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# Bladder Cancer Recurrence and Postoperative Outcomes: A Survey on Radiomics and Predictive Modeling in Medical Imaging

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## Abstract

Bladder cancer presents significant challenges due to high recurrence rates and complex management needs. This survey examines the interdisciplinary integration of radiomics and predictive modeling in enhancing bladder cancer diagnosis and treatment. Radiomics enables the extraction of quantitative features from medical images, providing insights into tumor heterogeneity crucial for personalized treatment strategies. Predictive modeling, employing statistical and machine learning techniques, forecasts disease recurrence and treatment efficacy, supporting tailored therapeutic interventions. The synergy between radiomics and molecular data enhances predictive accuracy, allowing for patient stratification based on tumor aggressiveness. Deep learning advancements, particularly convolutional neural networks, improve segmentation accuracy, refining tumor detection and classification. AI-driven frameworks, such as MDNet, facilitate the generation of interpretable diagnostic reports, bridging AI diagnostics and clinical practice. Despite challenges in data quality, model interpretability, and computational complexity, ongoing research aims to refine these approaches, enhancing their clinical utility. Future directions emphasize advancements in molecular characterization, treatment strategies, and AI applications, aiming to transform bladder cancer management. By integrating radiomics and predictive modeling, healthcare providers can deliver personalized care, improving patient outcomes and advancing oncology.

## 1 Introduction

### 1.1 Prevalence and Epidemiology of Bladder Cancer

Bladder cancer poses a significant public health challenge, marked by high morbidity and mortality rates primarily due to late diagnosis and complex management [1]. It ranks as the seventh most common cancer globally, impacting millions, and is the sixth most prevalent malignancy in the United States [2, 3]. With a rising incidence, particularly in developing countries, it is also the 10th most common cancer worldwide [4].

The increasing incidence among older adults contributes to its status as one of the most prevalent cancers, coupled with high treatment costs due to frequent recurrences that necessitate ongoing surveillance [5, 6]. Understanding the epidemiological aspects is crucial given the economic burden and need for effective management strategies.

Recent investigations into the urinary microbiome in bladder cancer patients have provided insights into its epidemiological characteristics compared to healthy controls [7]. Such research is vital for advancing our understanding of bladder cancer biology and therapy, addressing significant gaps in knowledge regarding its molecular mechanisms and treatment strategies [8]. The current epidemiological landscape emphasizes the necessity for continued research and innovation in diagnosis and management to reduce its global health impact [9].

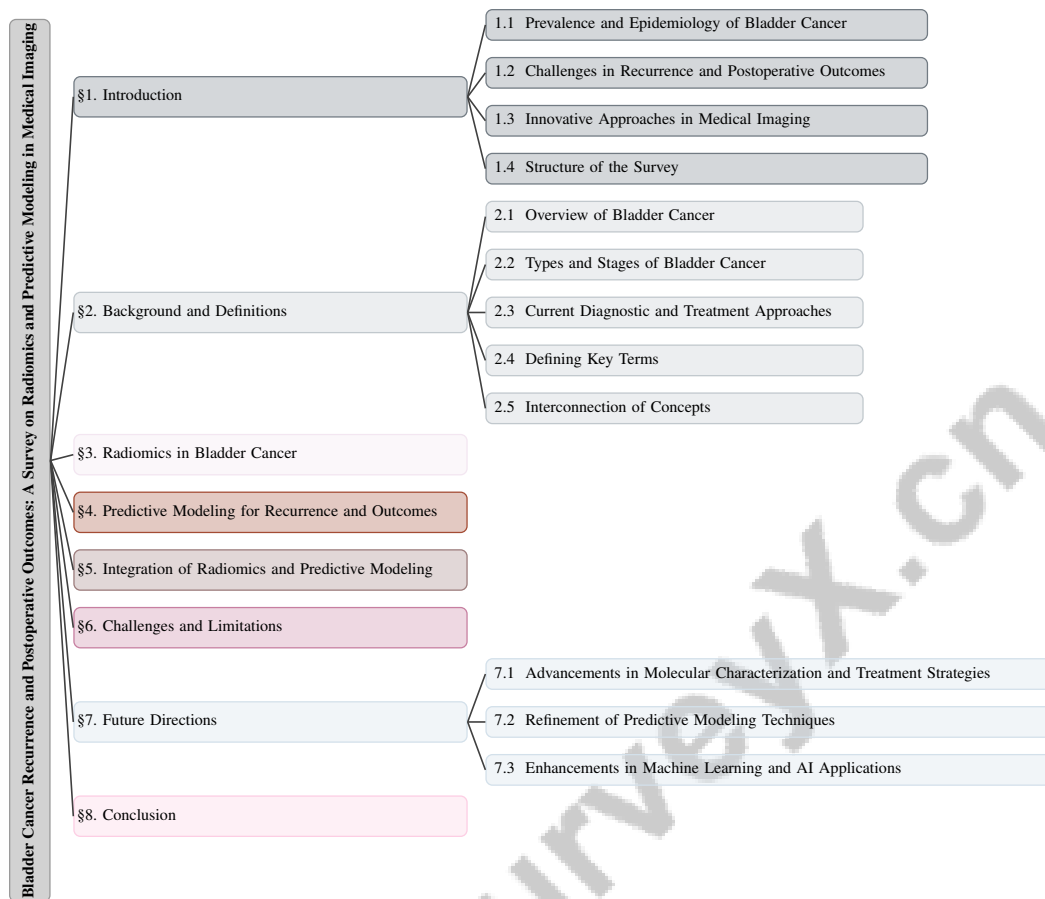


Figure 1: chapter structure

## 1.2 Challenges in Recurrence and Postoperative Outcomes

The management of bladder cancer recurrence and postoperative outcomes is fraught with challenges due to the disease's biological complexity and the limitations of existing diagnostic and therapeutic protocols. Non-Muscle-Invasive Bladder Cancer (NMIBC) is particularly susceptible to high recurrence rates, revealing inadequacies in current predictive tools and treatment strategies [10]. Traditional diagnostic methods, including cystoscopy and urine cytology, often suffer from low sensitivity and specificity, which can lead to misdiagnosis and undetected cases; these invasive procedures heavily depend on clinician expertise, resulting in variable outcomes and increased patient burden [6].

Bladder cancer's heterogeneity, encompassing various molecular subtypes and treatment resistance, complicates outcome prediction and necessitates personalized approaches. The intricate interactions among the immune system, treatments, and cancer cells add layers of complexity to predicting outcomes, underscoring the need for adaptive strategies [11]. Additionally, significant variability in bladder shape and tumor appearance, coupled with motion artifacts and weak boundaries, presents challenges in accurately segmenting bladder structures in imaging modalities, which is essential for assessing muscle invasion [12].

The role of the urinary microbiome in bladder cancer pathogenesis remains underexplored, creating critical gaps in understanding that could inform novel diagnostic and therapeutic strategies [7]. The high costs associated with bladder cancer management, driven by frequent recurrences and the need for continuous surveillance, underscore the necessity for innovative approaches to enhance patient outcomes [10]. Discrepancies between patient preferences for personalized treatments and the economic constraints faced by healthcare providers further complicate the implementation of personalized medicine [13].

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The absence of standardized screening tests for many cancers, including bladder cancer, results in insufficient data on preclinical latency periods, hindering accurate modeling and early detection efforts [14]. Furthermore, the assumption of conditional independence between measured and unmeasured confounders given treatment status is frequently violated, complicating the assessment of treatment efficacy [15]. These multifaceted challenges necessitate ongoing research and innovative strategies to enhance bladder cancer management and improve patient prognoses.

### 1.3 Innovative Approaches in Medical Imaging

Radiomics and predictive modeling represent cutting-edge methodologies in medical imaging, especially concerning bladder cancer. These approaches involve extracting quantitative features from medical images to predict tumor behavior and patient outcomes. Utilizing a supermodel composed of dynamically synchronized sub-models enhances the accuracy of tumor progression predictions, effectively capturing tumor dynamics [16]. This model integration fosters a nuanced understanding of tumor growth patterns, which is critical for tailoring individualized treatment strategies.

The incorporation of high-throughput sequencing methods, such as the utDNA CAPP-Seq (uCAPP-Seq), further enhances the diagnostic capabilities of radiomics by improving the sensitivity and specificity of bladder cancer detection [17]. This method exemplifies the potential of combining molecular data with imaging features, offering a comprehensive approach to early cancer detection and monitoring.

Advancements in deep learning, particularly through hybrid models that integrate convolutional neural networks (CNNs) with transformers and attention mechanisms, have also improved tumor detection and segmentation [6]. These models enhance the accuracy of identifying tumor boundaries and facilitate muscle invasion assessment, crucial for determining appropriate treatment courses.

Moreover, applying a universal growth law to tumor dynamics provides a unified framework for understanding tumor behavior across various cancer types, simplifying the modeling process and enabling consistent predictions [18]. The European Association of Urology (EAU) guidelines support these innovations by offering evidence-based recommendations for managing muscle-invasive and metastatic bladder cancer, emphasizing advanced imaging and predictive tools to enhance patient outcomes [19].

Incorporating socio-demographic factors into personalized mathematical models improves the predictive accuracy of treatment responses, facilitating the development of more effective and tailored therapeutic interventions [2]. Collectively, these innovative approaches signify substantial advancements in bladder cancer management, underscoring the transformative potential of radiomics and predictive modeling in medical imaging.

### 1.4 Structure of the Survey

This survey is systematically structured to provide a comprehensive examination of bladder cancer, focusing on the integration of radiomics and predictive modeling in medical imaging. The introduction highlights bladder cancer as the most common malignancy of the urinary tract, emphasizing its alarming global prevalence, with nearly 550,000 new diagnoses and approximately 200,000 deaths reported in 2018. It addresses significant challenges related to high recurrence rates and postoperative complexities, while discussing advancements in diagnosis and treatment aimed at improving patient care and reducing morbidity [3, 9, 1]. The innovative role of radiomics and predictive modeling in addressing these challenges is also underscored.

Subsequent sections provide a detailed background on bladder cancer, including its types, stages, and current diagnostic and treatment approaches. Key terms such as radiomics, predictive modeling, and postoperative outcomes are defined to establish a foundational understanding, while the interconnection of these concepts is explored to illustrate their relevance in bladder cancer management.

The survey focuses on the application of radiomics in bladder cancer, emphasizing quantitative feature extraction and its potential in diagnostics and recurrence prediction. It discusses the integration of radiomics data with molecular data, highlighting advanced deep learning techniques, such as fully convolutional neural networks and multi-task spatial feature encoder networks, to improve the analysis and segmentation of bladder cancer structures in MRI. These methods aim to enhance tumor

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classification and localization accuracy, providing critical insights for treatment decisions and patient prognosis [12, 20, 21, 22].

The exploration of predictive modeling techniques for assessing bladder cancer recurrence and enhancing postoperative outcomes encompasses a detailed analysis of advanced statistical and machine learning models, particularly focusing on their application in NMIBC, which has a recurrence rate of 70-80

The integration of radiomics and predictive modeling is discussed in the context of personalized medicine, exploring frameworks that support their applicability in clinical settings to improve patient management. The analysis highlights several challenges and limitations in medical diagnostics, including data quality issues, such as inconsistencies in electronic health records and imbalanced datasets, as well as model interpretability, which is crucial for understanding predictions made by complex algorithms like TandemNet and MDNet. Additionally, computational complexity arises from the high-dimensional nature of multi-omics data and the need for sophisticated techniques to manage it effectively. Addressing these challenges is essential for developing robust and interpretable models that can improve diagnostic accuracy and facilitate informed decision-making in clinical settings [23, 24, 20, 25, 26].

Finally, the survey outlines future directions, discussing potential advancements in molecular characterization, refinement of predictive modeling techniques, and enhancements in machine learning and AI applications for bladder cancer management. The conclusion emphasizes the transformative potential of innovative approaches, such as next-generation sequencing, machine learning for recurrence prediction, and advanced diagnostic techniques like AI-enhanced cystoscopy, in markedly improving outcomes for patients with bladder cancer. These strategies not only identify actionable therapeutic targets and enhance diagnostic accuracy but also offer personalized treatment options and better monitoring capabilities, ultimately leading to improved survival rates and quality of life for patients [8, 27, 28, 6]. The following sections are organized as shown in Figure 1.

## **2 Background and Definitions**

### **2.1 Overview of Bladder Cancer**

Bladder cancer predominantly affects urothelial cells, with tobacco use and environmental carcinogen exposure as primary risk factors [4]. It is categorized into non-muscle-invasive (NMIBC) and muscle-invasive bladder cancer (MIBC), each necessitating distinct diagnostic and therapeutic strategies due to their specific clinical and pathological traits [3]. NMIBC's high recurrence rate demands continuous surveillance, contributing significantly to healthcare costs and making it one of the most expensive cancers to manage [1].

The disease's progression involves complex molecular pathways and genetic mutations, crucial for comprehending its pathogenesis and developing targeted therapies [8]. Molecular diagnostics advancements, like RNA sequencing, have enhanced understanding of the bladder cancer transcriptomic landscape, aiding in biomarker identification for early detection and personalized treatment [29]. Despite cystoscopy's essential role, its efficacy varies with operator expertise, affecting tumor detection and grading.

Emerging research highlights the urinary microbiome's influence on bladder cancer pathophysiology, suggesting its potential in novel diagnostic and therapeutic strategies [7]. Identifying cancer driver genes remains pivotal for elucidating molecular mechanisms and informing future therapeutic interventions [30]. Current treatments include transurethral resection, radical cystectomy, and various chemotherapeutic and immunotherapeutic approaches, tailored to disease stages [9]. Continued research is essential to enhance patient outcomes, reduce recurrences, and improve quality of life.

### **2.2 Types and Stages of Bladder Cancer**

Bladder cancer is classified based on invasion depth into NMIBC, including stages Ta, T1, and carcinoma in situ (CIS), and MIBC, involving deeper invasion at stage T2 and above [3]. NMIBC is primarily managed through transurethral resection and intravesical therapies, emphasizing the need for precise diagnostics and treatment strategies to address high recurrence rates [1]. MIBC generally

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requires aggressive treatments like radical cystectomy and neoadjuvant chemotherapy to manage progression and minimize metastasis risk [3].

Challenges in accurately estimating tumor cell dynamics parameters, particularly in recurrent tumors, are exacerbated by the reliance on single time-point sequencing data, which may not capture tumor heterogeneity [31]. Identifying misregulated genes further complicates understanding bladder cancer's molecular underpinnings [32]. The cancer's heterogeneity necessitates personalized strategies targeting specific genetic and molecular alterations [8]. Advanced analytical methods, like structured tests for differential gene expression, offer potential for refined diagnostic and prognostic tools [33].

Understanding bladder cancer's types and stages is crucial for advancing clinical management and improving outcomes. Ongoing research into its molecular and genetic characteristics aims to develop more personalized and effective diagnostic and therapeutic strategies. Leveraging genomic sequencing, transcriptomics, and novel urinary biomarkers can enhance diagnostic accuracy, improve patient stratification, and tailor interventions to specific disease stages. These insights are expected to facilitate the translation of innovative therapies, such as immune checkpoint inhibitors, into clinical practice, ultimately improving patient outcomes and survival rates [17, 8, 29, 1, 28].

### **2.3 Current Diagnostic and Treatment Approaches**

Cystoscopy remains the gold standard for bladder cancer diagnosis, despite its invasiveness and limitations in sensitivity and specificity [17]. Molecular diagnostics advancements, exemplified by the NMP22 BladderChek test, underscore the need for more reliable, less invasive diagnostic tools due to performance variability across populations [5]. Advanced imaging techniques, such as the MMSFENet model, improve diagnostic accuracy by addressing challenges in delineating bladder walls and tumors [21]. Image registration processes in video sequences have been benchmarked to enhance detection accuracy and robustness [34].

Treatment approaches have shifted towards personalization, driven by advances in immunotherapy and targeted therapies [8]. Established diagnostic and management protocols have improved early detection and treatment outcomes [3]. For NMIBC, machine learning methodologies predict recurrence by leveraging radiomics, clinical, histopathological, and genomic data [27]. However, survival analysis models, like the proportional hazards model, face challenges with clustered observations, necessitating more robust statistical tools to avoid biased estimates [35].

The treatment landscape has expanded with targeted therapies focusing on molecular and genetic markers, such as high CDK1 and NDC80 expression, crucial for understanding disease progression and developing interventions [4]. The NMGrad method combines deep learning with histopathological expertise to enhance grading consistency and accuracy, reflecting the potential of integrating technological advancements with clinical expertise [10]. Traditional diagnostic methods' time-consuming nature underscores the need for more efficient approaches [36]. Reviews of urinary biomarkers for NMIBC, including FDA-approved tests and emerging markers like epigenetic, genetic, and exosomal markers, highlight efforts to refine diagnostic strategies [28]. The economic feasibility of implementing personalized medicine, particularly in resource-constrained environments, remains a significant concern [13]. These advancements reflect a shift towards more personalized and precise management, aiming to improve outcomes and reduce the economic burden associated with bladder cancer.

### **2.4 Defining Key Terms**

Key terms in bladder cancer diagnosis and treatment include radiomics, which involves extracting and analyzing large amounts of quantitative features from medical images to predict tumor behavior and patient outcomes. This process captures tumor heterogeneity through imaging biomarkers, integrated into predictive models to enhance diagnostic accuracy and treatment personalization [18].

Predictive modeling uses statistical and machine learning techniques to develop models forecasting disease recurrence and treatment effectiveness. These models incorporate dynamic resource allocation and predictive analytics to optimize management and outcomes [37]. In bladder cancer, predictive modeling assesses recurrence risk and tailors personalized treatments based on socio-demographic factors and individual characteristics [2].

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Medical imaging, including MRI, CT, and ultrasound, plays a crucial role in visualizing and assessing bladder cancer, providing foundational data for radiomics analysis. Advances in imaging technology have significantly improved the detection and characterization of bladder tumors, facilitating early intervention and monitoring of treatment response [7].

Postoperative outcomes encompass recovery following surgical interventions, including recurrence rates, survival, and quality of life. The complexity of bladder cancer's genetic landscape and high recurrence rates present challenges in predicting outcomes, necessitating effective biomarkers for early detection and treatment response [29]. Understanding gene expression and regulatory networks is essential for identifying misregulated genes that may influence these outcomes, offering insights into potential therapeutic targets and strategies [32].

The integration of advanced imaging techniques, such as the hybrid CNN-transformer model for cystoscopy and the multi-scale multi-task spatial feature encoder network (MM-SFENet) for MRI analysis, alongside predictive analytics powered by machine learning, enhances bladder cancer diagnosis and recurrence prediction accuracy. These approaches aim to personalize treatment models and improve patient outcomes by addressing high recurrence rates and diagnostic challenges, ultimately reducing the economic burden of this costly disease [21, 27, 6].

## **2.5 Interconnection of Concepts**

Integrating radiomics, predictive modeling, medical imaging, and postoperative outcomes forms a comprehensive framework for advancing bladder cancer management. Radiomics, by extracting quantitative features from medical images, provides detailed tumor heterogeneity characterization essential for accurate diagnosis and treatment planning [16]. This approach is significant given the exponential increase in time complexity associated with data assimilation in tumor evolution, necessitating efficient computational strategies to manage and interpret vast data [16].

Predictive modeling complements radiomics by employing statistical and machine learning techniques to forecast disease recurrence and treatment efficacy. These models address the challenges posed by high recurrence rates and the limited sensitivity of existing urinary biomarkers, which often result in false positives and insufficient predictive power when used alone [28]. Integrating predictive analytics allows for dynamic resource allocation and personalized treatment regimens, enhancing bladder cancer management precision [38].

Medical imaging serves as the foundational data source for radiomics analysis, facilitating tumor visualization and assessment. Imaging technology advances have significantly improved bladder cancer detection and characterization, providing critical information for developing predictive models and evaluating postoperative outcomes [9]. The synergy between imaging modalities and radiomics enables a nuanced understanding of tumor dynamics, vital for tailoring individualized treatment strategies and improving patient prognoses [31].

Postoperative outcomes, encompassing recurrence rates, survival, and quality of life, are inherently linked to diagnostic and therapeutic interventions' effectiveness. The complexity of bladder cancer's genetic landscape and competing risks complicate outcome prediction, underscoring the need for robust biomarkers and predictive models to guide clinical decision-making [38]. Understanding the interplay between molecular biology and treatment strategies is crucial for developing comprehensive management plans addressing bladder cancer's multifaceted challenges [9].

The interconnected concepts emphasize the need for an integrated bladder cancer management approach. This approach harnesses advanced imaging techniques, such as MRI, alongside radiomics and predictive modeling, to enhance diagnostic accuracy, refine treatment strategies, and improve postoperative outcomes. Innovations like the MM-SFENet for automated tumor classification, machine learning frameworks for predicting NMIBC recurrence, and deep learning models for precise bladder structure segmentation demonstrate these technologies' potential to transform clinical practices and patient care [21, 27, 6, 22, 12].

## **3 Radiomics in Bladder Cancer**

Radiomics in bladder cancer leverages advanced imaging and quantitative analysis to refine diagnostic and prognostic processes. This section delves into quantitative feature extraction, which is pivotal

for analyzing tumor characteristics through systematic medical image assessment. As illustrated in Figure 2, the hierarchical structure of radiomics in bladder cancer highlights key areas such as quantitative feature extraction, integration with molecular data, and the role of deep learning. Each section of the figure delves into specific methodologies, applications, and innovations that contribute to enhanced diagnostic and prognostic capabilities in bladder cancer management. Rigorous feature extraction methodologies provide crucial insights for clinical decision-making, with subsequent subsections detailing these processes and their technological foundations in bladder cancer research.

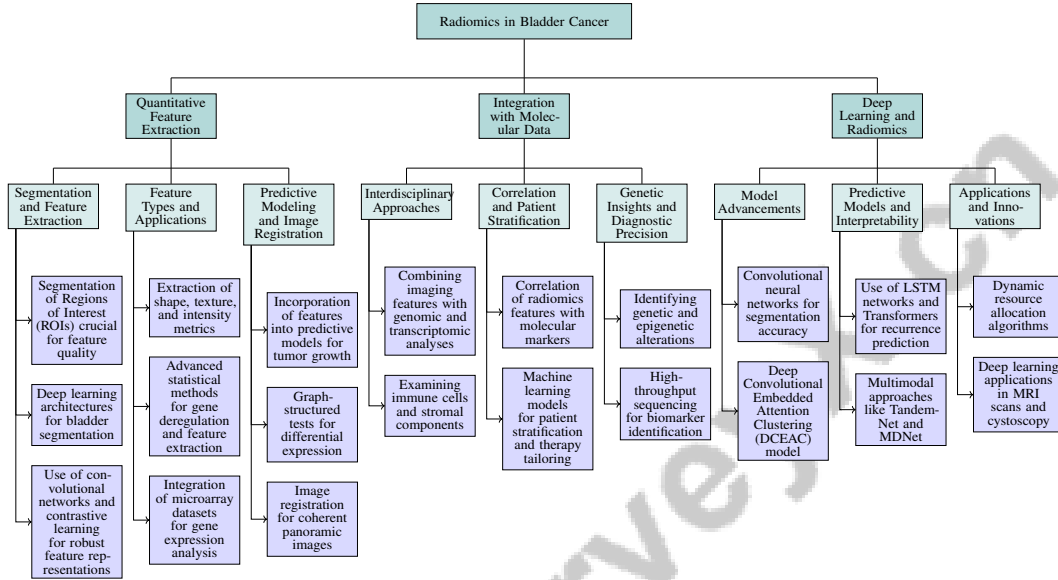


Figure 2: This figure illustrates the hierarchical structure of radiomics in bladder cancer, highlighting key areas such as quantitative feature extraction, integration with molecular data, and the role of deep learning. Each section delves into specific methodologies, applications, and innovations that contribute to enhanced diagnostic and prognostic capabilities in bladder cancer management.

### 3.1 Quantitative Feature Extraction

In radiomics, quantitative feature extraction is integral to bladder cancer diagnosis and prognosis, involving systematic image analysis to derive significant data. Initially, medical images undergo segmentation to identify Regions of Interest (ROIs), crucial for the quality of extracted features. Recent advancements underscore the need for specialized deep learning architectures for bladder imaging, such as frameworks that categorize deep learning models for bladder segmentation [12]. Techniques employing convolutional networks for ROI segmentation, followed by contrastive learning, have been crafted to develop robust feature representations [11].

Post-ROI establishment, a variety of quantitative features like shape, texture, and intensity metrics are extracted, offering a comprehensive tumor heterogeneity characterization vital for precise diagnosis and treatment planning. Advanced statistical methods, including the EM algorithm for posterior probabilities of gene deregulation, enhance feature extraction by elucidating gene expression patterns affecting tumor behavior [32]. Integrating microarray datasets to analyze gene expression differences between bladder cancer stages further elucidates the disease's molecular aspects [4].

These features are incorporated into predictive models, utilizing metrics such as recurrence time and mutant clone numbers to estimate tumor growth parameters, providing nuanced insights into tumor dynamics at the individual level [8]. Graph-structured tests for differential expression improve detection rates and biological interpretability of gene expression data, enhancing radiomics' predictive power [33].

Addressing the challenge of registering consecutive images from endoscopic video sequences to create coherent panoramic images of the bladder is critical. Benchmarking studies enhance quantitative feature extraction accuracy by ensuring consistent image alignment [34]. This comprehensive

approach to quantitative feature extraction not only boosts diagnostic accuracy but also facilitates personalized treatment strategies, ultimately improving bladder cancer management outcomes.

### 3.2 Integration with Molecular Data

Integrating radiomics with molecular data is an emerging frontier in bladder cancer research, enhancing analytical capabilities to improve diagnostic and therapeutic outcomes. This interdisciplinary approach combines quantitative imaging features with molecular profiles from genomic and transcriptomic analyses, offering a comprehensive understanding of tumor biology. Molecular characterization involves examining immune cells and stromal components, which significantly influence tumor behavior and treatment responses [8].

As illustrated in Figure 3, the integration of radiomics and molecular data is pivotal in bladder cancer research, showcasing key radiomics features, molecular characterization components, and the advanced methodologies employed in analysis. Radiomics features, such as texture and intensity metrics, correlate with molecular markers, identifying patterns not discernible through traditional imaging or molecular techniques alone. This correlation facilitates patient stratification according to tumor aggressiveness and anticipated treatment responses, enhancing personalized treatment development. Advanced methodologies like machine learning and microsimulation models enable healthcare providers to identify subpopulations likely to benefit from tailored therapies, improving patient outcomes and efficient resource allocation in clinical settings [27, 10, 13, 39, 14].

Incorporating molecular data aids in identifying specific genetic and epigenetic alterations driving tumor progression, informing targeted therapy decisions. High-throughput sequencing technologies like RNA sequencing uncover the transcriptomic landscape of bladder cancer, identifying potential biomarkers for early detection and monitoring [8]. This comprehensive approach augments diagnostic precision and provides insights into treatment resistance mechanisms, optimizing therapeutic regimens.

The synergy between radiomics and molecular data underscores the transformative potential of integrated analyses in clinical decision-making, significantly enhancing patient stratification and optimizing personalized medicine strategies, ultimately leading to improved healthcare outcomes and cost-effectiveness in resource-constrained settings [13, 20, 39, 27].

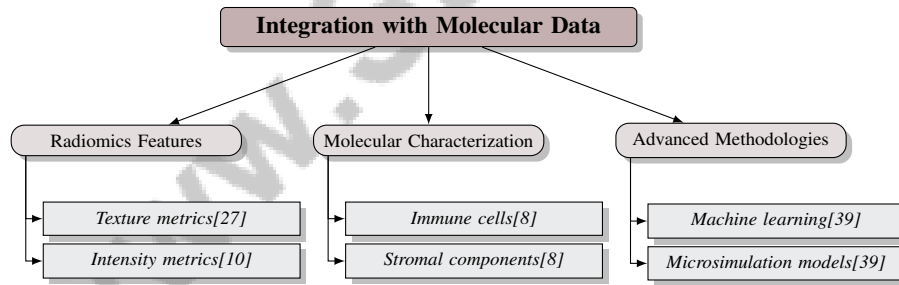


Figure 3: This figure illustrates the integration of radiomics and molecular data in bladder cancer research, highlighting key radiomics features, molecular characterization components, and advanced methodologies used in analysis.

### 3.3 Deep Learning and Radiomics

Deep learning integration into radiomics significantly enhances medical imaging capabilities in bladder cancer, offering improved diagnostic and prognostic insights. Deep learning models, especially convolutional neural networks (CNNs), refine bladder cancer segmentation accuracy by capturing complex spatial features and modeling intricate dependencies [36]. The Deep Convolutional Embedded Attention Clustering (DCEAC) model exemplifies this advancement by employing a self-learning framework to classify histological images into severity levels, facilitating precise diagnosis and treatment planning.

Advanced models like Long Short-Term Memory (LSTM) networks and Transformers enhance predictive accuracy for bladder cancer recurrence by capturing temporal dependencies and long-range interactions within imaging data. These models improve understanding of tumor dynamics



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through methodologies like supermodeling, which integrates multiple self-synchronized sub-models for enhanced trajectory predictions, and multimodal approaches like TandemNet and MDNet, which leverage both visual and semantic information from diagnostic reports to refine predictions and provide interpretability. Additionally, deep learning techniques, such as LSTM, effectively analyze complex, time-dependent recurrence data, identifying critical predictors of bladder cancer recurrence and improving clinical risk assessment and treatment strategies [40, 16, 20, 26]. Integrating attention mechanisms further enhances interpretability by focusing on relevant features, thus improving bladder cancer grading from histological slides.

Moreover, semantically and visually interpretable networks like MDNet establish direct multimodal mappings between medical images and diagnostic reports, enabling report generation and image retrieval based on symptom descriptions [26]. This capability enriches the diagnostic process and enhances the clinical decision-making framework by providing a holistic view of the patient's condition.

The adaptability of deep learning models is exemplified by their ability to dynamically adjust parameters based on socio-demographic data, as demonstrated in mathematical modeling approaches. This flexibility is complemented by dynamic resource allocation algorithms optimizing resource distribution in real-time, enhancing predictive modeling efficiency [38].

The synergy between deep learning techniques and radiomics not only improves bladder cancer diagnosis and treatment planning accuracy and efficiency but also facilitates novel biomarker discovery. Recent advancements in deep learning applications for radiomics significantly enhance bladder cancer management precision by enabling accurate segmentation of tumor and bladder structures in MRI scans, improving staging and personalized treatment strategies. For example, progressive dilated convolutional networks have achieved a mean Dice similarity coefficient of 0.84 for tumor regions, crucial for determining muscle invasion extent and guiding therapy selection. Hybrid CNN-transformer models have also been developed to improve diagnostic accuracy in cystoscopy, addressing misdiagnosis challenges due to reliance on clinician interpretation. Furthermore, novel multi-scale multi-task networks for bladder cancer localization and classification have demonstrated impressive performance metrics. Collectively, these innovations illustrate the transformative potential of deep learning in radiomics, paving the way for more precise and personalized approaches to bladder cancer management [21, 10, 6, 22, 12].

## **4 Predictive Modeling for Recurrence and Outcomes**

### **4.1 Overview of Predictive Modeling Techniques**

Predictive modeling in bladder cancer employs statistical and machine learning techniques to enhance recurrence predictions and treatment outcome assessments. These models integrate imaging, clinical, and molecular data, offering a comprehensive view of bladder cancer dynamics [2]. The Personalized BCG Treatment Model (PBCG) exemplifies this integration by leveraging patient-specific data for improved treatment predictions, facilitating personalized therapies. Gene expression profiling identifies hub genes as biomarkers crucial for patient stratification and individualized treatment [4]. Incorporating molecular insights into predictive models enhances their ability to forecast disease progression and treatment responses.

Hybrid models, combining deep learning and statistical methods, demonstrate high accuracy in real-time bladder cancer diagnosis [6]. Frameworks like DCEAC show promise in accurately grading bladder cancer severity, highlighting their potential as diagnostic tools [36]. Multi-region segmentation techniques refine segmentation accuracy by aggregating multi-scale contextual information, addressing sparsity issues [22]. Self-contrastive weakly supervised learning frameworks exhibit significant predictive power for BCG treatment outcomes and recurrence, achieving notable AUC values [11]. Integrating imaging and molecular data enhances predictive capacity and clinical applicability in bladder cancer management.

Two-stage cancer models estimate reductions in advanced-stage diagnoses based on stage-specific test sensitivities and testing ages, offering insights into early detection strategies' impact on patient outcomes [14]. The diverse predictive modeling techniques underscore their transformative potential in bladder cancer research, particularly for non-muscle-invasive bladder cancer (NMIBC) with high recurrence rates. Advanced machine learning algorithms, such as LSTM and hybrid CNN-transformer

models, refine personalized treatment strategies and improve patient outcomes through enhanced early detection capabilities. These models utilize multimodal data for accurate recurrence predictions and risk stratification, although challenges related to model generalizability and interpretability persist, necessitating collaborative efforts and robust datasets [40, 27, 41, 6, 12].

## 4.2 Advanced Statistical and Machine Learning Models

Advanced statistical and machine learning models play a crucial role in bladder cancer predictive modeling, enhancing accuracy and reliability of recurrence and outcome predictions. By integrating computational models with clinical and molecular data, these approaches deepen our understanding of disease mechanisms and patient heterogeneity, enabling tailored treatment strategies that are clinically effective and economically viable [13, 20].

The AE-GAN (Autoencoder-Generative Adversarial Network) significantly improves predictive accuracy for cancer outcomes, outperforming traditional methods like SMOTE-SVM-RBF and NMF-GA by capturing complex patterns in high-dimensional data [23]. The Generalized Survival Frailty Model (GSFM), a Bayesian framework, allows the baseline hazard function to vary by treatment strata and recurrence types, incorporating parametric and nonparametric frailty effects for survival analysis in bladder cancer [42]. Its ability to account for patient heterogeneity is valuable for tailoring treatment plans based on individual risk profiles.

The LSTM-Cox method combines Long Short-Term Memory (LSTM) networks with the Cox proportional hazards model, enhancing risk assessment for bladder cancer recurrence by capturing temporal dependencies in patient data [40]. This hybrid model improves recurrence prediction precision and informs clinical decision-making. Advanced machine learning models, particularly the LSTM-Cox model, analyze complex, time-dependent clinical data and integrate modalities such as radiomics, histopathology, and genomics, overcoming limitations of traditional survival analysis methods and achieving high prediction accuracy [40, 27, 6]. Their application supports individualized treatment strategies, improving patient management and outcomes.

## 4.3 Model Performance and Validation

Benchmark	Size	Domain	Task Format	Metric
NMP22BC[5]	8,724	Urology	Diagnostic Accuracy Evaluation	Sensitivity, Specificity
UBCMB[7]	9,713,510	Microbiology	Microbial Community Comparison	Simpson Index, Observed OTUs
AMI[34]	450	Bladder Cancer Detection	Image Registration	Mutual Information, Quadratic Distance

Table 1: Table presenting a selection of representative benchmarks used in the evaluation of predictive models for bladder cancer. The benchmarks vary in size, domain, task format, and metrics, providing a comprehensive overview of the datasets utilized for assessing model performance and generalizability.

Evaluating and validating predictive models for bladder cancer, particularly NMIBC, is essential for establishing clinical relevance and reliability. With NMIBC’s high recurrence rate and limitations of current predictive tools, robust machine learning techniques are needed. These models utilize diverse molecular and clinical data to enhance prediction accuracy and address generalizability and interpretability challenges. By refining existing algorithms, researchers improve their applicability in clinical settings, enhancing patient outcomes and reducing healthcare costs [41, 27, 28].

Statistical and machine learning models undergo rigorous evaluation using metrics to assess predictive accuracy and generalizability, often involving cross-validation techniques to prevent overfitting. A proposed model achieves a 14.8

Model validation involves using independent datasets to assess performance in real-world scenarios, ensuring reliability across medical contexts [43, 20, 26]. Advanced models like AE-GAN and GSFM are validated through comparisons with existing methodologies, demonstrating superior performance in risk stratification and outcome prediction. Ongoing evaluation and validation of predictive models are vital for enhancing bladder cancer management, particularly addressing NMIBC’s high recurrence rates. Integrating ML techniques leverages diverse data types to improve prediction accuracy and patient stratification. Advancements in deep learning, such as the hybrid CNN-transformer model,

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offer promising solutions for real-time diagnosis and segmentation, aiming to reduce misdiagnoses and improve outcomes. Collaborative efforts and robust datasets are essential to overcome challenges related to model generalizability and interpretability, paving the way for effective and cost-efficient bladder cancer management strategies [27, 10, 6]. These efforts ensure models remain reliable tools for guiding clinical decision-making, enhancing personalized medicine approaches.

## **5 Integration of Radiomics and Predictive Modeling**

### **5.1 Frameworks for Personalized Medicine**

The integration of radiomics with predictive modeling in personalized medicine frameworks marks a significant advancement in bladder cancer management, enhancing both clinical outcomes and economic viability. A key innovation is the nested multiple instance learning approach, which employs attention mechanisms to focus on pertinent regions in medical images, thereby improving diagnostic accuracy and treatment personalization [11]. This method extracts crucial features necessary for tailoring individualized treatment strategies, effectively addressing bladder cancer’s inherent heterogeneity.

Moreover, semantically and visually interpretable networks like MDNet bridge AI-based diagnostics with clinical practice. MDNet’s ability to generate interpretable diagnostic reports and visualize attention maps builds trust among medical professionals in AI-driven decision-making processes [26]. Such transparency is essential for successfully adopting AI technologies in clinical environments, ensuring that insights from complex models are actionable and reliable.

From an economic perspective, personalized medicine frameworks must address financial implications for healthcare service providers (HSPs). A proposed mathematical framework allows HSPs to select varying levels of treatment personalization, optimizing clinical outcomes alongside economic sustainability [13]. This framework balances personalization with cost-effectiveness, ensuring accessibility and feasibility across diverse healthcare settings.

These advancements underscore the promise of integrating radiomics and predictive modeling into personalized medicine frameworks. By merging advanced analytical methods with practical clinical and economic considerations, these frameworks facilitate more effective individualized strategies for managing bladder cancer. This approach not only addresses patient-specific needs but also highlights the importance of cost-effectiveness in resource-constrained healthcare environments. Innovations in urinary biomarkers and genetic profiling further enhance diagnostic accuracy and treatment personalization, leading to improved patient outcomes and optimized healthcare resource allocation [8, 13, 9, 28].

### **5.2 Integration and Applicability in Clinical Settings**

Integrating radiomics and predictive modeling into clinical settings for bladder cancer management offers a promising avenue for enhancing patient care through personalized treatment strategies. Advanced computational frameworks leverage quantitative features from medical imaging, alongside molecular and clinical data, to inform clinical decision-making. Deep learning models like MMSFENet facilitate precise localization and classification of bladder tumors, thereby augmenting diagnostic accuracy [21].

In clinical practice, advanced image segmentation techniques, including multi-region segmentation frameworks, enable accurate delineation of tumor boundaries, critical for assessing tumor invasiveness and planning surgical interventions [22]. These techniques empower clinicians to make informed treatment decisions, ultimately enhancing patient outcomes.

Moreover, incorporating socio-demographic factors into predictive models allows for customized treatment plans based on individual patient characteristics, addressing variability in treatment responses across populations [2]. This personalized approach is strengthened by frameworks with dynamic resource allocation algorithms, optimizing healthcare resource distribution and ensuring effective interventions based on unique patient profiles [38].

The clinical applicability of these integrated approaches is reinforced by AI-driven diagnostic tools, such as MDNet, which provide interpretable diagnostic reports and facilitate communication of

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complex model outputs to healthcare professionals [26]. This transparency fosters clinician trust and supports the integration of advanced analytical techniques into routine practice.

The integration of radiomics and predictive modeling represents a significant advancement in bladder cancer management, particularly for non-muscle-invasive bladder cancer (NMIBC), characterized by a recurrence rate of 70-80

## 6 Challenges and Limitations

### 6.1 Data Quality and Variability

In bladder cancer management, data quality and variability present significant challenges to the reliability and generalizability of radiomics and predictive models. Clinical datasets often contain heterogeneity, outliers, and missing values, complicating parameter estimation and model accuracy. For instance, electronic health records (EHRs) encompass diverse observations, complicating the estimation of disease-onset ages. The use of shared frailty survival models can lead to biased outcomes due to model misspecification, underscoring the need for flexible approaches that account for unmeasured heterogeneity and accurately fit baseline hazard functions. Non-negative Matrix Factorization (NMF) has improved feature extraction in clinical datasets, particularly in gene expression analyses for bladder cancer [44, 24, 45]. However, biases from RNA-Seq library preparation and high sequencing costs hinder clinical adoption. The noise inherent in weakly labeled data further necessitates validation across diverse datasets to ensure predictive modeling robustness.

MRI image segmentation is complicated by bladder shape variability, intensity inhomogeneity due to urine, weak boundaries, and motion artifacts [12]. These factors contribute to data quality inconsistencies, adversely affecting radiomics model performance. Class imbalance in medical images also leads to biased outputs, highlighting the need for effective mitigation strategies.

Current methodologies often rely on hypothesized sojourn times and constant test sensitivities, which may not reflect real-world scenarios [14]. Estimating parameters for models like the EGL distribution requires advanced computational techniques [46]. Misspecification in parametric models for the probability of cause of failure can compromise accuracy, emphasizing the need for precise model formulation [38]. The computational demands of fitting flexible parametric models may limit their practical applicability [44].

Low statistical power and high computational costs in testing interactions among numerous variables present additional obstacles in predictive modeling [47]. Simplifying real-world scenarios by focusing on a single time point and assuming patient homogeneity may not accurately capture patient diversity, affecting the economic feasibility of personalized medicine strategies [13].

Addressing complexities in EHR data and high-dimensional multi-omics datasets requires sophisticated statistical methods and advanced computational techniques. Innovations such as pairwise pseudolikelihood for age-at-onset estimation, Bregman proximal algorithms for robust NMF, and neural networks like autoencoders and Generative Adversarial Networks can enhance model performance in clinical and genomic contexts [23, 45, 41, 20, 24]. By improving data quality and managing variability, researchers can enhance model accuracy and generalizability, ultimately benefiting patient outcomes and personalized treatment strategies.

### 6.2 Model Interpretability and Generalizability

Model interpretability and generalizability are critical challenges in applying predictive modeling to bladder cancer, affecting clinical utility and acceptance. Convolutional neural networks (CNNs) face scrutiny for their opaque decision-making processes, which can diminish clinician trust and understanding of model predictions [20]. This necessitates developing models that offer clear, interpretable outputs for seamless clinical integration.

Generalizability is hindered when models are trained on limited datasets, risking overfitting and restricting applicability to broader patient populations [26]. Standard architectures may not be optimized for bladder cancer segmentation, underscoring the need for tailored solutions capable of consistent performance across diverse clinical environments [12].

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Model misspecification complicates selecting appropriate models for complex hazard functions, a core obstacle in developing effective solutions [44]. This challenge is amplified in high-dimensional data settings, where model assumptions may not hold, potentially compromising prediction robustness [47]. Effective evaluation of treatment effects must account for unmeasured confounders, as these can significantly influence model outputs and interpretability [15].

The dependency on specific parameters, such as those in the BPPR-NMF method, underscores challenges in model interpretability, as parameter selection can greatly impact performance [45]. Assumptions of independence among recurrences per subject may not capture data complexities, limiting applicability in certain contexts [42]. Similarly, assumptions of mutually exclusive groupings may fail to represent the intricacies of biological pathways, where genes may belong to multiple groups [25].

Addressing these challenges requires collaborative efforts to develop predictive models that ensure high accuracy while enhancing transparency and adaptability across clinical environments. Leveraging sophisticated methodologies, such as the pairwise pseudolikelihood approach for utilizing retrospective prevalent data from EHRs, along with advanced data science techniques to evaluate personalized medicine's economic feasibility, is essential. Incorporating multimodal neural networks like TandemNet can improve interpretability by integrating diagnostic reports with medical imaging. Additionally, microsimulation models analyzing therapy sequences using patient-level longitudinal EHR data can provide insights into the cost-effectiveness of treatment options, guiding healthcare providers in making informed, resource-optimized decisions tailored to individual patient needs [13, 20, 24, 39]. Enhancing model interpretability and generalizability will ultimately improve clinical utility and advance personalized treatment strategies for bladder cancer management.

### 6.3 Computational Complexity and Scalability

Radiomics and predictive modeling in bladder cancer management face significant computational challenges and scalability issues, hindering broader clinical application. The computational intensity of advanced modeling techniques, such as bootstrap resampling and multi-state models, is a primary limitation, requiring substantial resources for robust predictions [39]. This intensity constrains scalability, especially with large datasets prevalent in healthcare's big data era.

Processing high-dimensional data, such as multi-parametric MRI and genomic sequencing, exacerbates computational demands. Managing and interpreting large-scale datasets from multi-omics sequencing and EHRs necessitates advanced algorithms and high-performance computing infrastructure, essential for dimensionality reduction, feature extraction, and multimodal data integration critical for accurate predictions in complex medical scenarios [23, 24, 20, 6, 26]. The need for real-time analysis and decision-making in clinical settings adds complexity, necessitating efficient computational frameworks for timely, accurate results.

Scalability is further challenged by data quality variability and extensive preprocessing requirements to ensure consistency across imaging modalities and patient cohorts. The preprocessing phase incurs significant computational costs, especially when integrating heterogeneous data sources requiring harmonization for effective analysis. This challenge is intensified by managing diverse data types, such as EHRs containing retrospective information, necessitating advanced statistical methods for accurate modeling and interpretation [20, 25, 24, 23].

Developing scalable predictive models in healthcare necessitates balancing model complexity, which enhances predictive power, with interpretability and generalizability, crucial for clinical applicability and trust in model outputs. This complexity arises from the diverse nature of EHR data, often including retrospective prevalent information and high-dimensional multi-omics data, requiring advanced methodologies to effectively integrate and distill this information while remaining interpretable for healthcare professionals [20, 24, 23, 26]. As models become more complex to accommodate bladder cancer biology intricacies, they demand greater computational power and sophisticated optimization techniques, potentially limiting applicability in resource-constrained environments.

To address challenges in analyzing complex health data, current research focuses on enhancing algorithmic efficiency and creating scalable frameworks leveraging cloud computing and distributed processing technologies. This includes developing methods to extract retrospective prevalent information from EHRs, significantly improving disease-onset age distribution estimation. Innovative approaches are also being explored to optimize SMS reminder campaigns for cancer check-ups by

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integrating socio-demographic factors, potentially reducing mortality rates and improving patient outcomes [48, 24]. By enhancing computational efficiency and scalability in radiomics and predictive modeling, researchers aim to improve accessibility and applicability in diverse clinical settings, ultimately advancing personalized medicine strategies for bladder cancer management.

## 7 Future Directions

### 7.1 Advancements in Molecular Characterization and Treatment Strategies

Future progress in bladder cancer management is poised to revolutionize molecular characterization and treatment strategies through research and technological innovations. Key areas of focus include validating biomarkers like CDK1 and NDC80 in larger cohorts to better understand their roles in cancer progression and potential as therapeutic targets [4]. Understanding the biological mechanisms underlying bladder cancer is crucial for developing personalized treatments tailored to individual genetic and molecular profiles [9].

Integration of RNA-Seq technology provides comprehensive insights into gene expression changes, aiding early detection and personalized treatment strategies [29]. Future research aims to incorporate additional data types, such as copy number alterations, to enhance detection of misregulated genes and explore deregulations across cancer subtypes [32].

Incorporating radiomics features into clinical practice is expected to improve bladder cancer assessment, with a focus on expanding datasets and integrating 3D segmentation techniques for accurate tumor characterization [22]. Specialized architectures and multi-modal imaging data will further enhance model generalizability across diverse clinical settings [12].

Exploring self-contrastive weakly supervised learning models will refine feature discernment in complex datasets, incorporating clinical parameters to enhance prediction interpretability [11]. Advancements in graph-structured tests for differential expression will focus on refining graph construction and improving multiple testing correction methods [33].

Efforts will also prioritize building larger pathology image-report datasets, enhancing attention mechanisms for finer biomarker localization, and applying models like MDNet to whole slide diagnosis [26]. Methods like identifying control hubs in varying biological contexts may yield new insights into bladder cancer dynamics [30].

Key research areas include driver mutation identification through next-generation sequencing, advancing non-invasive diagnostics like liquid biopsies, and exploring immune checkpoint inhibitors. These innovations promise improved patient outcomes through personalized therapeutic options and better monitoring capabilities, addressing distinct molecular drivers in bladder cancer [29, 8].

### 7.2 Refinement of Predictive Modeling Techniques

Refining predictive modeling techniques for bladder cancer is crucial for enhancing accuracy and clinical applicability. Future research should integrate Long Short-Term Memory (LSTM) models with deep learning to improve predictions of cancer recurrence and treatment outcomes [40]. Refinement of PC priors, particularly in complex models like trivariate analyses, is necessary to enhance diagnostic accuracy [43].

In image registration, future efforts should combine the strengths of algorithms tested in benchmarking studies to enhance robustness while maintaining computational efficiency, vital for accurate tumor localization [34]. Enhancing dataset diversity and volume, alongside optimizing model architecture, will be essential for improving AI-driven cystoscopy applications [6].

Integrating multimodal data and developing advanced attention mechanisms could significantly enhance model interpretability, facilitating integration into clinical workflows [20]. Refinements in the NMGrad model architecture and creation of fully annotated datasets are anticipated to advance predictive modeling techniques, enhancing consistency and accuracy in bladder cancer grading [10].

Future research should focus on developing combination assays leveraging multiple biomarkers to improve diagnostic accuracy and predictive capabilities [28]. Addressing the complex heterogeneity observed in bladder cancer will involve improving classification accuracy in cases with multiple growth patterns within a single image [36].

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Exploring nonparametric or semiparametric models for failure-cause probabilities and applying these methods to time-dependent covariates will be essential for capturing the dynamic nature of bladder cancer progression [38]. Applying Bayesian estimation to complex models or different censoring schemes, while optimizing hyper-parameter selection, should be prioritized [49]. Developing more efficient algorithms for fitting complex models and exploring additional frailty distributions is also crucial [44].

These research directions highlight ongoing efforts to enhance predictive modeling techniques for bladder cancer management, focusing on accuracy, reliability, and clinical utility. By leveraging methodologies such as machine learning and deep learning, researchers are developing robust frameworks utilizing diverse data sources—including molecular, clinical, and imaging data—to better predict non-muscle-invasive bladder cancer (NMIBC) recurrence. This multidisciplinary approach aims to address existing limitations in current predictive tools, often overestimating risks, and facilitate the adoption of more effective diagnostic and therapeutic strategies, ultimately reducing healthcare costs and improving patient outcomes through precise and actionable insights [8, 41, 27, 6].

### 7.3 Enhancements in Machine Learning and AI Applications

Recent advancements in machine learning and AI applications have significantly improved bladder cancer management, enhancing diagnostic and therapeutic strategies. The integration of advanced AI models, such as convolutional neural networks (CNNs) and transformers, has refined tumor detection and segmentation in medical imaging, facilitating more accurate assessments of bladder cancer [6]. These models leverage deep learning techniques to capture intricate spatial features and dependencies, thereby enhancing the accuracy of bladder cancer diagnosis and treatment planning [36].

The development of hybrid AI models, combining CNNs with attention mechanisms, has further refined the classification of histological images into severity levels, enhancing diagnostic granularity and supporting tailored therapeutic interventions [26]. These advancements in AI-driven diagnostics are complemented by attention-based frameworks that provide interpretable outputs, crucial for clinical decision-making and fostering trust among healthcare professionals [20].

Moreover, machine learning's application in predictive modeling has been bolstered by the use of autoencoder-generative adversarial networks (AE-GAN), which enhance predictive accuracy by effectively capturing complex patterns within high-dimensional data [23]. This approach not only improves risk stratification but also supports the development of personalized treatment strategies, addressing the heterogeneity inherent in bladder cancer.

The integration of machine learning with socio-demographic data enables dynamic healthcare resource allocation, optimizing treatment plans based on individual patient profiles and improving overall efficiency in bladder cancer management [38]. Furthermore, advancements in image registration and segmentation techniques, such as multi-region segmentation frameworks, have enhanced tumor delineation accuracy, critical for assessing tumor invasiveness and planning surgical interventions [22].

These advancements in machine learning and AI applications are revolutionizing bladder cancer management by improving diagnostic accuracy, enhancing recurrence prediction, and enabling precise tumor segmentation. Addressing critical challenges, such as high misdiagnosis rates during cystoscopy and overestimation of recurrence risk in non-muscle-invasive bladder cancer (NMIBC), these technologies facilitate personalized treatment strategies based on accurate tumor staging. Innovative deep learning models integrating CNNs with transformers have shown promise in real-time bladder cancer detection and segmentation, while multimodal data-enhanced machine learning frameworks are boosting predictive capabilities for NMIBC recurrence. Collectively, these developments underscore the transformative potential of AI and machine learning to improve patient outcomes and reduce healthcare costs associated with bladder cancer treatment [12, 27, 6]. By enhancing diagnostic accuracy, refining predictive models, and facilitating personalized treatment strategies, these advancements promise significant improvements in patient outcomes and the advancement of oncology.

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## 8 Conclusion

The integration of radiomics and predictive modeling represents a pivotal development in bladder cancer management, significantly enhancing diagnostic precision and therapeutic strategies. By extracting quantitative features from medical images, radiomics provides a detailed characterization of tumor heterogeneity, which is crucial for accurate diagnosis and effective treatment planning. Predictive modeling, through the application of statistical and machine learning techniques, enables the anticipation of disease recurrence and the assessment of treatment efficacy, thus supporting personalized treatment regimens.

The confluence of radiomics with molecular data integration substantially improves the accuracy of predictive models, facilitating patient stratification based on tumor aggressiveness and therapeutic response. Advanced deep learning methods, particularly convolutional neural networks, have refined segmentation accuracy by capturing intricate spatial features, thereby improving the precision of tumor detection and classification.

AI-driven frameworks, such as MDNet, deliver interpretable diagnostic reports, effectively bridging the gap between AI diagnostics and clinical practice. These advancements underscore the transformative potential of sophisticated analytical techniques in enhancing clinical workflows in bladder cancer management.

Despite existing challenges concerning data quality, model interpretability, and computational demands, ongoing research endeavors aim to refine these methodologies, thereby enhancing their accuracy, reliability, and clinical applicability. By leveraging the capabilities of radiomics and predictive modeling, healthcare professionals can provide more effective and personalized care, ultimately improving patient outcomes and advancing the field of oncology.



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