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REVIEW

Recent Advances and Emerging Innovations in Transurethral Resection of Bladder Tumor (TURBT) for Non-Muscle Invasive Bladder Cancer: A Comprehensive Review of Current Literature

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Abstract: Bladder cancer management, particularly non-muscle-invasive bladder cancer (NMIBC), has evolved significantly due to advancements in imaging techniques and surgical methodologies. Enhanced tumor visualization methods, including Photodynamic Diagnosis (PDD) and Narrow-Band Imaging (NBI), offer improved detection rates for both papillary tumors and carcinoma in situ (CIS), compared to traditional white-light cystoscopy (WLC). Recent studies suggest that these technologies enhance diagnostic accuracy, reduce recurrence rates, and improve oncological outcomes. Additionally, transurethral resection of bladder tumors (TURBT), performed with advanced imaging, has demonstrated better resection quality, particularly in terms of detrusor muscle presence. Despite these innovations, challenges remain in the long-term impact on recurrence-free and progression-free survival. Artificial intelligence (AI) integration into cystoscopic imaging further promises enhanced diagnostic precision and cost-effective bladder cancer management. As personalized treatment paradigms emerge, predictive biomarkers, including genomic and pathological markers, may help stratify patients for aggressive treatment, sparing those at lower risk from unnecessary interventions. Future research should focus on validating these AI models and combining them with enhanced imaging modalities to refine treatment protocols further. These advancements collectively represent a significant leap toward precision medicine in bladder cancer care.

Keywords: bladder neoplasms, transurethral resection, photodynamic therapy, narrow-band imaging, artificial intelligence, recurrence-free survival, biomarkers, tumor, precision medicine

Introduction

Bladder cancer (BC) is one of the most common cancers globally, with an annual incidence of 570,000 new cases globally in 2020, and 212,000 deaths.[1] The majority (~76%) of patients are men.[2] This disparity between incidence and prevalence, coupled with high recurrence rates requiring prolonged surveillance, significantly impacts quality of life (QOL)[3–5] and places a substantial burden on healthcare systems in terms of resources and costs. Some researchers have even suggested that bladder cancer is the most expensive cancer to treat.[6,7]

TURBT is central to the diagnosis and management of bladder cancer, particularly in NMIBC, which accounts for approximately 75–80% of cases.[8,9] TURBT involves endoscopic examination, tumor sampling, and resection of visible tumors under white light.[10,11] Despite the relatively favorable prognosis for NMIBC, with cancer-specific survival rates of 66% at 15 years[12] and 88% at 8.7 years,[13] high recurrence and progression rates post-TURBT pose significant challenges. These rates vary widely based on clinical and pathological parameters, leading to recommendations for a second TURBT within 2–6 weeks in high-risk cases.[10,11,14] The method and quality of TURBT,[15] as well as the use of

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adjunctive treatments, significantly impact patient outcomes. However, there remains a need for a deeper understanding of optimal TURBT practices, predictive factors, and the benefits of new technologies in improving long-term outcomes and reducing recurrence.

All these factors, along with accumulating evidence regarding the initial diagnostic process, will be discussed in this review, with the aim of providing a comprehensive and up-to-date overview of the various aspects of TURBT surgery, as well as the therapeutic and prognostic value of innovations in this field. The recommendations of major urological associations for each topic reviewed are also summarized.

Methods: Systematic Review Process

A systematic literature review was conducted on PubMed between January 2018 and September 2024, using specific terms related to key components that were deemed relevant to a comprehensive review of different aspects of TURBT in NMIBC patients. The focus was on ways to improve its outcomes, based on a preliminary search for reviews, and the EAU and AUA guidelines. The search yielded a total of 1702 results since January 2018. After removing duplicates, 992 unique results were obtained, of which 493 abstracts were reviewed. A total of 121 full-text articles were thoroughly analyzed, including the relevant references. To provide a comprehensive assessment and augment our findings, we meticulously scrutinized the references cited within the articles and incorporated any additional relevant sources that we deemed necessary, as depicted in Figure 1. The detailed search strategy and process is described in the Supplementary material.

Unfortunately, due to space limitations, we could not include topics such as immediate instillation of chemotherapy, the role of TURBT in MIBC, or alternatives to TURBT (eg, active surveillance or radical cystectomy). Similarly, chapters on repeat TURBT, risk stratification, recurrence mechanisms, and TURBT complications were excluded. We also reviewed the current American Urological Association (AUA) and European Association of Urology (EAU) guidelines and commented accordingly on each topic, where available.

Aim of the Study

The primary aim of this review is to provide a comprehensive analysis of current literature pertaining to TURBT, including unique aspects such as patient selection, diagnostic approach, and surgical techniques. The review also focuses on methods to improve TURBT outcomes, particularly oncological results like recurrence, progression, and overall survival (OS). Finally, the study touches upon future directions for TURBT and identifies open questions for further investigation.

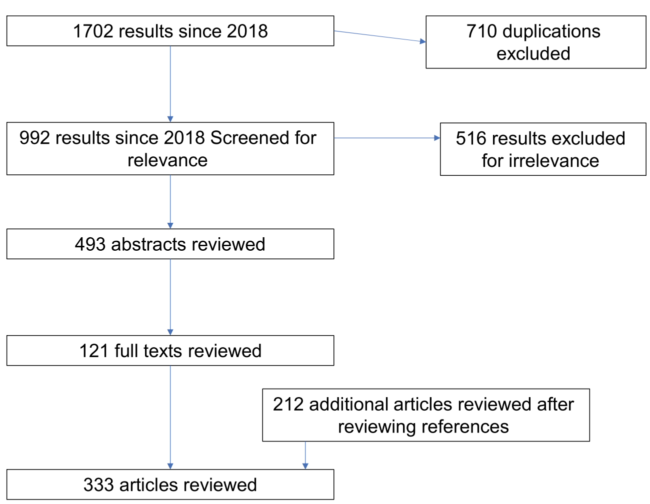

Figure 1 Flow diagram of the evidence acquisition in this systematic review on TURBT aspects.

Diagnostic and Pre-Procedural Approach to TURBT

Laboratory and Imaging Assessment

Before performing TURBT, several diagnostic tests are recommended, as they can influence the surgeon's approach. Urine cytology, which has a high sensitivity for high-grade (HG) tumors (60–84%)[16,17] and is highly specific (>95%),[18] should be included. However, urine cytology has low sensitivity for low-grade (LG) tumors (16–26%),[16,17] potentially necessitating random bladder biopsies to identify non-trivial flat reddish lesions. Novel molecular tumor markers cannot replace cystoscopy or urine cytology but may serve as adjunctive tools to detect tumors missed during cystoscopy and aid in surveillance.[11] Simultaneous upper urinary tract lesions occur in less than 2% of cases[19–21] but are more common when the tumor is located at the trigone (7.5%)[21] or in cases of multiple high-risk CIS tumors.[22]

Both the AUA and EAU guidelines recommend upper urinary tract imaging as part of the initial evaluation. The AUA suggests using computed tomography urography (CTU) or magnetic resonance urography (MRU) due to their ability to detect lymph nodes and filling defects, while the EAU recommends abdominal ultrasound or CTU as basic tests, with CTU/MRU recommended when bladder cancer is detected and the risk of simultaneous upper urinary tract carcinoma (UUTC) is high. Imaging should likely be risk-stratified and conducted within six months of initial diagnosis.[10] Positive imaging should direct the surgeon to inspect upper tract lesions during TURBT using ureteroscopes.

A newer modality, multiparametric magnetic resonance imaging (mpMRI), along with the VI-RADS system, is used to differentiate NMIBC from muscle-invasive bladder cancer (MIBC) prior to TURBT and can guide other decisions.[23] Over the past six years, five systematic reviews and meta-analyses involving thousands of patients have been published.[24–28] These studies reported sensitivities of 78–91%, specificities of 84–92%, and an area under the curve (AUC) of 0.93,[27,28] with good inter-observer agreement.[26] Integration of mpMRI into the diagnostic process has been shown to significantly reduce the time to appropriate treatment.[29] Despite these promising results, it is still too early to rely solely on mpMRI for accurate staging diagnosis. It is not a substitute for TURBT and is not yet recommended by major urological associations.[10,11]

Physical and Bimanual Examination in Preoperative Assessment of Bladder Cancer

Physical examination should include an assessment of body habitus, abdomen, and genitalia, as tumors located in the anterior or posterior bladder wall may be challenging to resect in obese patients. In men, the examination should include a digital rectal exam to assess the prostate, which may reveal tumor involvement. Bladder wall thickening may suggest MIBC, while a palpable or mobile mass could indicate cT3 disease, and a fixed mass may suggest cT4 disease. Although physical examinations rarely yield significant findings in NMIBC patients,[10] they remain a critical part of preoperative evaluation.[30] The EAU guidelines state, "A focused urological examination is mandatory, although it does not reveal NMIBC".

Bimanual examination under anesthesia (BEUA) is used before and after TURBT to establish clinical staging. A palpable mass post-resection suggests locally advanced disease and is associated with significant prognostic value. For instance, a palpable mass after TURBT predicted five- and ten-year survival rates of 83% versus 50%, and 70% versus 45%, respectively.[31] Ploeg et al found that BEUA accurately predicted the stage in 57.6% of patients, but resulted in understaging in 31% and overstaging in 11.3%.[32] Additionally, BEUA use has declined over time, with notable differences between teaching and non-teaching hospitals. Rozanski et al[33] found BEUA alone was correct in only 35% of cases (similar to findings by Mehrsai[34]), but combining BEUA with cross-sectional imaging improved staging accuracy for T3 disease or higher. The EAU guidelines recommend BEUA,[11] though the AUA guidelines consider it optional.[10]

Pre-TURBT Cystoscopy

Flexible cystoscopy is recommended on an outpatient basis prior to TURBT to identify and characterize suspicious lesions. Experienced practitioners can use tumor appearance to estimate stage and grade,[35–37] and this evaluation can help determine whether outpatient fulguration of low-grade tumors is appropriate.[38] However, cystoscopy is not always necessary prior to TURBT, especially when imaging results are definitive.

Anesthesia Considerations

Anesthesia strategy should be carefully discussed with the anesthesiologist, considering patient comorbidities and tumor characteristics. General anesthesia with paralysis is often preferred to ensure patient immobility, optimize bladder relaxation, and minimize bladder motion during breathing.[39] However, spinal anesthesia has been suggested to offer advantages over general anesthesia, with a hazard ratio for recurrence of approximately 0.6.[40] Adding an obturator nerve block (ONB) to spinal anesthesia can improve detrusor muscle (DM) sampling and prolong recurrence-free survival (RFS) while potentially reducing complications.[41–43] Muscle relaxation is particularly crucial for lesions near the ureteral orifices, as the obturator jerk reflex may increase the risk of bladder perforation.

Surgical Considerations

TURBT Quality and Its Influence on Outcomes

The primary goal of TURBT is to diagnose, stage, and treat bladder cancer by obtaining tissue for histopathological evaluation and removing visible tumors. TURBT serves as both a diagnostic and therapeutic procedure, guiding decisions for additional treatments, such as intravesical therapy or cystectomy.

Several indicators of high-quality TURBT have been proposed, some of which have been incorporated into broader national and population health programs.[39,44–48] One critical indicator is the presence of DM in the resected specimen. Numerous studies have demonstrated that the absence of DM is a significant predictor of poor oncological outcomes, including a higher likelihood of residual disease post-TURBT,[45,49–53] reduced RFS,[54–56] and increased recurrence rates, especially for T1 disease.[57] Studies have further shown a strong correlation—up to 3.58 times higher risk—between the absence of DM and progression to T2 disease.[54,56,58]

The EAU guidelines consider the presence of DM in the resected specimen a surrogate marker of resection quality and mandate its presence in all TURBT procedures, except for low-risk Ta LG tumors. When DM is absent, a second TURBT is typically recommended.[11] However, the AUA guidelines only state that a lack of DM increases the risk of understaging.[10]

Implications of Incomplete Resection and Positive Margins on TURBT Outcomes

Incomplete resection during TURBT is difficult to estimate due to the use of small tissue fragments. While some studies have found no significant correlation between complete macroscopic resection and RFS,[46,59] others have demonstrated that positive pathological margins are associated with higher rates of residual disease and recurrence. For instance, Jancke et al found that TURBT procedures with positive findings on additional marginal resection had significantly higher overall recurrence rates (83% vs 57%) and local recurrence rates (58% vs 19%), with a p-value of less than 0.001.[60] Similar findings have been reported for vertical[61] and lateral margins.[62] Both the EAU and AUA guidelines recognize complete resection as a key quality indicator for effective TURBT. Positive margins are considered a strong indication for repeat TURBT, except in cases where immediate cystectomy is planned.[10,11,15]

Impact of Surgeon Experience on TURBT Outcomes

Surgeon experience plays a critical role in determining TURBT outcomes. Brausi et al identified significant variability in residual disease rates across different institutions, underscoring the importance of surgeon skill and thoroughness.[15] TURBT is unique in that much of the procedure is performed by a single individual, meaning the surgeon's expertise greatly influences complex decisions, from determining whether TURBT would be overtreatment for an indolent tumor to assessing whether the patient would benefit from early cystectomy.[63]

Less experienced surgeons have been shown to obtain less DM in resected specimens, especially in high-risk cases or those involving tumors in challenging locations. This correlates with worse oncological outcomes, including higher rates of residual disease at the first follow-up cystoscopy, increased recurrence, and more postoperative complications.[50–52,64–69] Additionally, higher survival rates have been associated with surgeries performed by high-volume surgeons for T1 disease.[63] Studies assessing the learning curve of TURBT suggest that clinical outcomes improve markedly after approximately 101 operations, with optimal results seen after 170 procedures. The poorest results were observed in the first 45 cases, despite increasing case complexity during that period.[68]

While some studies have not demonstrated a significant association between surgeon experience and outcomes,[70–73] this could be due to factors such as the training environment, supervision, and teaching techniques.[74] Some alternative surgical techniques may also influence the findings.[75] Specific scoring systems have been developed to assess resident competency in TURBT.[76,77] Despite the potential benefits of centralizing TURBT to experienced surgeons, practical considerations mean that standard TURBT procedures cannot be restricted to a select few. Therefore, improving outcomes across a broad range of surgeons remains essential.[78]

The EAU guidelines endorse surgical training programs to improve outcomes, though they provide no concrete recommendations, while the AUA guidelines do not address this issue.[11]

The Impact of Surgical Checklists on TURBT Outcomes: Documentation, Implementation, and Clinical Implications

Surgical checklists play a crucial role in documenting patient outcomes and ensuring accurate, consistent management. They allow surgeons to record key factors, such as tumor invasion, incomplete resection, absence of DM, tumor grade, and administration of immediate chemotherapy, all of which influence surveillance decisions and additional interventions (chemotherapy, radiotherapy, or surgery). The use of bladder diagrams has been introduced as a quality performance indicator in national programs, such as Scotland's,[45] and is strongly recommended by the EAU guidelines.[11]

The introduction of surgical checklists has shown significant benefits. Haynes et al reported a 30-day mortality reduction and fewer complications after checklist implementation among 7,688 patients.[79] Other studies have shown similar positive outcomes.[80] A large study in Scotland's National Quality Improvement Program demonstrated strong responses to these initiatives, although it lacked a control group.[45] In the context of TURBT, controlled studies examining the impact of surgical checklists have shown improvements in documentation,[81–84] but the evidence regarding their impact on DM presence, recurrence rates, or RFS remains conflicting.[82,84–87] Nonetheless, the EAU guidelines strongly recommend using surgical checklists and documenting critical details of the patient, tumor, and operation, including a bladder diagram.[11]

Challenges and Considerations in TURBT Procedures

Limitations in Equipment Accessibility

TURBT is not always performed smoothly due to the availability of endoscopic equipment for bladder tumor resection. Several anatomical challenges, such as a large prostate or high bladder neck, can limit instrument access and maneuverability. For instance, a high bladder neck can make it difficult for the surgeon to reach certain areas, necessitating the use of specialized instruments or partial prostate resection to improve visibility. Additionally, urethral strictures may require urethral dilators or endoscopic incision tools such as Otis dilators.

Tumor Location and Surgical Considerations

Tumor location significantly affects treatment outcomes. Tumors situated in the bladder dome or anterior wall are associated with worse overall survival and RFS.[88] For bladder dome tumors, partial cystectomy may offer improved survival rates. Tumors located in the bladder neck, particularly on the dorsal aspect, have also been linked to poorer RFS and PFS.[89–92]

Special precautions are required when resecting tumors from the lateral bladder wall to avoid the obturator nerve reflex (ONR), which increases the risk of bladder perforation. Minimizing bladder distension, reducing energy levels, and using blunt dissection with the resection loop are strategies to avoid ONR.[74,93] Neuromuscular blockade, en bloc resection of bladder tumors (ERBT), and laser use have also been shown to reduce ONR incidence.

Special Considerations in Tumor Resection

Tumors in the anterior bladder wall present particular challenges and may require assistance, such as suprapubic pressure, to improve resectoscope access. Open-angled resection loops are recommended for more efficient resection. When

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operating near the ureteral orifices, coagulation should be avoided to prevent scarring and subsequent ureteric obstruction. For tumors affecting the ureteral orifices, resection should be performed using cutting settings to preserve renal function. Temporary ureteral stent placement can help reduce the risk of stricture formation. Postoperative imaging, such as renal ultrasound or CTU, is recommended to evaluate renal function.[74]

Tumors in Bladder Diverticula

Bladder diverticula, defined as outpouchings of the bladder wall, frequently lack a complete muscular layer, which poses significant challenges for surgical intervention. In cases of tumors located within these diverticula, particularly HG or T1 tumors, achieving complete resection is markedly difficult. The absence of a DM layer heightens the risk of bladder perforation, making the attainment of deep surgical margins nearly unattainable. Furthermore, the narrow neck of the diverticula may impose additional limitations on surgical access, thereby complicating the procedure even further. This anatomical constraint not only impairs visibility but also restricts the maneuverability of surgical instruments, ultimately increasing the risk of incomplete tumor resection or subsequent recurrence. Given these challenges, partial or radical cystectomy, or diverticulectomy, is frequently recommended in such cases.[10]

The Role of Random Biopsies in Staging and Diagnosis

Random biopsies are typically performed to detect concomitant CIS and to improve staging accuracy, especially in patients with positive cytology but no visible tumor on cystoscopy.[11] Random biopsies are more commonly performed in intermediate- and high-risk patients, as well as in cases with positive cytology.[94–98] However, random biopsies carry risks such as tumor reimplantation,[99] bleeding, and infection. Consequently, they should be reserved for specific cases where they are clearly indicated.

The current EAU guidelines recommend biopsies of suspicious areas, as well as random biopsies and urethral biopsies, in cases of positive cytology with normal-appearing cystoscopy.[11] The AUA guidelines recommend random biopsies for intermediate- to high-risk patients with persistent or recurrent disease or those who have undergone intravesical therapy.[10] A prostatic urethra biopsy is also recommended in cases of bladder neck tumors or visible prostatic urethral abnormalities.[11]

En Bloc Resection of Bladder Tumor (ERBT) Technique

ERBT is a relatively new but well-established technique, supported by comprehensive protocols.[100] It can be performed using a variety of instruments. The procedure begins with creating a circumferential incision approximately 5 mm from the tumor edge, deep to the muscularis mucosa layer, followed by the separation of the tumor from the surrounding tissue toward the center.[101] The primary goal of ERBT is to avoid tumor fragmentation by removing the tumor in one piece, ensuring clear margins and minimizing the risk of leaving residual disease. This approach adheres strictly to oncological principles, preventing the spread of floating cancer cells and enabling more accurate and reliable pathological staging,[61,102] reducing the risk of understaging[103,104] and improving predictions of disease progression.[61,105] Moreover, it helps ensure that DM is present in the specimen, which is crucial for improving oncological outcomes.

A review of the literature, including nine randomized controlled trials (RCTs) and several systematic reviews, demonstrates that ERBT is significantly safer, with fewer complications such as perforation and ONR.[69,101,106–111] Residual disease at the first follow-up cystoscopy or re-TURBT is also less frequent with ERBT.[106–109,112] While older studies showed similar recurrence rates between ERBT and traditional TURBT, more recent studies indicate better outcomes with ERBT, including a higher presence of DM in specimens and shorter hospitalization times.[106,107,110,111] However, the impact of ERBT on recurrence rates remains conflicting.[101,106–112]

While the extraction of large tumors through the urethra presents significant challenges,[113] a comprehensive collaborative statement has deemed en bloc resection feasible for tumors exceeding 3 cm in diameter.[101] Approaches to address this issue include utilizing specialized retrieval bags to extract the tumor's water component[114] or employing laparoscopic forceps to remove the detached specimen.[115] Alternative strategies involve morcellation of the exophytic portion of the tumor prior to ERBT of the tumor base, enabling more precise pathological examination of tumor base margins, or segmenting the whole specimen of broad-based tumors into two or three parts.[101] Due to these challenges,

Table 1 Summary of Evidence on ERBT Outcomes Compared to Conventional TURBT

Outcomes ERBT Seems to Have no Effect	Outcomes with Uncertainty Regard ERBT Effect	Outcomes ERBT Seems to Improve	Outcomes that ERBT has yet to be Studied
Operative time[107,109–111,129]	Recurrence-free survival (RFS) in 3, 6 and 12 months[101,106–112]	Obturator nerve reflex (ONR)[69,107,109–111,129]	Progression-free survival (PFS)
Risk of urethral stricture[130,131]	Catheterization time[107,109–111,129]	Bladder perforation[69,106–112,129]	Overall survival
	Irrigation time[109–111,129]	Higher rates of detrusor muscle in specimen[107,112,129]	
		Less frequent residual disease in first follow up[69,106–109,112]	
		Hospitalization time[107,109–111,129]	

Notes: However, the use of laser-assisted techniques in conjunction with ERBT has been shown to improve recurrence-free survival (RFS) and reduce hospitalization duration, without significantly impact on operative time or the risk of urethral stricture formation.

most larger studies have focused on tumors with diameters of less than 3 cm, potentially introducing bias in favor of ERBT, but few studies have demonstrated improved safety and efficacy of ERBT compared to conventional TURBT, even for tumors larger than 3 cm.[116,117]

Bipolar energy is the most commonly used energy source for ERBT.[118] Some studies report no significant difference between energy sources,[119] while others suggest that lasers, particularly thulium-based lasers, may offer superior safety and efficacy.[108,120–125] However, further discussion of these considerations is beyond the scope of this review.[93]

ERBT is estimated to be performed daily by about two-thirds of surgeons, with approximately half of them using the technique whenever feasible.[118,126] However, its use varies and is difficult to quantify.[127] The learning curve for ERBT is estimated to be around 13–20 procedures, depending on the surgeon's experience.[100,128] While the current AUA guidelines do not address ERBT,[10] the EAU guidelines mention ERBT as an option that increases the likelihood of obtaining DM in specimens, though it is not yet fully recommended.[11] Based on existing evidence, ERBT appears to be a safer and potentially more effective surgical approach when feasible, see Table 1.

Energy Source and Enhanced Cystoscopy

Comparison of Monopolar and Bipolar Electrocautery in TURBT

TURBT is typically performed using either monopolar or bipolar electrocautery. Monopolar electrocautery uses high voltage for tissue cutting, requiring current to flow from the resection electrode through the patient's body to a skin electrode, along with hypotonic fluid for irrigation. Bipolar TURBT confines energy between electrodes at the resectoscope site, allowing the use of a physiological irrigation medium and lower energy sources, which may reduce the risk of complications such as TUR syndrome.

While some studies favor bipolar TURBT for its reduced complications, the differences in outcomes like perforation rates, hospitalization time, catheterization time, and hemoglobin drop often lack statistical significance.[132–142] Although bipolar energy may result in better DM sampling[140,142] and less thermal damage to surrounding tissue,[136–138] there is no clear advantage in oncological outcomes such as recurrence rates. However, bipolar TURBT may yield better results for tumors larger than 3 cm.[143] The EAU summarizes the current evidence as controversial and inconclusive. The AUA states that bipolar electrocautery "may serve to enhance complete resection and reduce complications".

Advantages of LASER in TURBT Procedures

Laser technology has become highly regarded in urology due to its precision and versatility in treating various conditions. Lasers provide highly targeted energy, allowing for the precise cutting or ablation of tumor tissue while minimizing damage to surrounding healthy areas. This precision is especially advantageous in delicate surgeries like TURBT, where preserving

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healthy bladder tissue is critical. In addition, lasers offer superior hemostatic properties, reducing intraoperative bleeding,[144,145] which enhances surgical visibility and lowers the risk of complications. The minimally invasive nature of laser procedures also contributes to faster recovery times, shorter hospital stays,[130,131,146–150] and less postoperative pain,[145] making laser an appealing tool in modern urological practices.

However, laser technology has its drawbacks. One of the main limitations is cost—laser equipment is more expensive to acquire and maintain than traditional TURBT equipment. Laser procedures may also have a steeper learning curve for surgeons accustomed to traditional methods, requiring specialized training to ensure optimal outcomes. While it might be expected that laser use would increase operating time, most studies have not found a significant increase in procedure duration.[129–131,146,147,150]

Multiple studies and meta-analyses have demonstrated that laser TURBT, whether used with ERBT or conventional TURBT techniques, results in similar outcomes but with significantly lower rates of ONR and bladder perforation. Laser TURBT is also associated with reduced hospitalization, catheterization, and irrigation times compared to conventional TURBT.[130,131,146–150] However, evidence on laser technology's effect on recurrence rates remains inconclusive. The EAU guidelines mention laser use as a feasible alternative to electrocautery, while the AUA does not reference it. Current evidence suggests that laser technology is a safer and efficient tool, likely to be preferred when available.

Photodynamic Diagnosis (PDD) in TURBT

PDD enhances the detection of bladder tumors, particularly CIS, which are not easily identified through standard cystoscopy.[74,151] PDD involves intravesical administration of a photosensitizing agent that accumulates in tumor cells, causing them to fluoresce under specific wavelengths of light. The most widely studied photosensitizer for bladder cancer is hexaminolevulinic acid (HAL).[74] PDD has demonstrated advantages over white-light cystoscopy, with improved detection rates for papillary tumors (7–35.2%)[152,153] and CIS (20–40.7%).[154,155] Sensitivity rates of 90.1–95% have been reported.[152,153,155]

PDD has also shown a reduction in recurrence rates compared to standard cystoscopy, with recurrence rates reduced from 18% to 14%.[154] Estimates of recurrence rates in studies using PDD range from 19.8% to 37.2%.[156–158] However, PDD has a relatively high false-positive rate, ranging from 1% to 26%.[159] Despite its diagnostic benefits, PDD does not replace the need for other treatments, such as Bacillus Calmette–Guérin (BCG) therapy, particularly for high-risk cases.[160]

The EAU guidelines recommend PDD during TURBT, if available.[11] The AUA suggests offering PDD (often referred to as blue-light cystoscopy or BLC) at TURBT and considering its use in patients with positive cytology and normal cystoscopy findings.[10]

Narrow Band Imaging (NBI)

NBI enhances the visualization of bladder tumors by filtering light into blue and green wavelengths, which highlight blood vessels at different tissue depths. This enhances differentiation between normal and tumor tissue.[161] NBI was originally developed for gastrointestinal endoscopy[162] but has since been adapted for urological applications.

Most studies, including meta-analyses, have shown that NBI improves tumor detection rates when combined with WLC.[155,161,163–169] NBI has been particularly effective in detecting CIS,[168,170,171] with approximately 10% more bladder cancer patients being diagnosed with NBI than with standard WLC.[170]

However, the influence of NBI on recurrence rates remains mixed. Some studies have demonstrated significant improvements in recurrence rates at 3 and 12 months.[169,171–173] For instance, one systematic review and meta-analysis reported a hazard ratio (HR) of 0.63 for NBI compared to WLC.[172] However, other studies have found no significant differences, particularly in long-term follow-up.[164,174–176] Some have suggested that the addition of BCG may influence outcomes,[171] though further research is needed to clarify this effect. Notably, even in studies that did not show overall benefits, patients with low-risk tumors (TaG1, <3 cm) benefited from NBI, with 5.6% recurrence at 12 months compared to 27.3% with standard TURBT.[174]

Studies on PFS and OS with NBI are similarly inconclusive.[171,172,177] One recent Cochrane review found no difference in adverse events between NBI and WLC, despite concerns that higher false-positive rates might lead to overtreatment.[172]

Few studies have directly compared PDD and NBI. A study by Drejer et al[163] conducted in 2017 on 136 patients found no significant differences between the two imaging techniques, which was consistent with findings from a later meta-analysis[171] in 2023. However, other meta-analysis suggested that 5-aminolevulinic acid (5-ALA) might have a lower recurrence rate compared to HAL (OR for recurrence in 5-ALA compared to HAL was 0.48, 95% CI [0.26–-0.95]), but the superiority over NBI was insignificant (OR= 0.53, 95% CI [0.26–1.09]).[177]

The specificity of different imaging methods remains controversial. While some researchers[171] found that NBI had better specificity (similar to WLC, at 0.76) compared to PDD, Others[178] reported the opposite findings. Moreover, Chen et al observed that NBI had higher diagnostic accuracy, even after omitting studies with high risk of bias and those with less than 100 patients.[179] On the other hand, some studies found PDD to be significantly more sensitive in a retrospective study of 114 patients.[180]

More importantly, uncertainty persists regarding the oncological impact of NBI. While meta-analyses of RCTs suggest an insignificant advantage of HAL over NBI, the cost-effectiveness of NBI is in question, particularly when considering its use in routine practice.[181] Further complicating the decision between these methods is the need for instillation of a photosensitizing agent in PDD, which introduces additional costs and logistical considerations. Moreover, the reduced specificity of PDD after recent intravesical therapy (39.6% false positive rate for biopsy within six months, compared to 25.7% in patients who never underwent intravesical therapy) is a concern.[182]

In summary, NBI generally provides better detection rates and diagnostic accuracy and likely reduces recurrence at 12 months. However, further studies are required to assess its long-term effects on RFS, PFS, and OS. Additionally, there is a need for direct head-to-head comparisons between imaging techniques to establish clearer guidelines for their use.

The EAU guidelines weakly recommend the use of enhanced tumor visualization methods (PDD, NBI) during TURBT, if available.[11] The AUA guidelines suggest offering BLC or considering NBI during TURBT, and also consider BLC (along with urethral and random biopsies) in patients with positive cytology but normal-appearing cystoscopy.[10]

SPIES - IMAGE1 S (Formerly SPIES)

The "IMAGE1 S™" system is a software that processes cystoscopy images to create enhanced contrast without the need for physical filters,[183] which may reduce costs associated with expensive equipment. Early studies suggested that this system could improve diagnostic accuracy.[184,185] However, evidence regarding its overall impact remains limited.

One RCT found no significant differences in recurrence rates between groups at 18 months, except for low- to intermediate-risk primary tumors (p=0.035) and borderline effects in low- to intermediate-risk patients (p=0.068).[186] A recently published blinded RCT with 12-month follow-up (n=103) showed lower recurrence rates for the IMAGE1 S group (12.2% vs 25.9%, P =.080). Recurrence rates in low- and intermediate-risk groups were significantly lower (7.7% vs 30.8%, P =.003), and RFS was higher in the IMAGE1 S group (85.2% vs 62.8%, Log Rank: 0.021, HR=0.215). However, no differences were observed in high- and very-high-risk groups. Complications were primarily grade I and occurred more frequently with IMAGE1 S (20.4% vs 7.4%, P =.083).[187]

These findings leave an open question regarding whether IMAGE1 S can effectively reduce recurrence rates, especially in low- to intermediate-risk patients, and its potential to reduce the personal and economic burden of bladder cancer.

Future Directions

There are still many open questions regarding the integration of different imaging techniques and TURBT. For example, is restaging TURBT necessary when advanced imaging modalities and improved surgical techniques have already been used in the initial procedure? We look forward to future prospective studies to explore these questions. We also anticipate more extensive use of simulators and training programs to enhance the competency of new urologists. The role of artificial intelligence (AI) in interpreting cystoscopy images has been studied in multiple works, with high diagnostic accuracy.[188–190] Other AI models showed performance equivalent to expert interpretation, with faster image recognition.[191,192] These models still need to undergo prospective randomized trials and will likely require modifications for continuous video analysis. However, once fully operational, AI could revolutionize TURBT and cystoscopy.

Other intriguing developments include the "closing the loop" concept, with autonomous cystoscopy monitored by non-urologist staff,[193] as described by O'Sullivan in 2022. Although this approach is still in its early stages, it represents a promising direction for the future.

In other aspects of bladder cancer management, AI models are expected to play a more prominent role soon. These models may improve cytology accuracy,[17,194,195] as seen in studies like Lebret's 2022 analysis and Sokolov's 2018 research. AI also shows promise in pathology interpretation, with models like those developed by Abuhasenin[196] for staging accuracy based on CTU images, or Qureshi's 2024 MRI+mRNA marker model.[197]

Similarly, AI is being used to develop biomarkers to predict recurrence and progression. These include genomic and pathological biomarkers,[198] as demonstrated by Tokuyama in 2022, and models based on clinical data,[199,200] as reported by Sluzarcyzk in 2023 and Lucas in 2022. These predictive tools will play a key role in personalizing treatment, helping clinicians identify patients who need more aggressive treatments while sparing others from unnecessary interventions. However, these models are yet to be validated in prospective trials, and the effect of their integration into traditional decision-making processes on oncological outcomes remains unknown.

Urine biomarkers also represent a rapidly advancing area, especially for surveillance,[11,201,202] as shown in Singer's 2023 study. Such markers could eventually guide more personalized therapy, improving treatment outcomes for patients with bladder cancer. Advances in tumor classification, as mentioned by Teoh in 2022,[183] will also contribute to more tailored treatment approaches.

Emerging advancements from related fields, such as gastroenterological surgery, offer promising directions for urological innovation. Techniques like NBI and machine learning were already discussed earlier. Additionally, the integration of ultrasound technologies, particularly endoscopic ultrasound (EUS), could significantly enhance bladder cancer management. EUS can aid in tumor localization, assessment of invasion depth in suspected MIBC, and planning the extent of resection for large tumors. Innovative methods for bleeding control, such as injection therapy, in addition to thermal coagulation, also warrant exploration. Furthermore, genomic profiling of tumors could provide valuable insights for treatment planning, including decisions regarding adjuvant therapy. Techniques involving tissue ablation, such as argon plasma coagulation, heater probes, cryoablation, and radiofrequency or microwave ablation, present additional opportunities. These modalities could be utilized for achieving hemostasis or in palliative care settings where pathological examination is not required. Their application in managing recurrent LG NMIBC will remain outside the scope of this review. These emerging approaches could complement established energy sources, including bipolar technology, laser systems, and hydrodissection. We expect that a multidisciplinary approach to urological procedures would add to collaboration and innovation, ultimately improving TURBT and other related interventions.

Conclusions

TURBT remains the cornerstone of NMIBC diagnosis and treatment. The integration of enhanced imaging techniques such as PDD, NBI, and ERBT, alongside AI and biomarker advancements, promises to revolutionize patient outcomes by improving diagnostic accuracy and reducing recurrence rates. Surgeon experience and quality measures such as surgical checklists will continue to play an important role. Future research should explore the combined use of advanced diagnostic modalities and assess their long-term effects on oncological outcomes. With these innovations, bladder cancer management stands on the brink of a new era in precision medicine.

Disclosure

The authors report no conflicts of interest in this work.

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