has appreciated Movember's efforts of increasing awareness on prostate cancer on several occasions in the parliament. Movember has received similar recognition in the Scottish and Australian parliaments as well.

Aware politicians are more sensitive toward the need of their constituents. In 2013, when Rose Thompson launched Hear Me Now, a report that suggested that black men were twice more susceptible to prostate cancer than White Caucasian men, and recommended early screening for all black men 45 years and above, it was well received by UK MPs.

Local roundtable meetings were organised in London, Nottingham, and Birmingham, followed by the launch of first Black and Minority ethnic (BMe) prostate cancer project in Nottingham City, in 2016. Funded by NHS Nottingham City Clinical Commissioning Group, the project facilitated early screening of prostate cancer for Black, African and Black Caribbean communities.

Image description: UK parliamentarians including Minister Nicola Sturgeon, MSPs Liam McArthur & Edward Mountain supporting the Movember movement.

Image source: Prostate Cancer UK

In September 2017, moustache donning Australian MPs organized a barbeque event, to support prostate cancer awareness. Prime Minister Malcolm Turnbull announced that their government will continue to support prostate cancer care and doubled funding for 'Prostate Cancer Specialist Nursing Program'. The program provides nurses to support prostate cancer patients through different stages of their care journey—diagnosis, treatment, and aftercare. It was initiated by the Prostate Cancer Foundation of Australia in 2012, funded by a €2.5 million contribution from Movember.

Despite government support and rising awareness, prostate cancer remains one of the most diagnosed and lethal cancer in men. As per WHO, in 2012, 1.1 million men were diagnosed with prostate cancer, making it the second most diagnosed cancer in men (lung cancer was the most diagnosed cancer with 1.2 million new cases). Almost 70% of the cases occurred in developed regions (includes Europe, Northern America, Australia, New Zealand, and Japan).

Global Prostate Cancer Incidence (per 100,000, 2012)

Image source: GLOBOCAN, WHO

The developed regions faced a loss of about 142,000 men due to prostate cancer. Despite a high mortality rate, it remains one of the most under-studied cancer-types. Funding is much lower than that for other leading cancers. For instance, the National Cancer Institute in the US, one of the largest contributors to cancer research funding globally, funded prostate cancer research worth €195 million in 2015—less than half the funding for breast cancer research, the same year.

Incidence and Mortality Rates, by Type of Cancer and Sex – Developed Regions (2012)

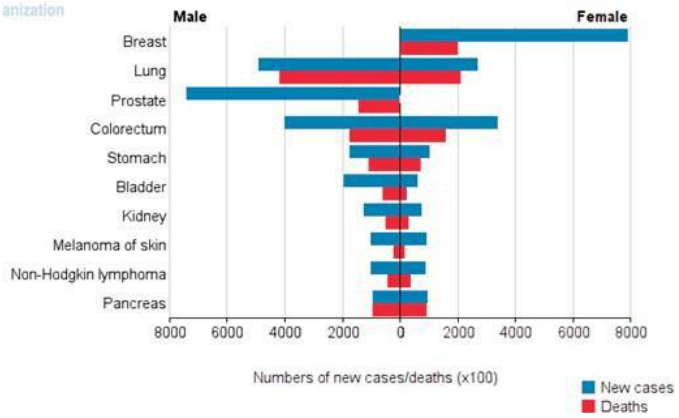


Image source: GLOBOCAN, WHO

This makes it all the more important for us to come together, and do our bit to promote research and equip our scientists with the arsenal that could defeat the deadly disease. Recent breakthroughs in prostate cancer diagnosis, therapies and research have been extremely promising.

Current Tests and Challenges

Prostate-specific antigen (PSA) test is usually the primary screening test. It involves analysis of blood sample for PSA levels. A reading of PSA level above 4 ng/ml is generally considered high and could be followed by a digital rectal examination (DRE), in which a physician uses the anal passage to examine the prostate surface for checking tumours or prostate enlargement.

One of the key challenges with PSA testing is that it is not accurate. PSA levels can be high due to several factors such as prostate inflammation or urinary tract infection. To counter this challenge, physicians usually conduct multiple PSA tests and DREs spread over a few weeks/months before recommending a biopsy.

Despite multiple tests, PSA is known to have a high rate of false-positive and false-negatives. A false-positive test means that a man's PSA level is elevated; however, he does not have prostate cancer. A false-positive test result creates unnecessary stress and anxiety for a man and his family and leads to additional medical procedures, such as a prostate biopsy, which has a risk of side effects including pain and bleeding.

As per the National Cancer Institute, US, *"only about 25% of men who have a prostate biopsy due to an elevated PSA level actually are found to have prostate cancer when a biopsy is done."*

Similarly, a PSA test may result in a false-negative result, which means that a man's PSA level is reported as low, even when he has prostate cancer. False-negative test results give false assurances and delay treatments.

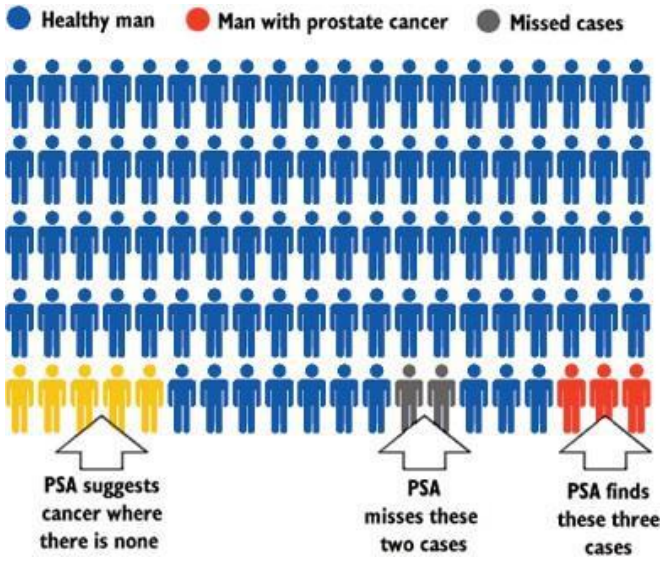


Image source: Article titled 'New Urine Test for Prostate Cancer Available; Unlike PSA Test, is Ultra- Specific for Prostate Cancer', published in Health.am (September 2013)

PSA and DRE tests are generally followed by a biopsy, in which several tissue samples from the prostate are examined by a pathologist to determine cancer. The test is associated with side effects including infection, bleeding, and pain.

Despite their challenges, PSA, DRE, and biopsy are the widely adopted tests available for screening and diagnosis of prostate cancer.

As per the National Cancer Institute, US, about 79% of prostate cancer cases at diagnosis are localized, while the remaining 21% are either spread to regional lymph nodes or metastasized to distant organs. Many countries, including the US, UK, and Australia have conducted studies to evaluate the possibility of a national screening program. However, each study has found that the risks outweigh the benefits.

This represents a huge unmet need. If the remaining 21% of metastasised cases are detected earlier at a localised state, thousands of lives can be saved. In monetary terms, it would result in avoiding the high costs involved in the chemical therapy of the metastasized cancers. This calls for high impetus on research and increase awareness and adoption of recently launched tests.

MOST PROMISING INNOVATIONS

MP-MRI

Multi-parametric MRI (MP-MRI) is being hailed as the *"biggest leap forward in prostate cancer diagnosis in decades"* by Angela Culhane, the chief executive at Prostate Cancer UK. MP-MRI provides a more accurate and painless method than biopsy for diagnosing prostate cancer.

In a trial on 576 men published in the Lancet, it was found that MP-MRI could avoid a primary biopsy in 27% of patients. Moreover, if MP- MRI directs subsequent biopsies, up to 18% more cases of clinically significant cancer might be detected compared with standard biopsies.

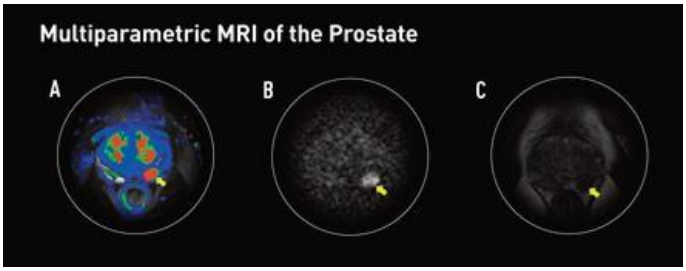


Image description: "Multiparametric MRI uses a dynamic contrast enhancement colour map (A), which shows intravenous contrast, allowing the radiologist to observe the rapidity with which the tissue is enhanced. Here, the image shows a focal area of abnormal perfusion indicated by the red colour. The T2- weighted image (B) can identify tumours by their inherent difference from other areas of tissue. Diffusion-weighted imaging (C) displays the rate of water diffusion in tissues, which can assist in tumour delineation."

Image source: Article titled, 'Multiparametric MRI/Ultrasound Fusion Biopsy and Prostate Cancer', published in Massachusetts General Hospital website (September 2017)

The study provides significant advantages and is being evaluated by NHS for widespread adoption. The cost should not be a deterrent as both the MP-MRI scan and biopsy cost around €500. The only challenge for wide-adoption remains the low availability of scanners and qualified radiologists.

PET/MRI

In a study funded by the Norwegian Cancer Society, published in October 2017 edition of the Journal of Nuclear Medicine, researchers at the Norwegian University of Science and Technology observed that fluciclovine F-18 PET combined with MP-MRI provided better images over either modality alone for detecting and characterizing high-risk prostate cancers. It was noted that the PET/MRI system costs more, which may hinder its usage in routine diagnosis. However, its high diagnostic potential could be utilised in selected cases, such as for diagnosis of patients at high risk for lymph node metastases and for planning of targeted prostate biopsies in highly suspected patients with previous negative biopsies.

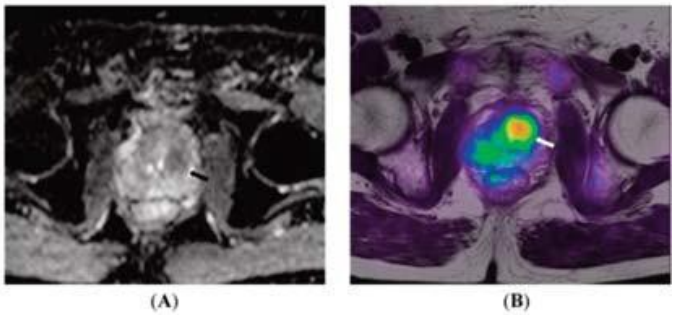


Image description: "A 72-year old patient with prostate cancer. (A) ADC map shows low signal intensity in the central gland (arrow), which is confirmed by F-18 choline PET/MRI (arrow in B) to be metabolically active central gland tumour."

Image source: Article titled, 'PET/MRI in Oncological Imaging: State of the Art', published in the Diagnostics Journal (July 2015)

Personalised Diagnosis

Use of genetic biomarkers in guiding prognosis and predicting therapy responses is one of the most promising areas in the field of prostate cancer research. The technology has the potential to be used in routine care, due to the rising clinical evidence supporting its efficacy and the ease of implementation it offers over traditional biopsy. Various biomarkers currently being evaluated in clinical studies include cell-free tumour DNA (cfDNA), circulating tumour cells (CTCs), circulating RNAs, cell-free proteins, and exosomes.

Image source: Frost & Sullivan

Cell-free tumour DNA (cfDNA)

Cell-free tumour DNA can be extracted from the blood of a patient. Its analysis can assist in evaluating a tumour at a genetic-level and avoid unnecessary treatment and associated side effects. Physicians can identify genetic mutations and tailor a therapy based on a patient's genetic makeup. For instance, if genetic analysis of cfDNA reveals a genetic mutation in the androgen receptor (AR) gene, then a physician can avoid drugs that modulate androgen receptors. cfDNA level, integrity, methylation, and mutational status have been identified to be useful predictors of monitoring prostate cancer therapy.

In a study published in journal Clinical Chemistry, it was reported that using cfDNA biomarkers in a clinical trial with around 433 participants, researchers were able to discriminate prostate cancer from controls with a diagnostic accuracy of 83% and differentiate benign prostatic hypertrophy and prostatitis from prostate cancer with an accuracy of 90%.

In various recent studies, researchers have identified several prognostic biomarkers using cfDNA. Pioneers in this space include the Institute of Cancer Research (UK), Medical University of Graz (Austria), and the Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, (Italy).

Although cfDNA offers high diagnostic potential, the current challenges in its widespread adoption include its low detection rate.

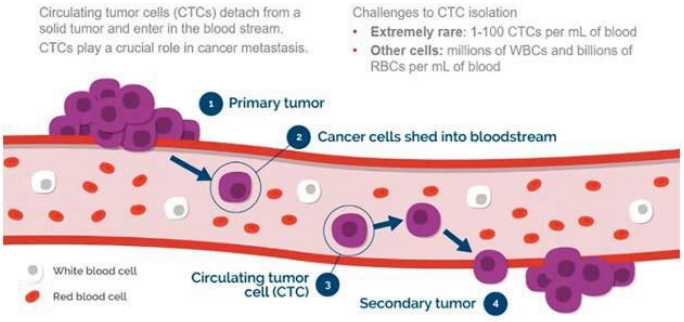
cfDNA Biomarkers

Biomarker	Description
Newly occurring focal amplifications (AR and MYC)	Indicates metastatic progression
High-level copy number gains in the androgen receptor (AR) locus	Present in castration-resistant prostate cancer (CRPC) patients but not in castration sensitive prostate cancer (CSPC) patients
Plasma AR mutations	Indicates enzalutamide- resistant and abiraterone-resistant patients with metastatic CRPC
AR and CYP17A1 copy number gain	Indicates shorter progression-free survival (PFS) and overall survival (OS) compared to metastatic CRPC patients with no gain

Circulating Tumour Cells (CTCs)

Circulating tumour cells (CTCs) are extracted from blood. They originate from a primary tumour or metastatic foci. They are present in extremely minute quantities, representing roughly a cell in a hundred million. Although they are difficult to extract, CTC can be a useful tool for monitoring treatment response.

CTCs Provide Direct Access to Intact Cancer Biology



CTCs are detected at high frequency in castration-resistant prostate cancer (CRPC) and are known to be associated with clinical outcomes. In different clinical studies, it was found that rising CTC levels and whole blood CTC count were strong indicators of overall survival. Currently, Menarini- Silicon Biosystems' CellSearch is the only FDA-approved CTC assay available for prognostic evaluation of prostate cancer in a clinic. Problems associated with sensitivity and specificity have hampered the wide adoption of CTC into clinical practice for guiding treatment decisions.

However, with new products such as the VTX-1 system from Vortex Biosciences, which can isolate CTC efficiently using microfluidic technology, usage of CTC for diagnosing prostate cancer in clinical settings is expected to increase.

Circulating RNA (cfRNA)

Circulating RNA can be analysed from a patient's blood and urine samples. Several cfRNA-based diagnostic tests have been commercialized, representing the huge potential the segment offers in alleviating pain arising from repeated biopsies in prostate cancer patients. All the tests have been launched in the previous 5 years.

Despite showcasing strong clinical performance when compared to biopsies, they are yet to witness wide adoption largely due to operational limitations (limited reimbursement, low visibility and so on). With time, as they gain more recognition from physicians, they are likely to play a significant role in diagnosing prostate cancer.

MDxHealth's SelectMDx is one such product which has immense potential for growth. It is a reverse transcription PCR (RT-PCR) assay performed on a urine sample that measures the mRNA levels of the distal-less homeobox 1 (DLX1) and urinary homeobox C6 (HOXC6) biomarkers, using the kallikrein-related peptidase 3 (KLK3) expression as an internal reference. The result assists in identifying patients with high-risk prostate cancer.

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MDxHealth has another commercialized test for diagnosing prostate cancer, ConfirmMDx, which uses residual tissue from previous negative prostate biopsies to rule out cancer-free men, avoiding the need for repeated biopsies. During 2012–2016, MDxHealth performed over 75,000 prostate cancer tests, of which 24,000 were in 2016. As per Taglich Brothers, the company is expected to nearly double the number of tests performed for prostate cancer by 2018, due to rising reimbursement coverage and increasing distribution network in Europe.

A recently launched RNA-based test in the market is the NeoGenomics Laboratories' NeoLAB Liquid Biopsy Prostate Test. It is a qRT-PCR test that can evaluate the cell-free RNA (cfRNA) levels of the genes AR, B2M, ERG, GAPDH, HSPD1, IMPDH2, PCA3, PDLIM5, PSA, PTEN, TMPRSS2, and UAP1 in urine and plasma samples. The test can be used to differentiate between no-risk, low-risk and high-risk prostate cancers. In a clinical study, it was demonstrated that NeoLAB Liquid Biopsy Prostate Test identified the presence of high-risk prostate cancer with 97% sensitivity, while the sensitivity of biopsy was 78%.

Another commercial RNA based test in the market is Hologic's Progensa PCA3 test, which can measure PCA3 levels from a urine sample.

Researchers have observed modulation in RNA levels between normal and prostate cancer patients, and during prostate cancer therapy, indicating their importance as biomarkers. Promising RNA biomarkers in research phase include microRNA-21 (miR-21), long non- coding RNA H19 (lncRNA H19), Metastasis Associated Lung Adenocarcinoma Transcript 1 (MALAT1), Carbonic anhydrase IX (CAIX) splice variant mRNA and human telomerase reverse transcriptase (hTERT) mRNA. Leading institutes involved in RNA biomarker research for prostate cancer diagnosis include University of Jean-Monnet (France), University of Heidelberg (Germany).

RNA Biomarkers in Research

Biomarker	Description
Serum miR-21 level	Indicates treatment effectiveness
Hypermethylation of the lncRNA H19	Helps to distinguish prostate cancer from controls
MALAT1 volume	Elevated levels are associated with prostate cancer
CAIX splice variant mRNA	Elevated levels are associated with prostate cancer
hTERT mRNA	Increased level indicate poor prognosis

Circulating Proteins and Peptides

Analysis of protein biomarkers has resulted in successful commercial launches including Beckman Coulter's Prostate Health Index (PHI) and OPKO Health's 4KScore. Similar to RNA-based tests, these proteomic tests have also displayed strong clinical outcomes and it is just a matter of time when they gain wide clinical adoption.

The Prostate Health Index (PHI) is a blood-based test that combines total PSA, free PSA, and proPSA for prostate cancer detection. Launched in 2014, the test is FDA-approved and has been recommended by the National Comprehensive Cancer Network for early detection of prostate cancer. The key barrier to its wide adoption is low insurance coverage.

The 4KScore is a multi-marker blood test that assesses four parameters including total PSA, free PSA, intact PSA, and human kallikrein to identify men with high-risk prostate cancer. It was launched commercially in 2014, and has been recognized by National Comprehensive Cancer Network and European Association of Urology as a blood test with greater specificity over the PSA test indicated for use prior to a first prostate biopsy or after a negative biopsy for defining high-risk prostate cancer. However, the test is still not reimbursed by many national payers, including Medicare, limiting its widespread adoption.

Exosomes

Due to their high expression in cancer patients and easy availability in various body fluids including urine and blood, exosomes are considered as a good source for diagnosing prostate cancer. A commercially available exosome- based test is Exosome Diagnostics' ExoDx Prostate (IntelliScore). Launched in 2016, it is a urine-based test that has been clinically proven to identify high- risk prostate cancer patients. The test faces reimbursement challenges that have limited its access to patients.

NGS Empowering Research

Big Data technologies and analysis of genetic information from large patient groups will be used to discover mutations and markers to provide valuable insight into prostate cancer diagnosis and prognosis. This is vital, as this emerging technology will help early detection and assist in the stratification of the patient population between low-risk and high-risk prostate cancer, for tailored, personalized treatment. Research in this field is expected to improve the understanding of prostate cancer biology and clinical variability of various genetic biomarkers.

Image source: Frost & Sullivan

In October 2017, Strata Oncology announced a partnership with the University of California San Francisco (UCSF) to offer free sequencing services for prostate cancer patients. The initiative—Stratify Prostate—is a part of the Strata Trial, an observational study that plans to sequence DNA of 10,000 men with metastatic prostate cancer. Stratify Prostate provides a good opportunity for men with advanced prostate cancer to explore experimental drugs based on their genetic mutation.

Another promising research in personalized medicine is a project funded by Prostate Cancer UK and the Movember Centre of Excellence.

Researchers at Queen's University Belfast tested a gene expression biomarker, known as Metastatic Assay (developed by Almac Diagnostics), on prostate biopsies from 248 patients who had previously been treated for prostate cancer. The assay provided genetic-level differentiation between tumours that assisted physicians in identifying tumours that required more aggressive management. As per Dr. Iain Frame, Director of Research at Prostate Cancer UK, *"this research could provide clinicians with the answers they need to identify which cancers are likely to spread. It's still early days but it's great to see how the work taking place at the Movember Centres of Excellence has the potential to bring about real change for men. We look forward to further results."*

Latest in Prostate Cancer Treatment

The most notable clinical findings for prostate cancer therapy in recent times were presented in American Society of Clinical Oncology (ASCO) and European Society for Medical Oncology (ESMO) 2017 annual meetings. These trials evaluated abiraterone and luteinizing hormone-releasing hormone (LHRH) analogues against LHRH analogues alone in patients with advanced prostate cancer.

It was observed that giving a combination of abiraterone and LHRH during early stages of treatment reduced the risk of dying by 37%. It also lowered the chance of cancer deteriorating by 71%. The results are promising and enhance the overall survival. Thought leaders in prostate cancer research have already started encouraging peers for using the combination therapy to treat their patients.

"It would be fair to say that in 2017, for patients with M1 prostate cancer at diagnosis, we have two standards of care: LHRH analogue and docetaxel, and LHRH analogues and abiraterone. The data presented at this meeting (ESMO 2017) would indicate that both are entirely satisfactory options. I urge you to ensure that your patients get all of the drugs that improve survival at some point in their lifetime." – Professor Johann de Bono, Professor of experimental cancer medicine at the Royal Marsden Hospital and the Institute of Cancer Research in London, Track chair ESMO 2017 prostate program.

Proton Beam Therapy (PBT)

Proton beam therapy is one of the most controversial therapies in recent times. While many physicians recommend it for treating early prostate cancer based on single-arm studies, critics site higher costs than IMRT (standard of care radiotherapy) as a wasted expenditure, as IMRT and PBT have not been evaluated together in a clinical trial. Despite its criticism, PBT has witnessed rapid growth. North America has 26 PBT centres, with multiple centres under construction. In Europe, PBT is offered through centres in many countries including Germany, France, Italy, UK, Switzerland, and Russia.

A recent study by researchers at the Northwestern Medicine Chicago Proton Centre, presented at the 4th Annual Particle Therapy Co-Operative Group North-America (PTCOG-NA) is likely to boost PBT adoption. The researchers reviewed the records of over 28,000 IMRT patients and 851 PBT patients who received treatment from 2006-2012, using the Medicare and Surveillance, Epidemiology and End- Results Reporting (SEER) databases.

It was observed that the five-year overall survival rate for proton therapy was higher (93% compared to 88% for IMRT). Patients treated with PBT reported fewer complications of bladder or endocrine, than those treated with IMRT. Additionally, there were fewer patients with secondary malignancies with PBT than IMRT (6.1% for PBT versus 10.5% for IMRT). As per the study's lead author William Hartsell, Medical Director of the Northwestern Medicine Chicago Proton Centre, *"the evidence shows that proton therapy is advantageous for younger patients who we are most concerned about developing secondary cancers later in life."*

Radioimmunoconjugates

Radioimmunoconjugates targeting prostate cancer, such as anti-prostate specific membrane antigen (PSMA) antibodies with a radioactive payload, have displayed promising results.

Notable among all is the radioligand 177Lu-PSMA-617 that targets PSMA. Results of a recently concluded study were presented in ESMO 2017 by Dr. Michael Hofman of the Peter MacCallum Cancer Center in Melbourne. The study showed 57% PSA response rate (>50% reduction) and 71% interim response rate in soft tissue lesions in patients who had previously failed conventional therapies such as docetaxel, cabazitaxel, enzalutamide and abiraterone. Median overall survival was 12.7 months. The drug was well-tolerated, with a low rate of adverse effects and no renal toxicity.

The radioligand was originally developed at DKFZ (German Cancer Research Center) and University Hospital Heidelberg and exclusively licensed by ABX GmbH in Germany. Due to the immense potential it holds, Endocyte acquired the exclusive worldwide license of PSMA-617 from ABX GmbH. The company will now be developing the drug further in phase-3 clinical trials.

Robot-assisted Surgery

Since 2000, robots have been assisting surgeons with prostate removal. Research suggests that robot-assisted surgery results in lesser bleeding and scarring leading to a quicker recovery and shorter stay in hospital, when compared to unassisted surgeries.

Studies also suggest a faster return of erectile function and urinary continence. However, the medical community at large has a divided opinion on the usefulness of robotics in prostate surgery. The critics of the surgery opine that the robots cost around €1.7 million, plus about €140,000 a year for maintenance, which is too high a price/patient when compared to a normal surgeon. Critics suggest that the research showing benefits of robot- assisted surgery over unassisted surgery have been based on small, non-randomized trials, and are thus inconclusive.

Despite lacking robust medical evidence of their usefulness, robots have found patronage among patients. They are travelling beyond the nearby prostate surgery centres that do not provide robot-assisted prostate surgery, to large centres at far-off places that have robots to assist in surgery.

In a recent study published in the Lancet Oncology it was observed that 16 hospitals in England had stopped offering prostate surgery because patients were travelling to far- off places where they could be operated using a robot. Northern Ireland's health officials are also considering offering robot-assisted surgery treatment for prostate cancer as currently patients in Northern Ireland are travelling to distant places such as the Robotic Prostate Centre at Addenbrookes Hospital in Cambridge rather than receiving surgery from a centre near their location.

The robot-assisted surgery market is dominated by US-based Intuitive Surgical that offers the ‘da Vinci’ robots. The company has enjoyed a monopoly in the global market since the launch of its da Vinci robots in 2000. However, new suppliers are likely to break this monopoly in the near future. This will largely be driven by advancing technology that will allow new suppliers to offer more features at lower costs.

Several suppliers that are currently researching on new robots for assisting in surgery include Cambridge Medical Robotics, Medical Microinstruments, Auris Robotics, Medtronic and Verb Surgical (a joint venture between Johnson & Johnson and Google’s life-science division, Verily).

To succeed in a market where thousands of surgeons have already been trained and are using da Vinci robots, a new supplier will need to provide convincing data to the medical community which displays the benefits of its robot over da Vinci and unassisted surgery. This is pivotal for gaining acceptance among surgeons and motivating them to get trained on a new robotic system.

Integrated Comprehensive Cancer Care

Cancer care is transforming. Traditionally, a cancer patient's journey moved between different stages including diagnosis, radiation therapy and chemotherapy, which often worked in silos and were disconnected. This was largely due to the fee-for-service payment model that reimbursed providers based on a service. There was no need for different teams to coordinate and provide a comprehensive treatment experience to a patient.

This is changing since the advent of performance-linked payment systems. In the evolved business model, payments are linked to clinical outcomes for a patient. Additional incentives are paid if the clinical outcomes of a provider are better than the national benchmarks set by a reimbursing agency.

For instance, Medicare's Hospital Value-Based Purchasing (VBP) Program reimburses hospitals based on their performance in comparison to their peers and their own performance in the previous year.

Today, hospitals are adopting a comprehensive and multidisciplinary approach to provide a coordinated management of prostate cancer across all the stages of cancer care— including prevention, survival and end-of-life care—while addressing key parameters such as survival and quality of life. Increasingly, hospitals are incorporating various programs such as options for genetic assessment and counselling and inclusion of survivorship care plan to differentiate their services from their peers. The focus is on providing state-of-the-art technology and a holistic treatment experience to patients, for improving the overall patient-reported outcomes.

Hospitals are also increasingly adopting different methods for tracking patient outcomes for monitoring their performance.

A recent case study published in the February 2017 edition of the New England Journal of Medicine Catalyst (NEJM Catalyst), demonstrated the initiative undertaken by the University of Texas MD Anderson Cancer Centre, which undertook a comprehensive assessment of disease-specific outcome measure sets, including provider-generated outcomes and patient-reported outcome measures for six cancer sites, including prostate. The goal was to capture these outcomes, integrate them with patients' electronic health records and use the final results for delivering a better prognosis.

Hospitals in the US are also increasingly adapting to the quality benchmarks set by the Commission on Cancer of the American College of Surgeons that collate performance of cancer hospitals that voluntarily participate in its various programs.

However, on a larger scale, there is currently no mechanism to compare the performance of different hospitals for managing prostate cancer care. Few organisations such as the International Cancer Benchmarking Partnership are working on creating benchmarks for comparison of the performance of global institutes for few cancer sites including breast and lung, however, none of them is involved in doing a similar comparison for prostate cancer.

Lack of such information hampers the ability for institutions involved in delivering cancer care in raising their standards through peer comparisons. This also results in lack of knowledge for patients, who are unable to select the best hospital that meets their needs.

Transforming Prostate Cancer Care through Digital Health

Several mobile apps assist physicians and patients in managing prostate cancer. The current apps landscape is largely targeted at educating a patient about the disease, various support groups and record and track PSA levels and other diagnostic parameters. Examples of such apps include AstraZeneca's Prostate Assistant and the ADT App, which was developed through the joint collaboration of Urologist Dr Jim Duthie, Australian Prostate Cancer Research, and Appster (an app production company).

A few apps are targeted at assisting physicians with their clinical decisions. For instance, the Prostate Cancer @Point of Care app uses IBM Watson's platform for providing evidence-based, tailored content to a physician.

AstraZeneca's Prostate Assistant App

Image source: Article titled, 'AstraZeneca Launches Prostate Cancer App', published in the Pharmafile (August 2012)

A few apps are targeted at assisting physicians with their clinical decisions. For instance, the Prostate Cancer @Point of Care app uses IBM Watson's platform for providing evidence-based, tailored content to a physician. The content is provided through a repository that contains thousands of case studies and journal articles. A physician can access relevant medical content, case studies, videos and interviews. This can be helpful in designing treatment options.

However, despite a number of prostate cancer apps in the market, there remains a wide gap to assist patients who suffer from psychological disorders due to prostate cancer treatment.

As per a study titled, 'Prevention and Management of Depression and Suicidal Behaviour in Men with Prostate Cancer', published in the February 2015 version of Front Public Health Journal, *"the lifetime prevalence of major depressive disorder in adults in the US is 17%, and research has shown that in patients with prostate cancer, particularly those treated with radiotherapy, the prevalence of depression is considerably higher in patients both pre-treatment (27%) and 5 years post- treatment (22%). Depression is associated with an increased risk of suicide; about 60% of people who commit suicide suffer from depression. In patients diagnosed with prostate cancer, as well as those who have survived the cancer, studies have shown an increase in suicidal ideation."*

Side effects from treatment are a major cause of depression among prostate cancer survivors. Common side effects that ail survivors are sexual dysfunction, urinary incontinence and bowel urgency. An app that could track these factors and associate them with psychological evaluation could be helpful in identifying patients who are on the verge of developing depression.

Patients could be asked simple questions about their feelings and emotions related to their relationships and daily life on a periodic basis, and physicians could be alerted if a patient's response suggests depressing ideation. This could assist in providing early intervention and increase the overall survival and quality of life for survivors.

CONCLUSION

If detected early, prostate cancer has a very promising survival rate. As per the American Cancer Society, the five-year relative survival rate for patients with local prostate cancer (cancer is confined to the prostate) is 100%. Even for regional stage cancer, i.e. cancer that has spread beyond the prostate in adjacent tissues such as the lymph nodes, the five-year relative survival rate is 100%. However, once cancer spreads through distant parts of the body, the five-year relative survival rate drops significantly low to about 29%.

This makes it important to have early diagnostic programs that can detect prostate cancer at its latent phase.
Men with a first-degree relative who had prostate cancer should get screened at 40 years of age. African American men are at a higher risk of having prostate cancer and should get screened annually beginning the age of 45 years. Remaining men should get themselves annually screened from 50 years of age.

Frost & Sullivan strongly suggests men to open up and discuss their health issues with physicians and proactively participate in early screening programs. In the words of Australian Prime Minister Malcolm Turnbull, *"stop being shy about asking the doctor for a check- up. Don't run away when you hear the snap of a rubber glove. More men will survive prostate cancer, if more men get a check-up."*

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