Non-Invasive Bladder Cancer Detection and Management: A Survey

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Abstract

Bladder cancer, ranking as the tenth most common cancer globally, presents significant challenges in diagnosis and management, particularly with its non-muscle-invasive form (NMIBC), which accounts for 75

1 Introduction

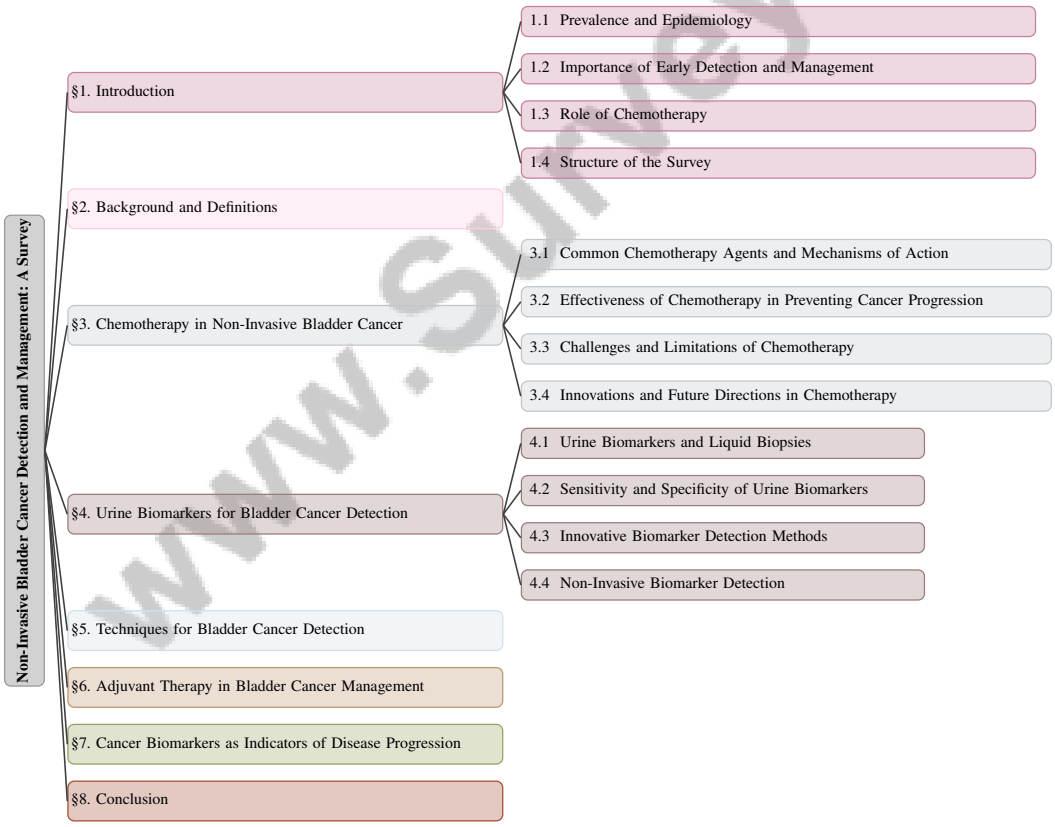


Figure 1: chapter structure

1.1 Prevalence and Epidemiology

Bladder cancer (BC) is the tenth most common cancer globally, with a notable rise in prevalence, particularly in developing nations [1]. In the United States, it ranks as the sixth most prevalent cancer, predominantly affecting individuals over 55 years, with men being three to four times more likely

to develop the disease compared to women [2]. BC is the second most frequent malignancy of the urinary tract, characterized by high relapse rates and a lack of reliable prognostic biomarkers [3].

Non-muscle-invasive bladder cancer (NMIBC) accounts for approximately 75% of all cases, exhibiting a high recurrence rate that necessitates ongoing monitoring and management [4]. The rising incidence of bladder cancer underscores the urgent need for improved diagnostic and therapeutic strategies. This survey evaluates and compares various tests based on molecular biomarkers for bladder cancer diagnosis, follow-up, and treatment response monitoring, particularly emphasizing non-invasive testing methods [5].

Current detection methods, such as cystoscopy, are invasive and often lack sensitivity, complicating early detection and management. The high incidence and recurrence rates further highlight the necessity of developing effective non-invasive diagnostic techniques and treatment modalities to enhance patient outcomes. This survey addresses critical areas, including risk factors—such as environmental and occupational carcinogens, notably tobacco use—pathophysiological mechanisms leading to different tumor types, current diagnostic methods like cystoscopy and urinary biomarkers, and various treatment strategies, including intravesical therapies and emerging immunotherapies. It also aims to identify future research directions to improve diagnostic sensitivity and specificity, enhance patient outcomes, and potentially replace traditional diagnostic methods like cystoscopy [6, 7, 8, 9].

1.2 Importance of Early Detection and Management

Early detection and management of NMIBC are crucial due to the disease's high recurrence and progression rates, which pose significant challenges in clinical management and increase patient burdens through the necessity for repeated diagnostic tests and treatments [10]. Current diagnostic methods, including cystoscopy and cytology, exhibit limited sensitivity, especially for low-grade tumors, potentially delaying treatment and escalating management costs [4]. This situation underscores the urgent need for non-invasive diagnostic tools with enhanced sensitivity and specificity [3].

The biological complexity and high incidence rates of bladder cancer further emphasize the need for early detection. Accurate diagnosis, particularly in differentiating non-invasive (Ta) from invasive (T1) bladder cancers, is vital for timely treatment, which directly affects patient outcomes and survival rates [2]. Implementing reliable diagnostic panels, such as those utilizing urinary extracellular vesicles (EVs), could significantly impact clinical practice by providing more accurate prognostic information [3].

Moreover, the invasiveness and cost of current diagnostic methods, such as cystoscopy, highlight the necessity for non-invasive alternatives. In the UK, the annual cost of cystoscopy exceeds £55M, illustrating the financial strain on healthcare systems. Improved non-invasive methodologies could reduce patient discomfort and associated risks, thereby enhancing overall bladder cancer management. The urgent need for effective non-invasive strategies is underscored by the disease's high recurrence and progression rates, which significantly impact patient outcomes and impose considerable economic and physical burdens on healthcare systems. Recent advancements, including innovative cystoscopy techniques and urine-based tumor biomarker screenings, hold promise for enhancing diagnostic accuracy, reducing recurrence risks, and improving overall bladder cancer management [11, 7, 4, 6, 9].

1.3 Role of Chemotherapy, Urine Biomarkers, and Adjuvant Therapy

Managing NMIBC involves a multifaceted approach that integrates chemotherapy, urine biomarkers, and adjuvant therapy to enhance patient outcomes. Intravesical chemotherapy, particularly Bacillus Calmette-Guérin (BCG) therapy, is a cornerstone treatment for NMIBC, demonstrating efficacy in reducing recurrence and progression rates, thereby improving patient prognoses [8]. Chemotherapy not only targets tumor eradication but also serves as an adjuvant treatment post-surgery to prevent recurrence and progression.

Urine biomarkers offer a promising non-invasive alternative for NMIBC detection and surveillance. While existing urine-based tests have modest sensitivities and specificities, ongoing research seeks to identify more reliable biomarkers [12]. Notably, urinary exosome-derived long non-coding RNA (lncRNA) panels represent an innovative approach that could enhance diagnostic accuracy and predict

recurrence [13]. Both established and emerging biomarkers are critical for overcoming current diagnostic limitations and improving early detection and monitoring.

Adjuvant therapy, encompassing both intravesical and systemic treatments, plays a significant role in comprehensive bladder cancer management. Advances in therapeutic strategies and improved surgical techniques for muscle-invasive bladder cancer (MIBC) have led to better patient outcomes [11]. Integrating these therapies into clinical practice is essential for optimizing treatment regimens and enhancing the quality of life for NMIBC patients.

1.4 Structure of the Survey

This survey provides a comprehensive examination of non-invasive bladder cancer detection and management strategies, beginning with an introduction that highlights the significance of early detection and the roles of chemotherapy, urine biomarkers, and adjuvant therapy. The introduction outlines the prevalence and epidemiology of bladder cancer, emphasizing the importance of early detection and management for improving patient outcomes. It also briefly reviews the roles of chemotherapy, urine biomarkers, and adjuvant therapy in NMIBC management.

Subsequent sections delve into the background and definitions of bladder cancer, detailing NMIBC's unique characteristics, which comprise approximately 75% of diagnoses, and contrasting it with muscle-invasive bladder cancer (MIBC), characterized by distinct molecular drivers and a higher progression risk. Clinical management strategies for NMIBC, including risk-adapted cystoscopic surveillance and intravesical therapies, are discussed, emphasizing the importance of differentiating between non-invasive and invasive stages for effective treatment [10, 14, 8, 15]. Key terms such as chemotherapy, urine biomarkers, bladder cancer detection, adjuvant therapy, and cancer biomarkers are defined to establish a clear understanding of the concepts discussed throughout the survey.

The subsequent sections focus on specific aspects of NMIBC management. The role of chemotherapy is explored in detail, discussing common agents, their mechanisms of action, and effectiveness in preventing cancer progression, alongside challenges and recent innovations.

The survey then examines urine biomarkers for bladder cancer detection, emphasizing their sensitivity, specificity, and comparison with traditional diagnostic methods. It provides a comprehensive review of various innovative biomarker detection methods and non-invasive techniques for bladder cancer diagnosis, highlighting their advantages over traditional approaches like cystoscopy and urine cytology, which often suffer from low sensitivity and false positives. The potential of emerging urinary biomarkers, including epigenetic and genetic markers, as well as mass spectrometry-based metabolomic analyses, to enhance diagnostic accuracy and streamline clinical decision-making is also discussed [16, 9, 7, 6].

The review further addresses various bladder cancer detection techniques, focusing on advanced imaging methods, machine learning algorithms, and molecular and genetic approaches, while evaluating their respective sensitivities, specificities, and clinical applicability. This analysis includes innovative non-invasive urine screening tests, such as DNA methylation-based assays, and the application of machine learning to distinguish between non-invasive and invasive tumor stages, ultimately aiming to improve diagnostic accuracy and patient outcomes [15, 11, 9, 6]. Emerging technologies in bladder cancer detection are highlighted for their potential to improve diagnostic accuracy.

The role of adjuvant therapy in bladder cancer management is critically examined, focusing on various types of adjuvant therapies, including intravesical treatments like BCG therapy and systemic approaches such as immunotherapy and targeted therapies. The integration of these therapies with surgical interventions and other modalities, alongside the underlying molecular mechanisms and predictive biomarkers informing treatment efficacy and patient prognosis, is also explored. Recent advancements in urine-based biomarkers and non-invasive diagnostic techniques are addressed, emphasizing their potential to enhance individualized treatment strategies and improve patient outcomes [11, 14, 8, 7].

The survey thoroughly examines cancer biomarkers, particularly their utility in bladder cancer as indicators of disease progression. It analyzes how these biomarkers can enhance diagnostic accuracy, facilitate individualized risk stratification, and inform treatment decisions, ultimately aiming to improve patient outcomes by potentially replacing or complementing traditional invasive methods like cystoscopy. Established and emerging urinary biomarkers are highlighted for their roles in

initial diagnosis, monitoring, and prognostic evaluation, while addressing limitations and the need for further standardization and validation in clinical practice [5, 9, 7]. Challenges in clinical application and the potential utility of emerging biomarkers are explored.

The conclusion synthesizes critical insights from the discussion, underscoring the significance of non-invasive methods for bladder cancer detection and management. It highlights advancements in urine-based biomarkers and enhanced cystoscopy techniques that promise to improve diagnostic accuracy, reduce recurrence risks, and personalize treatment strategies. Furthermore, it outlines future research directions aimed at establishing standardized protocols and evaluating the clinical utility of these innovative diagnostic tools, paving the way for enhanced patient outcomes in bladder cancer care [11, 7, 6].The following sections are organized as shown in Figure 1.

2 Background and Definitions

2.1 Characteristics of Non-Invasive Bladder Cancer

Non-invasive bladder cancer (NMIBC) is confined to the urothelial layer, unlike muscle-invasive bladder cancer (MIBC), which penetrates deeper into the bladder wall. This distinction is essential for prognosis and treatment strategies, as NMIBC accounts for about 75% of bladder cancer cases and is characterized by a high recurrence rate, necessitating diligent surveillance and management [4]. Pathologically, NMIBC includes Ta and T1 tumors, with Ta tumors restricted to the urothelium and T1 tumors invading the lamina propria without reaching the muscularis propria. The histological similarities between these tumor types pose diagnostic challenges, even for experienced pathologists, highlighting the need for precise diagnostic techniques to ensure appropriate treatment planning [4]. Clinically, NMIBC symptoms such as hematuria, dysuria, and increased urinary frequency overlap with various urinary tract conditions, complicating early diagnosis. Traditional diagnostic methods, particularly urine cytology, show limited sensitivity and specificity, especially for low-grade tumors [3]. This limitation has driven a shift towards novel diagnostic approaches incorporating molecular and genetic insights to improve detection accuracy [17]. The distinct molecular landscape of NMIBC, characterized by unique genetic and epigenetic alterations, provides a basis for targeted therapies and personalized treatment plans. The role of lncRNA-RMRP in bladder cancer progression exemplifies the complex interplay of molecular factors influencing tumor behavior [18]. Moreover, the tumor microenvironment in NMIBC, defined by specific immune profiles, presents potential therapeutic targets [4].

2.2 Current Diagnostic Challenges

Diagnosing non-invasive bladder cancer (NMIBC) is challenging due to the limitations of current diagnostic methods. Urine cytology, a widely used technique, has a sensitivity ranging from 22% to 62%, making it inadequate for detecting low-grade lesions [19]. The subjective nature of cystoscopy further complicates diagnosis, as variability in observer experience can lead to misdiagnosis or undetected tumors. Additionally, the high recurrence rates of NMIBC necessitate frequent and invasive follow-ups, imposing physical and psychological burdens on patients [17]. The inadequacy of current diagnostic and surveillance methods, particularly the low sensitivity and specificity of urine cytology and existing urinary biomarkers, underscores the urgent need for innovative approaches [9]. Despite advancements in molecular diagnostics, reliable biomarkers for bladder cancer diagnosis and progression remain elusive [20]. The complexity of the biological environment in urine samples further complicates the identification of dependable biomarkers, contributing to the low accuracy of existing urine diagnostic methods [21]. Moreover, historical control rates used to assess the efficacy of biomarker-targeted therapies often do not reflect the specific patient populations or treatment responses relevant to new therapies, complicating NMIBC management [22]. The variability in treatment responses among different populations and the high recurrence rates post-treatment underscore the need for more effective diagnostic strategies that can accurately detect tumors and monitor disease progression. Addressing these diagnostic challenges is crucial for improving patient outcomes, as advancements in innovative techniques, such as enhanced cystoscopy and urine-based biomarkers, can significantly enhance tumor detection accuracy, reduce recurrence rates, and inform personalized treatment strategies. These developments not only improve disease management but also hold promise for the future of bladder cancer therapy through better risk stratification and monitoring [11, 2, 9, 7].

Consequently, the development of more sensitive and specific biomarkers is imperative for enhancing early detection and providing reliable monitoring of disease progression.

3 Chemotherapy in Non-Invasive Bladder Cancer

Exploring chemotherapy agents and their mechanisms is crucial for managing non-invasive bladder cancer (NMIBC). This section examines common chemotherapy agents used in NMIBC treatment and their mechanisms, providing a foundation for assessing their clinical efficacy. As illustrated in Figure 2, the hierarchical structure of chemotherapy in non-invasive bladder cancer highlights the common agents and mechanisms of action, their effectiveness in preventing cancer progression, the challenges and limitations faced, and innovations and future directions for enhancing treatment precision and efficacy. This visual representation not only complements the discussion but also reinforces the complexity and multifaceted nature of chemotherapy strategies in NMIBC management.

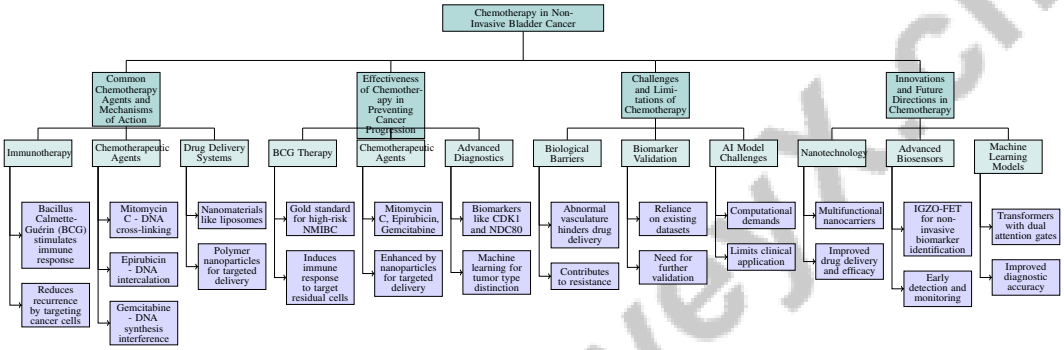


Figure 2: This figure illustrates the hierarchical structure of chemotherapy in non-invasive bladder cancer, highlighting the common agents and mechanisms of action, their effectiveness in preventing cancer progression, the challenges and limitations faced, and innovations and future directions for enhancing treatment precision and efficacy.

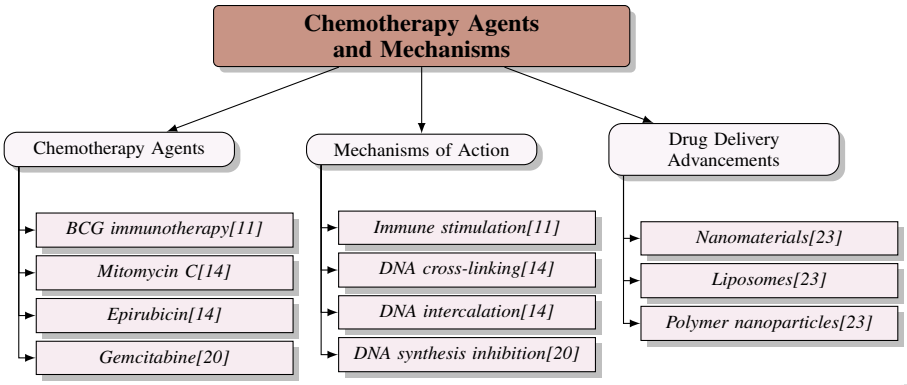
3.1 Common Chemotherapy Agents and Mechanisms of Action

NMIBC treatment often involves several chemotherapy agents with distinct mechanisms aimed at inhibiting cancer progression. Bacillus Calmette-Guérin (BCG) is a prominent immunotherapy that reduces recurrence by stimulating immune responses to target cancer cells [11]. Administered intravesically, BCG induces a localized immune response, enhancing the body's ability to eliminate cancerous cells in the bladder lining.

Other chemotherapeutic agents include mitomycin C, epirubicin, and gemcitabine. Mitomycin C, an alkylating agent, cross-links DNA strands, hindering DNA synthesis and cell division to prevent tumor proliferation [14, 20]. Epirubicin intercalates into DNA, disrupting replication and leading to cell death, while gemcitabine, a nucleoside analog, interferes with DNA synthesis, causing chain termination and apoptosis.

Advancements in drug delivery systems, such as nanomaterials like liposomes and polymer nanoparticles, have enhanced the efficacy of these agents by improving targeted delivery and reducing systemic toxicity [23]. These innovations allow for precise delivery to cancer cells, minimizing adverse effects and improving patient outcomes [14, 23, 11].

As illustrated in Figure 3, this figure provides a comprehensive overview of the common chemotherapy agents used in NMIBC treatment, their mechanisms of action, and advancements in drug delivery systems. It highlights the use of BCG immunotherapy and chemotherapeutic agents like mitomycin C, epirubicin, and gemcitabine, alongside their respective mechanisms such as immune stimulation, DNA cross-linking, and synthesis inhibition. Additionally, it emphasizes the role of nanomaterials in enhancing drug delivery efficacy. Understanding chemotherapy for NMIBC involves recognizing both the agents used and their mechanisms, as these images depict bladder cancer subtypes, advanced diagnostic tools, and gene expression profiles, underscoring the need for precision in treatment [14, 11, 18].



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3.2 Effectiveness of Chemotherapy in Preventing Cancer Progression

Chemotherapy's role in preventing NMIBC progression is well-documented, with BCG therapy being the gold standard for high-risk cases, effectively reducing recurrence and delaying progression to muscle-invasive bladder cancer (MIBC) [11]. BCG induces an immune response that targets residual cancer cells, preventing further growth.

Mitomycin C, epirubicin, and gemcitabine also contribute to reducing tumor proliferation through DNA synthesis disruption and apoptosis induction. Their effectiveness is enhanced by novel delivery systems like nanoparticles, allowing targeted drug delivery with reduced toxicity [23].

Optimizing chemotherapy for individualized care remains challenging. Biomarkers such as CDK1 and NDC80 could inform patient-specific responses and treatment regimens [1]. Advanced diagnostic technologies, including machine learning systems, offer promising avenues for distinguishing tumor types and enhancing chemotherapy effectiveness [15].

Integrating these advancements into clinical practice can significantly improve NMIBC management. By combining chemotherapy with advanced diagnostics and ongoing biomarker research, clinicians can enhance their ability to prevent NMIBC progression, leading to improved patient outcomes [14, 22].

3.3 Challenges and Limitations of Chemotherapy

Chemotherapy for NMIBC faces challenges such as biological barriers like abnormal vasculature, which hinder drug delivery and contribute to resistance [23]. These barriers complicate treatment and limit chemotherapy efficacy.

Another limitation is the reliance on existing datasets for biomarker identification, requiring further validation to ensure clinical applicability [1]. Without robust validation, biomarker-driven approaches remain limited, affecting treatment personalization.

The computational demands of AI models also pose challenges, limiting their clinical application [24]. These models require significant resources, hindering timely data analysis crucial for treatment decisions.

Non-invasive diagnostic methods, like those based on urinary extracellular vesicles, show potential but are still being integrated with chemotherapy protocols. Comprehensive strategies combining these diagnostics with chemotherapy are needed to optimize treatment and enhance patient care [3].

Addressing these challenges involves advancing drug delivery technologies, validating predictive biomarkers, and refining AI models for clinical use. By overcoming limitations in NMIBC manage-

ment, chemotherapy efficacy can be enhanced, reducing recurrence and improving patient outcomes [20, 14, 10, 11].

3.4 Innovations and Future Directions in Chemotherapy

Innovations in NMIBC chemotherapy focus on precision and efficacy through advanced molecular characterization and drug delivery systems. Persistent homology, as seen in Weighted Graph Topological Data Analysis (WGTDA), offers a novel approach for identifying biomarkers and personalizing treatment [25].

Nanotechnology advancements have led to multifunctional nanocarriers that improve drug delivery and efficacy [23]. These carriers can combine imaging and therapeutic functions, allowing real-time monitoring and enhanced targeting of cancer cells.

High stability indium gallium zinc oxide field effect transistor (IGZO-FET) biosensors offer potential for non-invasive bladder cancer biomarker identification from urine [21]. This approach could improve early detection and monitoring, providing insights into treatment efficacy [19].

Advanced machine learning models, like those combining transformers with dual attention gates, offer potential for capturing tumor features and improving diagnostic accuracy [24]. These models could revolutionize treatment planning by providing detailed analyses of tumor characteristics.

Research into lncRNA-RMRP's role in chemotherapy resistance and tumor progression underscores the importance of understanding molecular mechanisms [18]. Elucidating these pathways can identify therapeutic targets and strategies to overcome resistance, improving patient outcomes.

4 Urine Biomarkers for Bladder Cancer Detection

4.1 Urine Biomarkers and Liquid Biopsies

Urine biomarkers and liquid biopsies are pivotal in the non-invasive detection and management of bladder cancer, offering alternatives to traditional, invasive methods such as cystoscopy. These innovations enhance diagnostic accuracy, reduce patient discomfort, and lower recurrence rates through improved sensitivity and specificity in tumor detection [11, 26, 6]. The shift towards patient-centric diagnostic strategies is evident in the integration of urine biomarkers into clinical practice.

Exosomal components have become integral to cancer diagnostics, with exosomal PTENP1 emerging as a promising biomarker for bladder cancer diagnosis and progression monitoring [20]. Research frameworks categorizing exosomal biogenesis and isolation methods further highlight their diagnostic potential [27]. Detecting TERT promoter mutations in urine samples marks another advancement, correlating with urothelial bladder cancer (UBC) recurrence and enabling non-invasive disease monitoring [19].

Metabolomics approaches, both targeted and untargeted, reveal strengths and weaknesses in biomarker discovery strategies for bladder cancer diagnosis [16]. FDA-approved molecular, protein, and gene-related biomarkers underpin current surveillance frameworks, enhancing early detection and management while fostering personalized treatment strategies [17].

4.2 Sensitivity and Specificity of Urine Biomarkers

Assessing the sensitivity and specificity of urine biomarkers is crucial for accurately diagnosing bladder cancer. These metrics help differentiate malignant from benign conditions, reducing false positives and negatives. Current tests like UroVysion and NMP22 exhibit greater sensitivity and specificity than traditional cytology in certain contexts [5], though challenges remain, particularly with low-grade tumors [4].

UroVysion, which detects chromosomal abnormalities, offers enhanced sensitivity for high-grade tumors but may yield false positives in benign conditions [17]. Exosomal PTENP1 shows promise in distinguishing cancerous from healthy conditions, though further validation is required for routine use [20]. Mass spectrometry (MS) techniques provide high sensitivity and specificity in detecting miRNAs

Benchmark	Size	Domain	Task Format	Metric
IQGAP3[28]	293	Urology	Diagnostic Biomarker Identification	AUC, OR
EVBC[3]	43	Oncology	Biomarker Identification	miRNA expression levels, protein expression levels

Table 1: The table presents a comparative analysis of representative benchmarks utilized in the domain of urinary and oncological biomarker identification. It includes details on the benchmark name, dataset size, domain, task format, and evaluation metrics, providing a comprehensive overview for researchers in the field. This information is crucial for understanding the current landscape of diagnostic biomarker identification and its methodological approaches.

and proteins associated with bladder cancer, offering insights into the tumor microenvironment and potential novel biomarkers [27].

The TERT promoter mutation test in urine samples demonstrates promising sensitivity and specificity comparable to cytology and cystoscopy [19], yet high false positive rates and insufficient sensitivity of some biomarkers necessitate invasive confirmation [9]. Innovative technologies like electronic noses show remarkable sensitivity (93.3%) and specificity (86.7%) for bladder cancer detection, surpassing many traditional methods [29]. Table 1 provides an overview of representative benchmarks in the study of urinary and oncological biomarkers, highlighting key attributes such as dataset size, domain, task format, and evaluation metrics.

4.3 Innovative Biomarker Detection Methods

Advancements in urinary biomarker detection for bladder cancer focus on innovative methodologies that enhance diagnostic accuracy and offer non-invasive alternatives. The IGZO-FET biosensor, utilizing indium gallium zinc oxide's electronic properties, detects biomarkers with high sensitivity and specificity [21]. Mass spectrometry (MS) techniques enable comprehensive profiling of the urinary metabolome, leading to novel diagnostic markers [16].

Circular RNAs (circRNAs) are promising candidates for non-invasive cancer biomarkers due to their stability and abundance in bodily fluids [30]. Integrating circRNA analysis into clinical practice could improve detection precision. Electronic nose technology, leveraging a larger array of sensors, enhances diagnostic precision compared to previous systems [29].

Challenges remain in isolating and characterizing exosomes due to their heterogeneity and the complexity of biological fluids [27]. Overcoming these challenges is crucial for identifying specific exosomal proteins as reliable biomarkers, which could significantly improve diagnostic accuracy [20].

4.4 Non-Invasive Biomarker Detection

Non-invasive biomarker detection techniques represent a major advancement in bladder cancer diagnosis and management, reducing the need for invasive procedures like cystoscopy [17]. Technologies such as the IGZO-FET biosensor offer high stability and sensitivity in distinguishing urine samples from bladder cancer patients and healthy individuals [21]. The uCAPP-Seq technique provides improved sensitivity and specificity over standard methods, enhancing early diagnosis and disease monitoring [12]. Circular RNAs (circRNAs) are also gaining attention as stable, abundant biomarkers for non-invasive diagnostics [30].

Despite these innovations, challenges persist in surpassing traditional methods like cystoscopy. While many urine-based biomarkers exhibit superior sensitivity compared to cytology, none have yet matched cystoscopy's diagnostic accuracy [7]. Ongoing research is needed to develop more sensitive and specific biomarkers and validate existing tests in larger, diverse cohorts [31]. Future directions should focus on validating promising biomarkers like UroMark in multi-site trials and developing multi-target panels and novel detection technologies to enhance diagnostic accuracy and utility [32, 9].

5 Techniques for Bladder Cancer Detection

5.1 Advanced Imaging and Machine Learning Techniques

The integration of advanced imaging and machine learning has significantly enhanced bladder cancer detection, offering promising alternatives to traditional methods. Machine learning algorithms, particularly those designed for real-time data processing, have improved diagnostic accuracy and efficiency. CystoNet, for example, utilizes real-time video analysis during cystoscopic procedures, enhancing tumor detection rates beyond those achievable with static images [26]. In a study of 1,177 bladder tumor tissue images, machine learning classifiers effectively distinguished between non-invasive (Ta) and invasive (T1) tumors, demonstrating their potential in identifying subtle tumor characteristics that may be missed by conventional methods [15]. The computational efficiency of these models is particularly beneficial in resource-limited settings, supporting their broader clinical adoption [24]. Additionally, the Cyranose 320 electronic nose exemplifies the application of machine learning in analyzing volatile organic compound patterns in urine, further expanding the diagnostic toolkit for bladder cancer [29].

5.2 Molecular and Genetic Approaches

Molecular and genetic approaches have significantly advanced bladder cancer detection by elucidating tumor development mechanisms and identifying actionable targets. These methodologies focus on genetic mutations, epigenetic modifications, and molecular pathways, enhancing diagnostic sensitivity and specificity [11, 33, 19, 14, 9]. A key development is the identification of the TERT promoter mutation, detectable in urine and associated with cancer recurrence, serving as a non-invasive monitoring biomarker [19]. Epigenetic changes, such as DNA methylation and histone acetylation, influence bladder cancer pathogenesis by altering gene expression without changing the DNA sequence, providing insights into potential therapeutic targets [13, 3, 14, 7, 9]. MicroRNAs (miRNAs) and long non-coding RNAs (lncRNAs) are also pivotal, with miRNAs regulating gene expression related to cancer progression and lncRNAs, such as lncRNA-RMRP, implicated in key signaling pathways [27, 18]. These molecular insights facilitate early detection, tailored treatments, and improved patient outcomes. Continued research, particularly with next-generation sequencing, is crucial for identifying driver mutations and advancing therapeutic strategies, including liquid biopsies and immune checkpoint inhibitors [11, 14, 8, 7, 9].

5.3 Emerging Technologies in Bladder Cancer Detection

Method Name	Technological Innovations	Diagnostic Precision	Biomarker Utilization
IGZO-FET[21]	Igzo-FET Biosensor	High Sensitivity Specificity	Bladder Cancer Biomarkers
HCTM[24]	Dual Attention Gates	High Accuracy	-
C320[29]	Electronic Nose	Enhancing Diagnostic Precision	Volatile Organic Compounds

Table 2: Overview of emerging technologies in bladder cancer detection, highlighting their technological innovations, diagnostic precision, and biomarker utilization. The table compares IGZO-FET biosensors, dual attention gates in machine learning, and electronic nose technology, illustrating their unique contributions to enhancing diagnostic accuracy and biomarker detection.

Emerging technologies are poised to revolutionize bladder cancer diagnostics by enhancing sensitivity and specificity. Table 2 provides a comprehensive comparison of innovative methods used in bladder cancer detection, focusing on their technological advancements, diagnostic precision, and biomarker utilization. Notably, biosensors like indium gallium zinc oxide field-effect transistors (IGZO-FET) offer high stability and sensitivity for detecting urinary biomarkers, representing a leap in non-invasive diagnostics [21]. Combining advanced imaging with machine learning algorithms, such as positional-encoding-free transformers with dual attention gates, further improves diagnostic precision by analyzing complex imaging data [24]. Mass spectrometry (MS) plays a crucial role in biomarker discovery, enabling comprehensive profiling of urinary metabolites and identifying novel diagnostic markers with high sensitivity and specificity [16]. The potential of circular RNAs (circRNAs) as stable and abundant biomarkers in bodily fluids is gaining attention, offering new avenues for personalized treatment strategies [30]. Additionally, electronic nose technology, which analyzes volatile organic compound patterns in urine, demonstrates significant diagnostic potential, surpassing many traditional methods [29]. These innovations underscore the transformative potential

of integrating novel technologies into bladder cancer diagnostics, enhancing early detection and monitoring.

6 Adjuvant Therapy in Bladder Cancer Management

6.1 Overview of Adjuvant Therapies

Adjuvant therapies play a crucial role in bladder cancer management, aiming to prevent recurrence and progression after surgery by eradicating residual cancer cells. These therapies, encompassing systemic and localized treatments, are guided by the heterogeneity of bladder cancer and its molecular subtypes, necessitating effective biomarkers for optimizing patient outcomes [14]. DNA methylation tests are promising in predicting treatment responses and disease progression, though their clinical implementation requires navigating regulatory landscapes to ensure efficacy and safety [33]. Advanced imaging and machine learning are being explored to refine adjuvant therapy planning, with a focus on improving feature extraction and incorporating diverse histological patterns [15]. Innovative diagnostic methods like uCAPP-Seq offer real-time monitoring of treatment responses, with validation in diverse populations essential for clinical application [12]. Integrating advanced diagnostics and molecular insights into adjuvant regimens is vital for optimizing management, particularly considering the complexity of bladder cancer heterogeneity, including NMIBC, MIBC, and metastatic forms. Advancements in non-invasive urine screening, liquid biopsies, immunotherapy, and targeted treatments can help tailor therapies to specific molecular characteristics, enhancing efficacy and improving outcomes by reducing recurrence and progression rates [11, 14].

6.2 Types of Adjuvant Therapies

Adjuvant therapies for bladder cancer include systemic and localized treatments to prevent recurrence and progression post-surgery. Intravesical treatments are crucial for managing NMIBC and MIBC, serving as adjuncts to surgery and improving outcomes by addressing the disease's complex clinical course [14, 10]. Bacillus Calmette-Guérin (BCG) is the cornerstone for NMIBC treatment, leveraging immunomodulatory effects to enhance local immune responses against tumor cells [8]. Other intravesical agents, such as mitomycin C, epirubicin, and gemcitabine, provide cytotoxic effects directly to the bladder urothelium [23]. Systemic chemotherapy, particularly for high-risk or advanced bladder cancer, includes cisplatin-based regimens like gemcitabine and cisplatin (GC) or MVAC, effectively reducing metastasis and improving survival [11]. Emerging therapies, including targeted therapies and immunotherapies, show promise due to their potential for personalized treatment based on tumor molecular characteristics. Agents targeting specific pathways, such as FGFR inhibitors and immune checkpoint inhibitors like pembrolizumab and atezolizumab, modulate the immune system to sustain anti-tumor responses [14, 11]. Successful integration of diverse adjuvant therapies requires evaluating patient-specific factors, such as tumor stage and molecular profile, to ensure optimal outcomes and effective tailoring of immunotherapeutic strategies [22, 34].

6.3 Integration with Other Treatment Modalities

Incorporating adjuvant therapies, such as immunotherapy, targeted therapy, and intravesical treatments, alongside conventional approaches is essential for optimizing therapeutic effectiveness and enhancing survival and quality of life. Recent advancements in diagnostic techniques, like non-invasive urine screening and enhanced cystoscopy, support a multifaceted treatment strategy tailored to NMIBC and MIBC [2, 11, 14, 8]. CystoNet improves tumor detection rates during cystoscopy, potentially reducing recurrence and enhancing surgical outcomes [26]. Integrating adjuvant therapies with other modalities faces challenges such as nanocarrier cytotoxicity in chemotherapy delivery and complex tumor microenvironments [23]. Addressing these challenges is crucial for optimizing drug delivery systems and effective therapy combinations. Incorporating emerging biomarkers into clinical practice is critical, with large-scale studies necessary to validate their utility and guide treatment decisions [17]. Innovative clinical trial designs, like optimal efficiency predictive probability methods, offer promising avenues for monitoring biomarker subpopulations [22]. Integrating adjuvant therapies requires a multifaceted approach combining advanced diagnostics, personalized biomarker analysis, and innovative clinical trial designs. By employing techniques like enhanced cystoscopy and urine-based biomarkers alongside intravesical immunotherapy and targeted therapies, clinicians can improve

detection and treatment accuracy, reducing recurrence and progression while facilitating personalized therapy decisions, ultimately leading to better outcomes and quality of life [11, 2, 7].

6.4 Molecular Mechanisms and Predictive Biomarkers

Exploring molecular mechanisms and predictive biomarkers is crucial for advancing adjuvant therapy efficacy in bladder cancer. Understanding the molecular pathways driving tumor progression and treatment responses is essential for developing personalized therapies. Genomic analyses and next-generation sequencing have identified key driver mutations, actionable therapeutic targets, and improved prognostic assessments. Characterizing tumor microenvironments and developing non-invasive diagnostics, like liquid biopsies, enhance treatment strategy tailoring. These innovations, along with immune checkpoint inhibitors, contribute to improved outcomes through precise and effective interventions [34, 14, 22, 11]. Dysregulation of signaling pathways in bladder cancer involves lncRNAs like lncRNA-RMRP, presenting potential therapeutic targets [18]. Predictive biomarkers guide therapy decisions, allowing regimen tailoring based on tumor molecular characteristics. Biomarkers like exosomal PTENP1 offer promising avenues for diagnostic accuracy and personalized strategies [20]. Future research should prioritize validating biomarkers and exploring their clinical integration [35]. Integrating molecular mechanisms and predictive biomarkers into adjuvant therapy regimens enhances treatment by enabling personalized strategies, improving diagnostic accuracy through non-invasive methods, and facilitating better risk stratification, ultimately optimizing outcomes and survival [11, 7, 14, 8, 9]. Leveraging these insights allows clinicians to enhance therapy personalization and advance bladder cancer management.

7 Cancer Biomarkers as Indicators of Disease Progression

7.1 Novel Classification Frameworks

Innovative classification frameworks are essential for enhancing bladder cancer diagnostics and treatment strategies, addressing its high recurrence and progression rates. Advances such as next-generation sequencing, liquid biopsies, enhanced cystoscopy, and novel therapeutic approaches like immunotherapy and targeted therapy significantly improve patient prognosis and outcomes [11, 14]. These frameworks leverage computational techniques and molecular insights for precise cancer categorization, enabling personalized patient management. Machine learning algorithms, including persistent homology and Weighted Graph Topological Data Analysis (WGTDA), reveal gene interaction patterns and identify biomarkers predictive of disease progression [25]. This enhances understanding of bladder cancer's molecular landscape, facilitating targeted therapies.

Molecular and genetic profiling has identified distinct bladder cancer subtypes, informing treatment decisions and tailoring therapies to tumor-specific molecular characteristics. Differentiating luminal and basal subtypes correlates with varying chemotherapy and immunotherapy responses, emphasizing accurate tumor classification's role in treatment efficacy. Machine learning advancements improve differentiation between early-stage tumors, optimizing treatment strategies and patient outcomes [14, 2, 8, 15].

Integrating advanced imaging with molecular data enriches classification frameworks, providing comprehensive tumor characterization. Machine learning models combining imaging and genetic data improve subtype classification accuracy, enhancing treatment planning. Techniques achieving 91–96

These frameworks facilitate identifying molecular drivers across cancer stages—NMIBC, MIBC, and metastatic forms—enhancing prognostic accuracy and therapeutic targeting. Incorporating insights from sequencing and machine learning transforms tumor biology understanding and management strategies. Emerging non-invasive methods, like liquid biopsies and urinary biomarkers, improve treatment outcomes and patient survival [14, 9, 11, 15]. Continued research is essential to fully realize these classification systems' clinical potential.

7.2 Challenges in Clinical Application

Clinical application of cancer biomarkers in bladder cancer management faces challenges that hinder widespread adoption. Variability in biomarker expression across patient populations complicates

establishing standardized diagnostic criteria, reflecting bladder cancer's heterogeneous nature [27]. This limits biomarker-based diagnostics' reproducibility and reliability, necessitating further research for universally applicable markers.

Integrating biomarker data into clinical workflows is complex, requiring advanced computational tools and expertise often unavailable in clinical settings [25]. User-friendly platforms are needed to incorporate biomarker analysis seamlessly into practice, enabling informed treatment decisions.

Regulatory hurdles also impede biomarker clinical application, with lengthy approval processes demanding extensive validation studies [33]. This delays translating promising biomarkers from research to clinical settings, limiting patient access to personalized strategies.

High costs and inadequate reimbursement pose substantial barriers to adopting biomarker testing, which enhances detection sensitivity and specificity compared to traditional methods [9, 7]. Financial implications, especially in resource-constrained settings, necessitate cost-effective testing methods and supportive reimbursement policies.

Ethical considerations surrounding genetic information use in care, particularly regarding diagnosis and surveillance, must be examined. Urine-based biomarkers and genetic testing raise privacy, consent, and discrimination concerns [11, 17, 7, 12, 9]. Addressing these concerns requires robust ethical guidelines and patient education to ensure responsible genetic data use.

7.3 Emerging Biomarkers and Their Clinical Utility

Emerging biomarkers significantly advance bladder cancer diagnostics and treatment. Techniques like Weighted Graph Topological Data Analysis (WGTDA) uncover significant gene signatures, offering deeper insights into cancer progression [25]. This aids in precise clinical assessments and personalization of treatment by tailoring strategies to unique genetic landscapes, improving efficacy and outcomes.

Advanced computational methods like WGTDA identify biomarkers predicting treatment response, enhancing prognostic precision. These biomarkers guide tailored interventions, refining treatment plans and improving outcomes. Non-muscle invasive bladder cancer research highlights the need for prospective studies to validate biomarkers' utility, particularly in predicting BCG treatment responses [25, 35, 22].

Emerging biomarkers also monitor cancer progression and recurrence, providing real-time therapy effectiveness insights and supporting timely treatment modifications [35, 9, 17, 7]. Integrating these biomarkers into practice transforms management, offering accurate prognostic information and facilitating early interventions.

Ongoing research and validation are critical to harnessing emerging biomarkers' potential, given their diverse nature, including epigenetic, genetic, and exosomal elements enhancing diagnostic sensitivity and specificity [16, 7, 9]. Large-scale studies are necessary to confirm reliability across populations. Developing standardized testing protocols ensures successful clinical integration.

8 Conclusion

The survey highlights the critical importance of non-invasive techniques in the detection and management of bladder cancer, emphasizing their potential to improve diagnostic precision and patient outcomes. Despite advancements, these methods often lack optimal sensitivity and specificity, necessitating continued research to refine these aspects. The integration of novel diagnostic and therapeutic strategies is vital for enhancing bladder cancer care, underscoring the need for ongoing studies to address existing gaps in patient management.

Early diagnosis and effective treatment protocols are essential for boosting survival rates in bladder cancer patients, making non-invasive methods crucial for timely detection. Although urine-based tests offer benefits such as ease of sample collection and reduced discomfort, their effectiveness requires further validation and exploration.

Future investigations should aim to improve adherence to clinical guidelines, examine new treatment options, and rectify current management shortcomings. This includes standardizing procedures for extracellular vesicle isolation and analysis, as well as identifying additional biomarkers for bladder

cancer. The potential of exosomal proteins in liquid biopsies is promising but demands further validation through standardized approaches.

Moreover, exploring the in vivo functions of lncRNA-RMRP and its interactions with other regulatory RNAs and pathways may provide valuable insights for bladder cancer treatment strategies. Progress in early-phase oncology trial designs that optimize sample sizes while maintaining statistical power could facilitate the integration of new therapies and diagnostics. Additionally, the development of electronic nose technology for detecting volatile organic compounds offers a novel, non-invasive approach to bladder tumor diagnosis, meriting further investigation.

References

[1] S. Sajedeh Mousavi and Mohammad Jalil Zorriehzahra. High expression of cdk1 and ndc80 predicts poor prognosis of bladder cancer, 2021.

[2] Katharine C DeGeorge, Harry R Holt, and Stephanie C Hodges. Bladder cancer: diagnosis and treatment. *American family physician*, 96(8):507–514, 2017.

[3] Zoraida Andreu, Renan Otta Oshiro, Alberto Redruello, Soraya López-Martín, Cristina Gutiérrez-Vázquez, Esperanza Morato, Ana Isabel Marina, Carlos Olivier Gómez, and María Yáñez-Mó. Extracellular vesicles as a source for non-invasive biomarkers in bladder cancer progression. *European Journal of Pharmaceutical Sciences*, 98:70–79, 2017.

[4] Marine Charpentier, Charly Gutierrez, Thierry Guillaudeux, Grégory Verhoest, and Rémy Pedeux. Noninvasive urine-based tests to diagnose or detect recurrence of bladder cancer. *Cancers*, 13(7):1650, 2021.

[5] Rui Batista, Nuno Vinagre, Sara Meireles, João Vinagre, Hugo Prazeres, Ricardo Leão, Valdemar Máximo, and Paula Soares. Biomarkers for bladder cancer diagnosis and surveillance: a comprehensive review. *Diagnostics*, 10(1):39, 2020.

[6] Chao-Zhe Zhu, Hua-Nong Ting, Kwan-Hoong Ng, and Teng-Aik Ong. A review on the accuracy of bladder cancer detection methods. *Journal of Cancer*, 10(17):4038, 2019.

[7] Igor Duquesne, Lars Weisbach, Atiqullah Aziz, Luis A Kluth, Evanguelos Xylinas, Young Academic Urologist Urothelial Carcinoma Group of the European Association of Urology, et al. The contemporary role and impact of urine-based biomarkers in bladder cancer. *Translational andrology and urology*, 6(6):1031, 2017.

[8] Oner Sanli, Jakub Dobruch, Margaret A Knowles, Maximilian Burger, Mehrdad Alemozaffar, Matthew E Nielsen, and Yair Lotan. Bladder cancer. *Nature reviews Disease primers*, 3(1):1–19, 2017.

[9] Kenrick Ng, Arnulf Stenzl, Anand Sharma, and Nikhil Vasdev. Urinary biomarkers in bladder cancer: A review of the current landscape and future directions. In *Urologic Oncology: Seminars and Original Investigations*, volume 39, pages 41–51. Elsevier, 2021.

[10] Solomon L Woldu, Aditya Bagrodia, and Yair Lotan. Guideline of guidelines: non-muscle-invasive bladder cancer. *BJU international*, 119(3):371–380, 2017.

[11] Xinzi Hu, Guangzhi Li, and Song Wu. Advances in diagnosis and therapy for bladder cancer. *Cancers*, 14(13):3181, 2022.

[12] Jonathan C Dudley, Joseph Schroers-Martin, Daniel V Lazzareschi, William Y Shi, Simon B Chen, Mohammad S Esfahani, Dharati Trivedi, Jacob J Chabon, Aadel A Chaudhuri, Henning Stehr, et al. Detection and surveillance of bladder cancer using urine tumor dna. *Cancer discovery*, 9(4):500–509, 2019.

[13] Yao Zhan, Lutao Du, Lishui Wang, Xiumei Jiang, Shujun Zhang, Juan Li, Keqiang Yan, Weili Duan, Yinghui Zhao, Lili Wang, et al. Expression signatures of exosomal long non-coding rnas in urine serve as novel non-invasive biomarkers for diagnosis and recurrence prediction of bladder cancer. *Molecular Cancer*, 17:1–5, 2018.

[14] Linda Tran, Jin-Fen Xiao, Neeraj Agarwal, Jason E Duex, and Dan Theodorescu. Advances in bladder cancer biology and therapy. *Nature Reviews Cancer*, 21(2):104–121, 2021.

[15] Peng-Nien Yin, Kishan Kc, Shishi Wei, Qi Yu, Rui Li, Anne R Haake, Hiroshi Miyamoto, and Feng Cui. Histopathological distinction of non-invasive and invasive bladder cancers using machine learning approaches. *BMC medical informatics and decision making*, 20:1–11, 2020.

[16] Mona M Khamis, Darryl J Adamko, and Anas El-Aneed. Mass spectrometric based approaches in urine metabolomics and biomarker discovery. *Mass spectrometry reviews*, 36(2):115–134, 2017.

[17] Sukumar S Sugeeta, Anand Sharma, Kenrick Ng, Arvind Nayak, and Nikhil Vasdev. Biomarkers in bladder cancer surveillance. *Frontiers in Surgery*, 8:735868, 2021.

[18] H-L Cao, Z-J Liu, P-L Huang, Y-L Yue, and J-N Xi. lncrna-rmrp promotes proliferation, migration and invasion of bladder cancer via mir-206. *European Review for Medical & Pharmacological Sciences*, 23(3), 2019.

[19] Françoise Descotes, Norelyakin Kara, Myriam Decaussin-Petrucci, Eric Piaton, Florence Geiguer, Claire Rodriguez-Lafrasse, Jean E Terrier, Jonathan Lopez, and Alain Ruffion. Non-invasive prediction of recurrence in bladder cancer by detecting somatic tert promoter mutations in urine. *British journal of cancer*, 117(4):583–587, 2017.

[20] Rui Zheng, Mulong Du, Xiaowei Wang, Weidong Xu, Jiayuan Liang, Wenying Wang, Qiang Lv, Chao Qin, Haiyan Chu, Meilin Wang, et al. Exosome–transmitted long non-coding rna ptenp1 suppresses bladder cancer progression. *Molecular cancer*, 17:1–13, 2018.

[21] Yingxue Li, Bo Zeng, Yujie Yang, Huageng Liang, Yanbing Yang, and Quan Yuan. Design of high stability thin-film transistor biosensor for the diagnosis of bladder cancer. *Chinese Chemical Letters*, 31(6):1387–1391, 2020.

[22] Emily C. Zabor, Alexander M. Kaizer, Nathan A. Pennell, and Brian P. Hobbs. Optimal predictive probability designs for randomized biomarker-guided oncology trials, 2022.

[23] Zhen Li, Shirui Tan, Shuan Li, Qiang Shen, and Kunhua Wang. Cancer drug delivery in the nano era: An overview and perspectives. *Oncology reports*, 38(2):611–624, 2017.

[24] Meryem Amaouche, Ouassim Karrakchou, Mounir Ghogho, Anouar El Ghazzaly, Mohamed Alami, and Ahmed Ameur. Redefining cystoscopy with ai: bladder cancer diagnosis using an efficient hybrid cnn-transformer model, 2024.

[25] Ndivhuwo Nyase, Lebohang Mashatola, Aviwe Kohlakala, Kahn Rhrissorrakrai, and Stephanie Muller. Wgtda: A topological perspective to biomarker discovery in gene expression data, 2024.

[26] Eugene Shkolyar, Xiao Jia, Timothy C Chang, Dharati Trivedi, Kathleen E Mach, Max Q-H Meng, Lei Xing, and Joseph C Liao. Augmented bladder tumor detection using deep learning. *European urology*, 76(6):714–718, 2019.

[27] Chunmiao Hu, Wei Jiang, Mingjin Lv, Shuhao Fan, Yujia Lu, Qingjun Wu, and Jiang Pi. Potentiality of exosomal proteins as novel cancer biomarkers for liquid biopsy. *Frontiers in Immunology*, 13:792046, 2022.

[28] Won Tae Kim, Ye Hwan Kim, Pildu Jeong, Sung-Pil Seo, Ho-Won Kang, Yong-June Kim, Seok Joong Yun, Sang-Cheol Lee, Sung-Kwon Moon, Yung-Hyun Choi, et al. Urinary cell-free nucleic acid iqgap3: A new non-invasive diagnostic marker for bladder cancer. *Oncotarget*, 9(18):14354, 2018.

[29] Hendrik Heers, Josef Maximilian Gut, Axel Hegele, Rainer Hofmann, Tobias Boeselt, Akira Hattesohl, and Andreas Rembert Koczulla. Non-invasive detection of bladder tumors through volatile organic compounds: a pilot study with an electronic nose. *Anticancer Research*, 38(2):833–837, 2018.

[30] Shujuan Meng, Hecheng Zhou, Ziyang Feng, Zihao Xu, Ying Tang, Peiyao Li, and Minghua Wu. Circrna: functions and properties of a novel potential biomarker for cancer. *Molecular cancer*, 16:1–8, 2017.

[31] Felice Crocetto, Biagio Barone, Matteo Ferro, Gian Maria Busetto, Evelina La Civita, Carlo Buonerba, Giuseppe Di Lorenzo, Daniela Terracciano, and Jack A Schalken. Liquid biopsy in bladder cancer: State of the art and future perspectives. *Critical Reviews in Oncology/Hematology*, 170:103577, 2022.

[32] Andrew Feber, Pawan Dhami, Liqin Dong, Patricia de Winter, Wei Shen Tan, Mónica Martínez-Fernández, Dirk S Paul, Antony Hynes-Allen, Sheida Rezaee, Pratik Gurung, et al. Uromark—a urinary biomarker assay for the detection of bladder cancer. *Clinical epigenetics*, 9:1–10, 2017.

[33] Warwick J Locke, Dominic Guanzon, Chenkai Ma, Yi Jin Liew, Konsta R Duesing, Kim YC Fung, and Jason P Ross. Dna methylation cancer biomarkers: translation to the clinic. *Frontiers in genetics*, 10:1150, 2019.

[34] Yu-Pei Chen, Yu Zhang, Jia-Wei Lv, Ying-Qin Li, Ya-Qin Wang, Qing-Mei He, Xiao-Jing Yang, Ying Sun, Yan-Ping Mao, Jing-Ping Yun, et al. Genomic analysis of tumor microenvironment immune types across 14 solid cancer types: immunotherapeutic implications. *Theranostics*, 7(14):3585, 2017.

[35] Francesco Soria, Michael J Droller, Yair Lotan, Paolo Gontero, David D'Andrea, Kilian M Gust, Morgan Rouprêt, Marek Babjuk, Joan Palou, and Shahrokh F Shariat. An up-to-date catalog of available urinary biomarkers for the surveillance of non-muscle invasive bladder cancer. *World journal of urology*, 36:1981–1995, 2018.

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