ISSN: 3033-3326

Review Article

Journal of Chemotherapy and Cancer Research

Recent Progress and Upcoming Paths: Current Developments in Chemotherapy for Metastatic Prostate Cancer Treatment

Niladri Shekhar Dey[1*] and Rahul Kundu[2]

[1]*Mata Gujri College of Pharmacy (Constituent Unit of Mata Gujri University), Kishanganj-855107, Bihar, India*
[2]*Jiaganj Institute of Pharmacy, Jiaganj-742123, Murshidabad, India*

[*]**Corresponding author**
Dr. Niladri Shekhar Dey, Mata Gujri College of Pharmacy (Constituent Unit of Mata Gujri University), Kishanganj-855107, Bihar, India.
E-mail: niladrisekhar111@gmail.com

Received: January 22, 2026; **Accepted:** January 29, 2026; **Published:** February 04, 2026

ABSTRACT
Prostate cancer is the most frequently identified cancer in men and remains a major cause of cancer-related deaths. Precise and prompt diagnosis is crucial for differentiating clinically relevant tumours from non-aggressive lesions and for guiding treatment choices. Multiparametric magnetic resonance imaging (mp MRI) has transformed prostate cancer detection through accurate lesion localization, risk assessment, and enhanced biopsy targeting. Fusion biopsy, integrating mp MRI results with real-time transrectal ultrasonography (TRUS), has become a highly efficient technique for sampling concerning lesions. Over the past thirty years, there have been swift advancements in the diagnosis and treatment of prostate cancer, such as multiparametric magnetic resonance imaging, positron emission tomography, robotic surgery, image-guided hypo fractionated and stereotactic radiotherapy, new anti-androgens, and radioligand therapies. This review addresses the current management of every stage of prostate cancer in view of recent advancements, allowing for comprehensive personalization of treatment, and highlights the potential of future studies to enhance results even further. In this document, we provide an extensive overview of the evidence backing the use of chemotherapy in the current management of advanced prostate cancer, focusing particularly on the application of chemotherapy for aggressive variant prostate cancer (such as neuroendocrine prostate cancer) and the integration of chemotherapy with androgen signalling inhibitors. As prostate cancer research advances quickly, producing new agents and treatment methods, chemotherapy remains vital for extending the lives of patients with advanced and metastatic prostate cancer.

Keywords: biopsy targeting, magnetic resonance imaging, robotic surgery, stereotactic radiotherapy, signalling inhibitors.

Introduction

Prostate cancer (PC) is a form of cancer that develops in a small gland in males known as the prostate. The primary role of the prostate is to generate the seminal fluid that feeds and carries sperm. PC ranks as one of the most prevalent cancers in men, constituting a significant public health concern since approximately one in six men receives a PC diagnosis; however, it is very manageable if caught early. Prostate cancer is typically detected through a blood test that measures prostate-specific antigen levels (PSA), (PSA > 4 ng/ml), a glycoprotein typically produced by prostate tissue and/or a digital rectal exam [1].

Prostate cancer (PCa) is characterized by the National Cancer Institute (NCI) as a type of cancer that develops within the prostate's tissues. The occurrence of PCa is increasing globally due to demographic influences, a growing elderly population, and the number of cases diagnosed through prostate-specific antigen (PSA) tests [2]. PCa primarily affects older men, with nearly two-thirds diagnosed in those aged 65 or above. The typical age range for a PCa diagnosis is from 60 to 70 years, and approximately 1 in 6 men will receive a PCa diagnosis at some point in their lives. Men with a single-family history of PCa are twice as likely to develop the illness, whereas those with two or more relatives are almost four times more likely to have PCa [3]. The risk increases further if the impacted family members were diagnosed prior to turning 65. Another potential risk factor involves lifestyle elements like dietary habits (animal fats,

Citation: Niladri Shekhar Dey, Rahul Kundu. Recent Progress and Upcoming Paths: Current Developments in Chemotherapy for Metastatic Prostate Cancer Treatment. J Chem Can Res. 2026. 4(1): 1-10. DOI: doi.org/10.61440/JCCR.2026.v4.35

meats, milk, and dairy), supplement consumption (Vitamin D, Calcium), exposure to sunlight, occupational chemical exposure, smoking, obesity, alcohol intake, physical activity levels, and men with a background of vasectomy. There have also been proposals that socioeconomic factors, sexual behaviour, and sexually transmitted infections might affect the likelihood of developing or being diagnosed with PCa [4].

Prostate cancer denotes a malignancy that starts in the prostate gland, primarily adenocarcinoma, although infrequently, other types like small cell/neuroendocrine carcinoma may arise. Metastatic prostate cancer is characterized by the dissemination of prostate cancer to areas beyond the prostate. The most frequent locations for metastatic disease are lymph nodes and the axial skeleton, though more aggressive and advanced forms can spread to other areas like the liver and lungs [5]. Localized prostate cancer can be treated effectively, but metastatic prostate cancer is generally not curable. Consequently, the aim of treatment for metastatic prostate cancer is to manage the disease for an extended period to enhance survival and preserve quality of life. Nevertheless, with sufficient time, metastatic prostate cancer frequently acquires resistance to conventional treatments and advances to a fatal stage [6]. Uncontrolled metastatic prostate cancer may lead to serious complications, such as bone pain, pathological fractures, spinal cord compression, and mortality. Prostate-specific antigen (PSA) is a protein generated uniquely by both cancerous and non-cancerous prostate cells, and blood PSA levels act as a reference indicator for diagnosing and monitoring prostate cancer, including evaluating treatment effectiveness [7].

Prostate cancer staging is a classification system determined by the T (tumour size and penetration in prostate tissue), N (involvement of nearby lymph nodes and tissues), and M (spread to distant organs, typically pelvic and spinal bones) criteria. Stages I and II indicate prostate cancer that is confined to the gland ("clinically localized"), with Stage II being identifiable through digital rectal examination and/or imaging techniques like ultrasound or magnetic resonance imaging [8]. Stage III describes locally advanced cancer that has extended beyond the prostate capsule but has not metastasized systemically. Stage IV signifies the local invasion of other organs (bladder, rectum, pelvic wall) or metastasis to different organs, commonly involving bone or retroperitoneum. When stages I and II were less advanced, the five-year survival rate was significantly higher. The significant occurrence of advanced prostate cancer and its massive impact on healthcare have prompted recent significant breakthroughs in diagnosis and treatment utilizing state-of-the-art bioimaging, genomic studies, and adaptive therapeutic agents [9].

This review aims to identify and comprehend the risk factors and preventive strategies in PCa. It is essential to identify and handle these risk factors effectively to select the appropriate treatment, reduce negative effects, and protect quality of life. Healthcare providers must assess if patients are at elevated or diminished risk for PCa [10]. This paper will detail how this significant accomplishment was achieved by outlining crucial events in the history of PCa discovery and treatment. This review aimed to offer a brief and comprehensible overview of the historical development of PCa treatment and diagnostics [11]. Grasping the advancements is essential and intriguing not just for urologists, oncologists, radiologists, and pathologists dealing with PCa, but also for patients with PC and various healthcare professionals, including pharmacists and nurses [12].

Assessment

The majority of early prostate cancer cases show no symptoms. Numerous patients come in with unrelated urologic concerns that lead to a PSA examination. These consist of urinary issues, like increased frequency, urinating at night, difficulty starting, incomplete emptying, and challenges in attaining an erection [13]. Advanced or metastatic disease can manifest with pain, often in the back or bones, alongside sexual side effects such as difficulties. Severe disease may result in metastatic spinal cord compression, causing radiating pain in the back or legs, weakness in the legs, numbness, tingling sensations, paralysis, or loss of bladder control. The likelihood of identifying a clinically significant prostate cancer is influenced by several factors: age, family history, PSA level, and, in advanced cases, a DRE. Risk calculators exist that take these factors into account [14]. The most frequently observed result on DRE is a hard, immobile nodule. Additional findings could consist of asymmetry or rigidity. A stony, firm prostate felt during DRE indicates advanced local disease. A DRE is not always required if an MRI will be performed [15]. A multiparametric MRI is advised when there is a clinical suspicion of prostate cancer, before conducting a biopsy. MRI-guided biopsies are at least twice as effective in detecting clinically significant cancer compared to systematic transrectal biopsies alone [16].

MRI also enables over 25% of individuals to skip follow-up biopsies that would probably identify non-significant disease. An MRI that is deemed suspicious (≥3 per the Prostate Imaging Reporting and Data System, PIRADS) necessitates both targeted and systematic biopsies. A biopsy may be skipped if the MRI result is negative (PIRADS≤2) or with minimal clinical suspicion, assuming high-quality MRI and reader expertise are available [17]. It is always advised to have an MRI prior to a biopsy. Worldwide implementation of this approach with proper quality assurance may be difficult. MRI offers information on the local extent, involvement of seminal vesicles, and disease outside the prostate, assisting in surgical technique planning to enhance negative margins, especially concerning neurovascular bundle preservation and removal of potential extra prostatic sites, though it can lead to stage migration. A histologic diagnosis of prostate cancer is established by examining the loss of normal glandular structure, disruption of the basal membrane, absence of adjacent basal cells, and nuclear atypia in luminal cells (Figure 1) [18].

The degree of differentiation observed in histopathology reflects the aggressiveness of an adenocarcinoma and is assessed using the Gleason score (GS). Numerous adjustments have occurred over the years, involving alterations to evaluation and communication [19]. The GS on biopsy is the total of two values: the grade of the primary pattern combined with the grade of the highest pattern observed. Gleason grade varies from 3 (moderately differentiated cancer cells) to 5 (lack of glandular structures, clusters of atypical cells). If just one Gleason grade is found in the biopsy, it is multiplied by two [20].

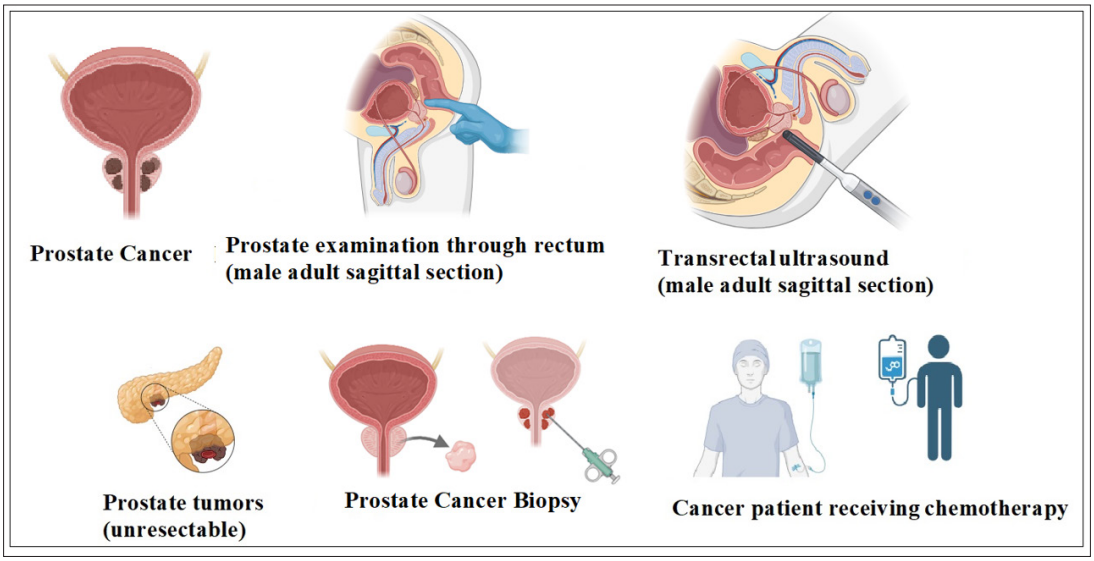

Figure 1: Prostate Cancer Diagnosis and Chemotherapy

Innovative Methods for Bioimaging Prostate Cancer

An increasing blood level of prostate-specific antigen following treatment of prostate cancer with surgery or radiation indicates a possible return of local disease or the development of metastases. Localization and staging of post-treatment recurrences typically involved computed tomography (CT), magnetic resonance imaging (MRI), and/or bone scans [21]. Recent advancements in imaging utilize positron emission tomography (PET) radiotracers that significantly enhance the detection of microscopic disease in the prostate and across the body. A radiotracer of this kind is 68gallium prostate-specific membrane antigen-11, which attaches to the enzyme of the prostate-specific membrane antigen present on the surface of prostate cancer cells and produces positrons [22]. The accuracy and speed of recurrent prostate cancer detection using gallium-prostate-specific membrane antigen-11 PET is associated with blood prostate-specific antigen levels, showing at least 84% accuracy for levels at 1.0 ng/ml and 97% for levels of ≥5.0 ng/ml [23]. Gallium-prostate-specific membrane antigen-11 PET has emerged as a standard element for post-therapy assessment of recurrence according to recent updates in national clinical guidelines (National Comprehensive Cancer Network, 2025) [24].

Management of prostate cancer

Various standard treatments for prostate cancer are:

- Chemotherapy
- Innovative hormone treatments

Chemotherapy

The chemotherapy treatment approach includes the use of medications such as docetaxel, cabazitaxel, and mitoxantrone. Docetaxel has been among the most effective medications to enhance overall survival in metastatic castration-resistant prostate cancer [25]. Enhancements in overall survival symptoms, prostate-specific antigen levels, and quality of life were observed in patients with metastatic castration-resistant prostate cancer who received docetaxel and prednisolone. Docetaxel is usually given through intravenous infusion every three weeks for a total of 10 recommended cycles [26]. The mechanism of action, while not completely clear, has been noted to affect microtubules during both mitosis and interphase, resulting in stabilization of the mitotic spindle, which leads to mitotic and cell growth arrest, ultimately causing cell death. Cabaxitaxel is another authorized chemotherapy medication, approved for the treatment of prostate cancer [27]. Cabaxitaxel operates in a manner akin to docetaxel by interfering with microtubule activity, leading to cell death. Cabaxitaxel is generally given intravenously every 3 weeks. Cabaxitaxel is additionally advised for a regimen of 10 cycles, considering the patient's condition (Figure 1) [28].

New Hormone Treatment

The most common method for treating metastatic prostate cancer has been castration, a practice that has lasted for almost a century. The management of treatment through castration showed a success rate of 60%–70% based on various criteria [29]. A reduction in the success rate was noted alongside a rise in the secretion of adrenal androgens, related to the development of upregulated or mutated androgen receptors. During its developmental phase, prostate cancer depends on androgenic hormones for growth. A sensible approach to halting the advancement of prostate cancer is by reducing androgen hormone levels or inhibiting androgenic activity [30].

Various forms of hormonal treatment for prostate cancer include:

- **Bilateral orchiectomy:** Almost a hundred years ago, a treatment method for prostate cancer was developed that included the removal of both testicles. This is a very methodical approach to treatment since it eliminates the origin of testosterone production [31].
- **LHRH agonists:** LHRH agonist, or luteinizing hormone releasing hormone agonist, are drugs that inhibit the testicles from generating testosterone. The sole distinction between the LHRH agonist treatment approach and orchiectomy is that the actions of LHRH agonists are reversible, restoring testosterone production quickly once the treatment ceases [32].
- **LHRH antagonists:** LHRH antagonists, a group of medications called gonadotropin-releasing hormone (GnRH) antagonists, induce the suppression of testosterone-like LHRH agonists by the testicles at a quicker rate without the flare associated with LHRH agonists [33]. The FDA

has authorized an injectable medication named degarelix (Firmagon), given monthly, for treating advanced prostate cancer; however, it can lead to serious allergic responses. The FDA has approved an oral LHRH antagonist called relugolix (Orgovyx) for treating advanced prostate cancer [34].

- **Androgen synthesis inhibitors:** Other body parts, such as the adrenal gland, besides the testicles, also generate testosterone that can stimulate the growth of prostate cancer cells. Therefore, androgen synthesis inhibitors are compounds that focus on an enzyme known as CYP17 and prevent cells from producing testosterone [35].

Examples of androgen synthesis inhibitors are abiraterone acetate and ketoconazole.

Radiation and Hormonal Therapies for Testosterone-Sensitive Prostate Adenocarcinoma

For any form of cancer, the prostate cancer treatment strategy should be tailored to each individual patient considering clinical risk, life expectancy, and collaborative decision-making. The patient's age, additional health issues, personal preferences, tumour size, spread extent, and unique features identified through specialized tests are all taken into account [36]. For patients diagnosed with low-risk prostate cancer (stage I or II) who commit to diligently following a structured active surveillance protocol as advised by clinical guidelines, this approach offers a safe option compared to immediate definitive treatment without diminishing the chances of a cure if the disease advances [37]. Surgery and radiation therapy, with or without androgen deprivation therapy (ADT), are the main active methods for intermediate or high-risk prostate cancer that has not metastasized. Significant recent progress in the radiation therapy of metastatic prostate cancer encompasses various techniques for delivering radiation, including the implantation of particles that release radiation from isotopes like palladium-103 or cesium-137, as well as the intravenous administration of the alpha-emitting radiopharmaceutical radium-223, which targets bony metastatic sites [38].

Another significant developing progress is the intensification of hormone therapy when prostate cancer advances to radiographically visible metastatic disease or there is biochemical (prostate-specific antigen-based) indication alone of recurrence. This method is particularly successful for high-volume metastases identified as four or more bone lesions or one or more bone lesions located outside the pelvis or spine [39]. Hormone enhancement therapy has proven effective in various types. Fundamental androgen deprivation therapy (ADT) through bilateral orchidectomy or the suppression of testosterone production in the testes using gonadotropin releasing hormone agonists/antagonists or testosterone production inhibitors like abiraterone markedly enhances overall survival [40].

Therapeutic Drugs for Metastatic Prostate Cancer with Alterations in DNA Repair Genes

In patients with metastatic prostate cancer who have impaired mismatch repair of damaged DNA, the occurrence of somatic mutations significantly exceeds that of germline mutations that impair mismatch repair capability. Both groups gain advantages from treatment with the immune checkpoint inhibitor pembrolizumab when disease progresses following initial therapy [41]. The action of pembrolizumab results from its inhibition of Programmed Death Ligand-1 receptors on T cells, preventing Programmed Death Ligand-1 and Programmed Death Ligand-2 from attaching to Programmed Death-1, thus allowing T cells to attack prostate cancer cells. Prostate cancer cell damage caused by T cells likely decreases their ability to repair DNA mismatches. Germline mutations in BRCA1 and BRCA2 lead to a deficit in double-stranded DNA break repair via homologous recombination, an inability to mend collapsed DNA replication forks, and a failure to inhibit the formation of R-loops, causing genomic instability [42]. These abnormalities elevate the risk of prostate cancer by three to eight times, cause the disease to develop at an earlier age, and lead to a greater occurrence of nodal involvement and distant metastases [43]. Medications like poly (ADP-ribose) polymerase (PARP) inhibitors harm the DNA of prostate cancer cells, resulting in the destruction of those cancer cells. Deficiency in homologous recombination repair in prostate cancer cells with BRCA1/2 or similar mutations hinders the repair of DNA damaged by PARP inhibitors, thereby increasing the mortality of prostate cancer cells (Figure 2) [44].

PARP inhibitors play significant roles in both first- and second-line therapies for metastatic prostate cancer with homologous recombination repair deficiency, whether used alone or alongside androgen deprivation in second-line treatments. Numerous early and late somatic mutations in prostate cancer are linked to tumour size, prostate-specific antigen levels, concurrent genomic characteristics, and enzymatic functions, yet they do not exhibit a clear connection with the pathogenicity of prostate cancer [45]. Recurrent missense mutations in speckle-type poxvirus and zinc finger protein represent the most prevalent point mutations in primary prostate cancer, arising early at a rate of 10% in both localized and metastatic cases, leading to a selective loss of certain biochemical functions. Speckle-type poxvirus and zinc-finger protein variants engage with various oncogenes, oncogenic co-activators, and tumor suppressors, yet none have an established role in the development of prostate cancer [46]. Numerous investigations on 70-110 cancer driver mutations involving approximately 2000 patients revealed notable rises in the prevalence of four linked to metastatic advancement of localized disease. The most frequent mutation in metastatic prostate cancer is an increase in androgen receptor expression [47].

Single-Incision Robotic-Assisted Radical Prostatectomy

The launch of the Single Port (SP) robotic system is the primary surgical advancement of the past seven years. Following FDA approval in 2018, the SP robot entered the European market in 2024, and its appeal is increasing among robotic surgeons in Europe. The single incision, the 3DHD fully articulate scope, and the double-jointed tools are crafted to function effectively in confined areas, enabling SP urological surgical operations to take place extra peritoneally [48]. In addition, the 360◦ rotation of the single arm allows for a standard supine position to be utilized for almost all SP robotic urologic surgeries. The one incision lowers postoperative discomfort and opioid consumption, the supine posture reduces anaesthetic complications, and the extraperitoneal approach lessens the chances of bowel damage and postoperative ileus. These benefits ultimately enable nearly all SP procedures to be conducted in an outpatient environment [49].

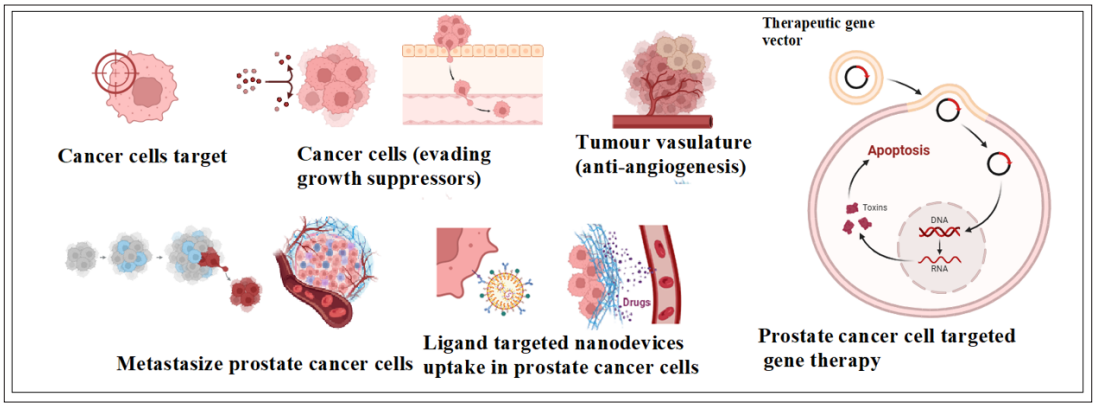

Figure 2: Prostate Cancer Targeted by Uptake of Nanodevices and Gene Therapy

Single-Incision Robotic-Assisted Radical Prostatectomy

The launch of the Single Port (SP) robotic system is the primary surgical advancement of the past seven years. Following FDA approval in 2018, the SP robot entered the European market in 2024, and its appeal is increasing among robotic surgeons in Europe. The single incision, the 3DHD fully articulate scope, and the double-jointed tools are crafted to function effectively in confined areas, enabling SP urological surgical operations to take place extra peritoneally [48]. In addition, the 360◦ rotation of the single arm allows for a standard supine position to be utilized for almost all SP robotic urologic surgeries. The one incision lowers postoperative discomfort and opioid consumption, the supine posture reduces anaesthetic complications, and the extraperitoneal approach lessens the chances of bowel damage and postoperative ileus. These benefits ultimately enable nearly all SP procedures to be conducted in an outpatient environment [49].

Function of Artificial Intelligence (AI) in Prostate Cancer Operations

Artificial Intelligence (AI) has infiltrated all facets of human existence and is widely utilized in healthcare to enhance patients' results and maximize the efficiency of healthcare professionals' time. Although the initial mention of AI dates to World War II, notable attempts to incorporate AI into medicine were not reported until recent advancements [50]. For example, the initial ground breaking innovation in this area has been the launch of the Cardio AI tool, which utilizes a deep learning algorithm to rapidly analyse cardiac MRI with exceptional precision. Radiology is likely the medical field that has seen the greatest integration of innovative AI technologies [51]. However, numerous companies have arisen in the realm of medical AI, impacting various aspects of healthcare, including data gathering, treatment recommendations, and financial evaluation. In surgery, especially in robotic-assisted procedures, AI is widely utilized for segmenting surgical operations, identifying crucial phases, gathering feedback, and recognizing anatomical structures [52].

Partial Prostate Removal

RP, the primary treatment choice for localized PCa, is a standardized and efficient procedure, featuring low rates of mortality, complications, and recurrence. However, the prevalence of long-term urinary incontinence and erectile dysfunction following RP varies from 4% to 40% and 14% to 90%, respectively, influenced by patients' preoperative function, the surgical method, and the techniques used [53]. The comparatively elevated rates, combined with the high number of PCa survivors, create an unaddressed issue with a considerable impact on patients' quality of life and healthcare costs. Focal therapies like high-intensity focused ultrasound (HIFU) have become a viable option for certain low- and intermediate-risk PCa patients who have favourable life expectancy and maintain good preoperative erectile function and continence [54]. Nonetheless, for carefully chosen patients, the reported rates of residual cancer and retreatment vary from 25% to 81%, and 25% to 27%. In this case, partial prostatectomy has been suggested as a safe and practical treatment choice, offering similar benefits for erectile function and continence preservation as focal therapy, along with the cancer-fighting effectiveness of surgically excising the tumour [55].

Radio Guided Surgery (RGS)

A significant drawback of RARP is the absence of real-time visualization during surgery for tumour size and lymph node metastases. Negative surgical margins and the dissection of lymph node metastases during ePLND are critical elements for long-term cancer management and rates of biochemical recurrence. Imaging before surgery and precise staging of lymph nodes continues to be essential. Currently, intraoperative imaging-guided surgery has advanced, focusing on a more accurate, efficient, and patient-oriented surgical method [56].

Nanotechnology

Nanotechnology is a collaborative domain that merges pharmacology, biomedical science, and nanotechnology. Nanoparticles possess traits that enhance drug effectiveness, easily infiltrate tumours, inhibit drug breakdown, and can be engineered to focus on particular tissues. Nanoparticles including liposomes, polymers, metal nanomaterials, and porous silicon nanoparticles have been extensively studied for use in the treatment and prognosis of prostate cancer [57]. Targeted nanoparticles possess altered surfaces with bound antibodies, affibody molecules, peptides, or oligosaccharides. These ligands aim at receptor cells on malignant cells, like the prostate-specific membrane antigen (PSMA) receptors found on prostate cancer cells [58]. There is a growing interest in creating nanoparticles for prostate cancer treatment because of the difficulties encountered with existing therapies. The gold silica nanoparticles absorbed infrared light at a wavelength capable of penetrating biological tissues. The gold nanoparticles exhibited plasmon resonance that could significantly reduce side effects

associated with the treatment [59]. Integrating nanotechnology with various therapeutic approaches can significantly boost and elevate the efficacy of medications. "2-(3-((S)-5-amino-1-carboxypentyl) ureido) pentane dioic acid, also known as ACUPA or a Lys-C(O)-Glu derivative,is a highly effective small molecule that strongly binds to PSMA.This compound functions as targeting molecule, helping radiopharmaceuticals to locate and identify metastatic tumours. It also serves as a carrier in the development of PSMA targeted therapies, such as PSMA-directed docetaxel nanoparticles known as BIND-014". In prostate cancer, nanotechnology plays a role in both diagnosis and treatment (Table 1). Nanoparticles serve as effective delivery systems while enhancing the solubility of poorly soluble drugs, and multifunctional nanoparticles show sufficient specificity for urological cancers, including bladder, renal, and prostate cancer (Figure 2) [60].

Table 1: Nano Formulations for Prostate Cancer

Nano particle type	Active Pharmaceutical ingredient	Ligand on nanoparticle	Target on neoplastic cells
PNP (PLGA-PEG polymer)	Docetaxel	prostate-specific membrane antigen (PSMA) aptamer	increase targeted delivery of docetaxel increase tumor cell apoptosis
	Toremifene	Anti-PSMA antibody	enhance tumor necrosis enhance Toremifene uptake by tumor cells decrease growth of prostate tumor and proliferation
	Docetaxel	ACUPA	Enhance targeted delivery of docetaxel
CNTs	Thionine (electrochemical probe)	Anti-PSA antibody	Linear behaviour of PSA concentrations was detected between 0.2 and 1 ng/ml and 1-40 ng/mL
	Carboplatin	NA (In vitro)	Increase accumulation of the chemotherapeutic drugs in malignant cells
Silver NP (AgNPs)	Berberis thunbergia leaf extract	NA (In vitro)	Dose dependent toxicity on malignant cell
AuNPs	gastrin-releasing peptide (GRP)	Bombesin	Enhance quality of molecular imaging via X-ray

Creating New Treatment Approaches for Metastatic Prostate Cancer

The main objective of creating targeted treatments for metastatic prostate cancer is to direct a recognized prostate cancer cytotoxic agent or immune cytokines to primary and metastatic sites while minimizing off-target effects. This method utilizes recent, more targeted radioligands combined with therapeutic agents to enhance delivery to the tumour itself and reduce off-target effects [61]. A category of these agents includes small molecules like prostate-specific membrane antigen-617 and monoclonal antibodies like J591, which attach to prostate-specific membrane antigen and are linked to radionuclides to create radioligands suitable for intravenous delivery [62]. The radionuclides consist of beta-emitters, such as lutetium-177, or alpha-emitters, like actinium-225. Lutetium-177-prostate-specific membrane antigen-617 was the initial radioligand granted FDA approval for treating prostate-specific membrane antigen-positive metastatic androgen deprivation-resistant prostate cancer [63]. The intravenous administration of 200 mCi of lutetium 177-prostate-specific membrane antigen-617 every six weeks for four to six cycles improved imaging outcomes and overall survival (15 months vs. 11 months) when combined with standard care. Many studies involving radioligands, either individually or in conjunction with other substances, are currently underway [64].

Importance of Targeting Primary Tumour in Oligometastatic PCa

Oligometastatic prostate cancer (OMPC) is an intermediate phase of prostate cancer progression from localized to extensive metastasis, characterized by a limited number (3-5) and specific locations of radiographically significant sites [65]. OMPC was conventionally managed with systemic treatment. Given its advantageous biology and slower natural progression, OMPC has recently been investigated to evaluate the best imaging techniques and treatment results [66]. Specifically, the extended survival provided by new systemic agents and the enhanced disease profiling obtained through advanced molecular imaging has enabled research to concentrate on the incorporation of metastasis-directed therapy (MDT) and radiotherapy (RT) of the primary tumour into the treatment repertoire for OMPC. Recently, evidence is surfacing regarding the function of radical prostatectomy as a cytoreductive approach, especially considering the lower morbidity linked to robotic-assisted surgery [67].

Radical Prostatectomy in OMPC

Cytoreductive surgery or radiotherapy of the primary tumour is a crucial investigational method in managing OMPC. Numerous studies have shown that lowering primary tumour burden can reduce circulating and spread tumour cell populations with metastatic ability, while boosting immune responses by raising T

helper to regulatory T cell ratios [68]. The SOLAR trial integrated systemic therapy (leuprolide, apalutamide, and abiraterone) along with MDT through SBRT, and primary tumour management using either RP or RT. At six months after treatment, 83% of patients met the primary PSA endpoint, with all patients staying progression-free at a median follow-up of 31 months, indicating the promise of this approach [69]. Cytoreductive prostatectomy (CRP) has become a possible treatment choice for men with low-volume metastatic disease. Extensive retrospective studies have revealed notable survival advantages for patients who undergo RP or prostate brachytherapy, in contrast to those who receive no local treatment, while maintaining an acceptable safety profile [70]. In a retrospective study, Heidenreich et al. found a five-year OS rate of around 80% and identified neoadjuvant ADT, low metastatic burden, and favourable PSA levels as indicators of better outcomes and fewer complications. Multiple potential clinical trials are presently in progress [71]. Currently, the Italian multicentre experimental trial APPROACH is an active study assessing if a treatment regimen of apalutamide combined with ADT for 6 months, followed by locoregional treatment with RT or RP, shows greater efficacy compared to medical treatment with apalutamide plus ADT alone regarding radiographic PFS in hormone-sensitive OMPC patients [72].

Surgery for the Prostate Using a Holmium Laser

Holmium laser prostate surgery, known as holmium laser enucleation of the prostate (HOLEP), is a minimally invasive procedure for treating benign prostatic hyperplasia. Benign prostatic hyperplasia, or BPH, is a condition in which the prostate enlarges more than normal. When the prostate enlarges excessively, it exerts pressure on the tube responsible for transporting urine out of the body, known as the urethra. This can obstruct the passage of urine [73].

HOLEP utilizes a laser to eliminate prostate tissue, allowing urine to flow without obstruction. A different instrument is subsequently employed to slice the prostate tissue into smaller fragments for easier removal [74].

HOLEP and conventional prostate surgery share certain similarities, yet there are notable differences. Conventional prostate surgery requires incisions in the skin, whereas HOLEP requires no incisions at all. HOLEP can offer rapid alleviation of BPH symptoms. The excised tissue can also be examined in a laboratory for different conditions, like prostate cancer. HOLEP provides quicker recovery and alleviation of symptoms compared to conventional prostate surgery. Seldom, a second HOLEP procedure might be required [75].

Conclusion

To sum up, prostate cancer stands out as a major cancer type worldwide due to its common occurrence in men, its likelihood of returning after initial treatments, and its resistance to conventional therapeutic approaches. Many genes associated with the beginning and advancement of this illness have yet to be studied, resulting in numerous possibilities that could improve success rates in cancer treatments. Currently, the common diagnostic and prognostic techniques include PSA tests and invasive prostate biopsies, with few viable alternatives present. Although alternative markers are being studied, significant research gaps remain that, if filled, could improve our understanding of prostate cancer advancement. Therefore, discovering new biomarkers is essential while simultaneously continuing the research on existing markers.

Numerous epidemiological studies have linked the risk of PCa to various factors, such as age, ethnicity, family history, insulin-like growth factors, lifestyle, diet, as well as environmental and occupational exposures. Epidemiological, in vivo, in vitro, and early clinical research suggested that specific dietary components and supplements could play a role in the prevention of PCa. Further studies are required to explore and identify the risk factors and preventive measures for the onset of PCa. Healthcare providers need to elaborate on this information for teaching purposes to lower PCa risks and advocate for PCa prevention.

Nanomedicine approaches demonstrate significant advancements in drug delivery research. The NP's design and function vary greatly regarding their potential or usefulness. Improving the selectivity of a nanoparticle (NP)-based drug delivery system can be accomplished via surface modification of a specific NP of interest. Selecting a suitable surface marker is crucial for precise therapeutic delivery through NPs. Overall, drug delivery using nanotechnology has shown remarkable effectiveness in cancer treatment, especially for PCa, offering multiple advantages (such as passive tumour accumulation, active tumour targeting, and the ability to cross tissue barriers) along with drawbacks (like toxicity and possible organ harm).

References

1. Pritchard CC, Mateo J, Walsh MF. Inherited DNA-repair gene mutations in men with metastatic prostate cancer, N Engl J Med. 2016. 375: 443-53.
2. Fendler WP, Calais J, Eiber M. Assessment of 68Ga-PSMA-11 PET accuracy in localizing recurrent prostate cancer: a prospective sin gle-arm clinical trial. JAMA Oncol. 2019. 5: 856-63.
3. Cotter K, Rubin MA. The evolving landscape of prostate cancer somatic mutations, Prostate 2022. 82: 13-24.
4. Lenis AT, Ravichandran V, Brown S. Microsatellite instability, tumor mutational burden, and response to immune checkpoint blockade in patients with prostate cancer. Clin Cancer Res. 2024. 30: 3894-903.
5. Eule CJ, Kuna EM, Robin TP, Gershman B, Flaig TW, et al. Treatment intensification in metastatic hormone-sensitive prostate cancer: an analysis of real-world practice patterns from the cancer Lin Q database. Urol Oncol. 2024. 42: 447.
6. Lampe H, Tam L, Hansen AR. Bi-specific T-cell engagers (BiTEs) in prostate cancer and strategies to enhance development: hope for a BiTE-r future. Front Pharmacol. 2024. 15: 1399802.
7. Chalker C, Chun B, Sokolova AO. Germline and somatic mutations in prostate cancer: implications for treatment. Curr Probl Cancer. 2024. 50: 101101.
8. Goddard JC. The history of the prostate, part one: say what you see. Trends Urol Mens Heal. 2019. 10: 28-30.
9. Obaldo JM, Hertz BE. The early years of nuclear medicine: a retelling, Asia Ocean J Nucl Med Biol. 2021. 9: 207-219.
10. Huh HD, Kim S. History of radiation therapy technology. Prog Med Phys. 2020. 31: 124-134.

11. Davies AH, Zoubeidi A. Targeting androgen receptor signalling: a historical perspective. Endocr Relat Cancer. 2021. 28: 11-18.
12. Quinn DI, Sandler HM, Horvath LG. The evolution of chemotherapy for the treatment of prostate cancer. Ann Oncol. 2017. 28: 2658-2669.
13. Epstein JI. Prostate cancer grading: a decade after the 2005 modified system. Mod Pathol. 2018: 31: 47-63.
14. Kweldam CF, van Leenders GJ, van der Kwast T. Grading of prostate cancer: a work in progress. Histopathology. 2019. 74: 146-160.
15. Bercovich E, Javitt MC. Medical imaging: from roentgen to the digital revolution, and beyond, Rambam Maimonides Med J. 2018: 9: e0034.
16. Hamid AA, Huang HC. Wang V. Transcriptional pro filing of primary prostate tumor in metastatic hormone-sen sitive prostate cancer and association with clinical outcomes: correlative analysis of the E3805 CHAARTED trial. Ann Oncol. 2021. 32: 1157-1166.
17. Satapathy BS, Mukherjee B, Baishya R, Chatterjee Debnath M, Dey NS, et al. Lipid nanocarrier-based transport of docetaxel across the blood brain barrier. RSC Adv. 2016. 6: 85261-85274.
18. Dey NS. Mechanistic approach of nano carriers for targeted in cancer chemotherapy: a newer strategy for novel drug delivery system. Polymers. 2022. 2321: 1-17.
19. Dey NS, Mukherjee B, Maji R, Satapathy BS. Development of linker-conjugated nanosize lipid vesicles: a strategy for cell selective treatment in breast cancer, Current Cancer Drug Targets. 2016. 16: 357-372.
20. Mukherjee B, Dutta L, Mondal L, Dey NS, Maji R, et al. Nanoscale formulations and diagnostics with their recent trends: a major focus of future nanotechnology, Current Pharmaceutical Design. 2015. 21: 5172-5186.
21. Maji R, Dey NS, Satapathy BS, Mukherjee B. Preparation and characterization of tamoxifen citrate loaded nanoparticles for breast cancer therapy, International Journal of Nanomedicine, 2014. 9: 3107-3118.
22. Dey NS, Sarkar S, Mohanta T, Pramanik S. Nano formulation devices technology for targeting breast cancer chemotherapy, J Chem Can Res. 2025. 3: 1-9.
23. Mukherjee B, Satapathy BS, Dey NS, Ruma Maji R. Potentials and challenges of active targeting at the tumor cells by engineered polymeric nanoparticles, Current Pharmaceutical Biotechnology. 2013. 14: 1250-1263.
24. Mukherjee B, Dey NS, Maji R, Bhowmik P, Das PJ, et al. Current status and future scope for nanomaterials in drug delivery, Hard copy of the book "Application of Nanotechnology in Drug Delivery" in INTECH OPEN book chapter, 2014. 16: 525-544.
25. Dey NS, Dasgupta RK, Deb Roy S. Nanomedicine for targeted drug delivery in cancer chemotherapy, in recent advances in smart drug delivery, INTECH OPEN book chapter. should be "edited volume, Smart drug delivery systems - futuristic window in cancer therapy. 2023. 02: 1-21.
26. Dey NS, Pal S, Saha P, Samanta A, Ram PK, et al. Development of metronidazole loaded multiple emulsion for sustained release medication, International Journal of Pharmaceutical Sciences. 2025. 03: 2661-2670.
27. Pal S, Dey NS, Ram PK, Shahjaha MD. Multiple emulsions for sustainable drug delivery, International Journal of Pharma Growth Research Review. 2025. 05: 42-48.
28. Ni Raghallaigh H, Eeles R. Genetic predisposition to prostate cancer: an update, Fam Cancer. 2022. 21:101-114.
29. Eldred Evans D, Burak P, Connor MJ. Population-based prostate cancer screening with magnetic resonance imaging or ultrasonography: the IP1-PROSTAGRAM study, JAMA Oncol. 2021. 7: 395-402.
30. Hugosson J, Månsson M, Wallström J. Prostate cancer screening with PSA and MRI followed by targeted biopsy only. N Engl J Med. 2022. 387: 2126-2137.
31. Hugosson J, Godtman RA, Wallstrom J. Results after four years of screening for prostate cancer with PSA and MRI, N Engl J Med. 2024. 391: 1083-1095.
32. Bratt O, Godtman RA, Jiborn T. Population-based organised prostate cancer testing: results from the first invitation of 50-year-old men. Eur Urol. 2024. 85: 207-214.
33. Bancroft EK, Page EC, Brook MN. A prospective prostate cancer screening programme for men with pathogenic variants in mismatch repair genes (IMPACT): initial results from an interna tional prospective study. Lancet Oncol. 2021. 22:1618-1631.
34. Benafif S, Ni Raghallaigh H, Mc Growder E. The BARCODE1 pilot: a feasibility study of using germline single nucleotide poly morphisms to target prostate cancer screening0 BJU Int. 2022. 129: 325-336.
35. Eeles RA, Bancroft EK, McHugh JK. Effect of polygenic risk score for clinically significant prostate cancer in a screening program: the BARCODE 1 study results, J Clin Oncol. 2024. 42:10500.
36. Moghul M, Tran A, Croft F. The Man Van: a pilot study of using mobile targeted case-finding to address health inequalities in prostate cancer. Int J Cancer. 2024. 155: 2246-2252.
37. Burki T. Prostate Cancer UK launches the TRANSFORM trial. Lancet. 2024. 403:1738.
38. Wei JT, Barocas D, Carlsson S. Early detection of prostate cancer: AUA/SUO guideline part I: prostate cancer screening. J Urol. 2023. 210: 46-53.
39. Cornford P, van den Bergh RCN, Briers E. EAU-EANM ESTRO-ESUR-ISUP-SIOG guidelines on prostate cancer-2024 update. Part I: screening, diagnosis, and local treatment with curative intent, Eur Urol. 2024. 86: 148-163.
40. Denijs FB, Van Harten MJ, Meenderink JJL. Risk calculators for the detection of prostate cancer: a systematic review, Prostate Cancer Prostatic Dis. 2024. 27: 544-557.
41. Anger CM, Stallworth JL, Rais-Bahrami S. Integrating risk calculators into routine clinical workflow for the detection of prostate cancer: next steps to achieve widespread adoption, Prostate Cancer Prostatic Dis. 2024. 27: 365-366.
42. Basourakos SP, Tzeng M, Lewicki PJ. Tissue-based bio markers for the risk stratification of men with clinically localized prostate cancer. Front Oncol. 2021. 11: 676716.
43. Tward JD, Huang HC, Esteva A. Prostate cancer risk strati f ication in NRG Oncology phase III randomized trials using multi modal deep learning with digital histopathology. JCO Precis Oncol. 2024: e2400145.
44. Barbato F, Fendler WP, Rauscher I. PSMA PET for the assessment of metastatic hormone-sensitive prostate cancer volume of disease. J Nucl Med. 2021. 62:1747-1750.
45. Weiner AB, Agrawal R, Valle LF. Impact of PSMA PET on prostate cancer management. Curr Treat Options Oncol.

2024. 25:191-205.
46. Hennrich U, Eder M, Pluvicto TM. The first FDA-approved radio therapeutical for treatment of prostate cancer. Pharmaceuticals. 2022. 15:1292.
47. Miyahira AK, Soule HR. The history of prostate-specific membrane antigen as a theranostic target in prostate cancer: the cornerstone role of the prostate cancer foundation. J. Nucl. Med. 2022. 63: 331-338.
48. Jani AB, Ravizzini GC, Gartrell BA, Siegel BA, Twardowski P, et al. Diagnostic performance and safety of 18f-rhpsma-7.3 positron emission tomography in men with suspected prostate cancer recurrence: results from a phase 3, prospective, multicenter study (SPOTLIGHT). J. Urol. 2023. 210: 299-311.
49. Wang Y, Chen Z, Zhu Y, Zhao H, Li L, et al. Total-body [(68)Ga]Ga-PSMA-11 PET/CT improves the detection rate compared with conventional [(68)Ga]Ga-PSMA-11 PET/CT in patients with biochemical recurrent prostate cancer. Eur. J. Nucl. Med. Mol. Imaging. 2023. 50: 4096-4106.
50. Uribe C, Iravani A, Savir Baruch B, Jacene H, Graves SA, et al. Summary: SNMMI/ACNM Procedure Standard for Posttreatment Imaging of 177Lu-Based Radiopharmaceuticals. J Nucl Med. 2025. 66: 1528-1537.
51. Wen X, Xu P, Zeng X, Liu J, Du C, et al. Development of 177Lu-LNC1003 for radioligand therapy of prostate cancer with moderate PSMA expression. Theranostics. 2022. 12: 422-433.
52. Kratochwil C, Fendler WP, Eiber M, Hofman MS, Emmett L, et al. Joint EANM/SNMMIprocedure guideline for the use of 177Lu-labeled PSMA-targeted radioligand-therapy (177Lu-PSMA-RLT). Eur. J. Nucl. Med. Mol. Imaging. 2023. 50: 2830-2845.
53. Kwon WA, Joung JY. Neoadjuvant 177Lutetium-PSMA-617 radioligand therapy for high-risk localized prostate cancer: rationale, early clinical evidence, and future directions. Cancers. 2025. 17: 3330.
54. Holzgreve A, Armstrong WR, Clark KJ, Benz MR, Smith CP, et al. Thin P, Nickols NG, Kishan AU. PSMA-PET/CT findings in patients with high-risk biochemically recurrent prostate cancer with no metastatic disease by conventional imaging. JAMA Netw. Open. 2025. 8: e2452971.
55. Hope T, Antonarakis ES, Bodei L, Calais J, Iravani A, et al. SNMMI consensus statement on patient selection and appropriate use of 177lu-psma-617 radionuclide therapy. J. Nucl. Med. 2023. 64: 1417-1423.
56. Schuchardt C, Zhang J, Kulkarni HR, Chen X, Mueller D, et al. Prostate-Specific membrane antigen radioligand therapy Using 177Lu-PSMA I&T and 177Lu-PSMA-617 in patients with metastatic castration-resistant prostate cancer: comparison of safety, biodistribution, and dosimetry. J. Nucl. Med. 2022. 63: 1199-1207.
57. Wurzer A, De Rose F, Fischer S, Schwaiger M, Weber W, et al. Preclinical comparison of [177Lu] Lu-rhPSMA-10.1 and [177Lu] Lu-rhPSMA-10.2 for endoradiotherapy of prostate cancer: biodistribution and dosimetry studies, EJNMMI Radiopharm. Chem. 2024. 9: 18.
58. Morris MJ, Castellano D, Herrmann K, de Bono JS, Shore ND, et al. PSMAfore Investigators. 177Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naive patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): A phase 3, randomized, controlled trial, Lancet, 2024. 404: 1227-1239.
59. Hansen AR, Probst S, Beauregard JM, Viglianti BL, Michalski JM, et al. Initial clinical experience with [177Lu] Lu-PNT2002 radioligand therapy in metastatic castration-resistant prostate cancer: Dosimetry, safety, and efficacy from the lead-in cohort of the SPLASH trial. Front. Oncol. 2024. 14: 1483953.
60. Nordquist L, Lengyelova E, Saltzstein D, Josephson D, Franklin GE, et al. Assessment of safety and efficacy of 64Cu-SAR-bisPSMA in patients with biochemical recurrence of prostate cancer following definitive therapy. J. Clin. Oncol. 2024. 42: 5100.
61. Freedland SJ, de Almeida Luz M, De Giorgi U, Gleave M, Gotto GT, et al. Improved outcomes with enzalutamide in biochemically recurrent prostate cancer, N. Engl. J. Med. 2025. 393: 832.
62. Lafata KJ, Wang Y, Konkel B, Yin FF, Bashir MR. Radiomics: A primer on high-throughput image phenotyping. Abdom Radiol. 2022. 47: 2986-3002.
63. Liu Z, Duan T, Zhang Y, Weng S, Xu H, et al. Radiogenomics: A key component of precision cancer medicine. Br. J. Cancer. 2023. 129: 741-753.
64. Ferro M, de Cobelli O, Musi G, del Giudice F, Carrieri G, et al. Radiomics in prostate cancer: An up-to-date review. Ther. Adv. Urol. 2022. 14: 17562872221109020.
65. Yazdani E, Geramifar P, Karamzade Ziarati N, Sadeghi M, Amini P, et al. Radiomics and artificial intelligence in radiotheranostics: a review of applications for radioligands targeting somatostatin receptors and prostate-specific membrane antigens. Diagnostics. 2024. 14: 181.
66. Herrmann K, Giovanella L, Santos A, Gear J, Kiratli PO, et al. Joint EANM, SNMMI and IAEA enabling guide: How to set up a theranostics centre, Eur. J. Nucl. Med. Mol. Imaging. 2022. 49: 2300-2309.
67. Rebello RJ, Oing C, Knudsen KE, Loeb S, Johnson DC, et al. Prostate Cancer. Nat. Rev. Dis. Primers. 2021. 7: 9.
68. Desai MM, Cacciamani GE, Gill K, Zhang J, Liu L, et al. Trends in incidence of metastatic prostate cancer in the US. JAMA Netw. Open. 2022. 5: e222246.
69. Sandhu S, Moore CM, Chiong E, Beltran H, Bristow RG, Cancer. Lancet. 2021: 398: 1075-1090.
70. Park JJ, Kim CK. Paradigm shift in prostate cancer diagnosis: pre-biopsy prostate magnetic resonance imaging and targeted biopsy, Korean J. Radiol. 2022. 23: 625-637.
71. Kipriyanov EA, Karnaukh PA, Vazhenin IA, Vazhenin AV. Radical prostatectomy and robotic radiosurgery as treatment options for localized prostate cancer. Sib. J. Oncol. 2020. 19. 50-56.
72. Mateo L, Duran Frigola M, Gris Oliver A, Palafox M, Scaltriti M, et al. Personalized cancer therapy prioritization based on driver alteration co-occurrence patterns, Genome Med. 2020. 12: 78.
73. Giri VN, Morgan TM, Morris DS, Berchuck JE, Hyatt C. Genetic testing in prostate cancer management: Considerations informing primary care. CA Cancer J Clin. 2022. 72: 360-371.
74. Desai N, Momin M, Khan T, Gharat S, Ningthoujam RS, et al. Metallic nanoparticles as drug delivery system for the

treatment of cancer. Expert Opin. Drug Deliv. 2021. 18: 1261-1290.

75. Yao Y, Zhou Y, Liu L, Xu Y, Chen Q, et al. Nanoparticle-based drug delivery in cancer therapy and its role in overcoming drug resistance. Front. Mol. Biosci. 2020. 7: 193.