

The use of blue-light cystoscopy in the detection and surveillance of nonmuscle invasive bladder cancer

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Abstract

Nonmuscle invasive bladder cancer is associated with a high risk of recurrence as well as progression to muscle-invasive disease. Therefore, adequate visualization and identification of malignant lesions as well as complete resection are critical. Traditional white-light cystoscopy is limited in its ability to detect bladder cancer, specifically carcinoma in situ. Blue-light cystoscopy makes use of the intravesical instillation of a heme precursor to differentiate areas of malignancy from normal tissue. A narrative review of the literature on the use of blue-light cystoscopy in bladder cancer was conducted. Blue-light cystoscopy has been shown in several randomized clinical trials to increase detection of Ta, T1, and carcinoma in situ, as well as reduce risk of recurrence at 12 months as compared with traditional white-light cystoscopy. Research into the effects of blue-light cystoscopy on risk of disease progression has produced mixed results, in part due to changing definitions of progression. However, more recent research suggests a correlation with decreased risk of progression. Whereas the use of blue-light was initially limited to rigid cystoscopy in the operating room, results from a recent randomized clinical trial showing enhanced detection of recurrent disease using blue-light in-office surveillance flexible cystoscopy have led to expanded Food and Drug Administration approval. Overall, blue-light cystoscopy offers promise as an enhancement to white-light cystoscopy for the detection of nonmuscle invasive bladder cancer and may yield additional benefits in reducing disease recurrence and progression. Further prospective research is needed to evaluate the true benefit of blue-light cystoscopy in terms of disease progression as well as the cost-effectiveness of this technique.

Keywords: Nonmuscle invasive bladder cancer; Blue-light cystoscopy; White-light cystoscopy

1. Introduction

Bladder cancer is the most common malignancy of the urinary tract and the fifth most common cancer in the United States.^[1] An estimated 81,000 new cases of bladder cancer and 17,000 deaths are expected in 2022.^[2,3] Bladder cancer treatment costs per patient are higher than any other cancer in the United States.^[2,3] Between 75% and 85% of patients diagnosed with bladder cancer are diagnosed with nonmuscle invasive bladder carcinoma (NMIBC), categorized as stages Ta, T1, and carcinoma in situ (CIS).^[1,4] Despite the use of intravesical chemotherapy and immunotherapy, NMIBC is associated with a 30%–70% 5-year risk of recurrence, and 5%–25% of recurrent cases eventually progress to muscle-invasive disease.^[1,4,5]

Bladder cancer is diagnosed using a combination of urine cytology, cystoscopy, and transurethral resection of bladder tumor (TURBT).^[1] Cytology may be negative in stage Ta and T1 disease, but these lesions are usually visible on TURBT because of their papillary appearance.^[1] In contrast, CIS usually produces positive cytology but is often missed on TURBT.^[1] Not only is CIS more difficult to visualize, but it is also associated with more aggressive disease and an increased risk of progression.^[5,6] Given the risks

of recurrence and progression associated with NMIBC, visualization and complete resection during diagnostic TURBT and surveillance cystoscopies are crucial to improving outcomes.^[4]

Cystoscopy and TURBT are typically performed using traditional white-light cystoscopy (WLC), which has limited sensitivity in detecting suspicious lesions.^[7] The limitations of WLC in identifying malignant lesions may lead to incomplete resection during TURBT.^[8] Residual tumor has been found in 30%–44% of resected cases up to 8 weeks after TURBT.^[9,10] It has been hypothesized that early recurrence may arise from growth of residual tumor or undetected lesions left behind at the time of resection.^[11,12] Therefore, because of limitations with WLC, enhanced imaging techniques have been developed.

Blue-light cystoscopy (BLC), also known as photodynamic diagnosis fluorescence cystoscopy, is an enhanced imaging technique with the ability to detect bladder carcinoma better than white light alone.^[1] Blue-light cystoscopy is made possible because of the preferential accumulation of heme precursors in malignant tissue.^[1] Intravesical instillation of hexyl-aminolevulinate (HAL; marketed as Hexvix/Cysview® by Photocure, Norway), a lipophilic ester of heme precursor 5-aminolevulinic acid, is performed 1 hour before cystoscopy.^[1,12] This molecule is transported into the urothelial cytoplasm and incorporated into heme biosynthesis. Cell abnormalities in malignant tissue lead to accumulation of protoporphyrin IX in mitochondria, whereas in normal urothelial tissue the drug is eliminated.^[1] During cystoscopy, the bladder wall is illuminated with blue light at a 380- to 450-nm wavelength, which induces porphyrins in abnormal cells to emit a red fluorescence while normal cells appear blue.^[1] This allows the physician to differentiate malignant from benign tissue, facilitating improved detection and resection of bladder cancer. Enhanced demarcation between normal and cancerous tissue enables more complete

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resection during TURBT.^[8] The resulting reduction in residual tumor is thought to lower the risk of recurrence and progression, which are significant concerns in the treatment of NMIBC.

2. Materials and methods

A narrative review of relevant literature was conducted. Searches were performed in PubMed and Google Scholar databases restricted to English-language original articles published between January 1964 and March 2022 using the following search terms: non-muscle invasive bladder cancer, blue-light cystoscopy, blue-light flexible cystoscopy, blue-light cystoscopy AND detection, blue-light cystoscopy AND recurrence, blue-light cystoscopy AND progression, blue-light cystoscopy AND cost-effectiveness, blue-light cystoscopy AND safety. Systematic reviews, original articles, and case reports/series were included. Commentaries and news articles were excluded. Full-text articles meeting inclusion and exclusion criteria were independently reviewed by all authors. Bibliographies were reviewed for potential missed studies. In addition, all articles identified in previously published systematic reviews were included.

A supplemental search for clinical trials was conducted in www.clinicaltrials.gov, accessed in January 2022, using combinations of the search terms “bladder carcinoma” and “blue-light cystoscopy.” Trials were classified as completed if their status was listed as “completed” on www.clinicaltrials.gov. Trials were classified as ongoing if their status was listed as “active,” “recruiting,” “active, not yet recruiting,” “active, not recruiting,” or “suspended.” Trials were excluded if they were listed as “terminated” or “withdrawn.”

3. Results

3.1. Evidence supporting the use of BLC

3.1.1. Detection and recurrence Six multicenter phase III clinical trials have demonstrated improvement in detection and/or decreased rate of recurrence of NMIBC with use of BLC. Table 1 summarizes the characteristics and findings of these 6 clinical trials.

Multiple trials have shown improved detection of NMIBC using BLC. Jichlinski et al.^[6] published the first multicenter study evaluating

the sensitivity and specificity of HAL fluorescence cystoscopy in patients with bladder cancer. In their study, 52 patients underwent both white and blue light cystoscopy. Blue-light cystoscopy identified 43 patients with a diagnosis of bladder cancer, whereas WLC only identified 33 patients, yielding a sensitivity of 96% for BLC and 73% for WLC.^[6] Subsequent studies using BLC have found similar detection rates.^[13,14,16] One study reported that BLC detected residual tumor in 49% of patients after WLC TURBT.^[17]

Research has shown BLC to be especially useful in detecting CIS. Jichlinski et al.^[6] reported that 12 of 13 patients with CIS tumors were diagnosed or confirmed by BLC, as compared with only 3 patients diagnosed by WLC. In a similar study, Schmidbauer et al.^[13] found that 22% of CIS cases were detected using BLC alone, 75% were detected using both BLC and WLC, and only 2% were detected using WLC alone.

Grossman et al.^[15] examined the use of BLC in the detection of Ta and T1 papillary lesions. In patients with Ta tumors, 29% had at least one more tumor detected by BLC as compared with WLC. Of those patients, 19% had no lesions detected on WLC.^[15] For T1 tumors, at least one more tumor was detected by BLC in 15% of patients. Overall detection rates for Ta tumors were 95% for BLC and 83% for WLC ($p < 0.05$), and for T1 tumors, 95% were detected by BLC and 86% by WLC ($p > 0.05$).^[15]

A 2013 meta-analysis of 9 clinical trials involving 2212 patients to determine the effect of BLC on detection of Ta, T1, and CIS tumors found that BLC detected 14.7% more Ta tumors and 40.8% more CIS tumors compared with WLC.^[11] In addition, 25% of patients had an additional Ta/T1 tumor detected by BLC. Importantly, CIS was detected by BLC in only 26.7% of patients. The 2021 meta-analysis by Russo et al.^[18] similarly compared the diagnostic sensitivity of BLC versus WLC across 11 studies. They found that TURBT with BLC was more sensitive (0.93; 95% confidence interval [CI], 0.85–0.97) compared with WLC (0.73; 95% CI, 0.66–0.79) in detecting bladder cancer.^[18]

Jocham et al.^[14] examined how the use of BLC impacted treatment decisions. Because of improved detection of disease, 10% of patients underwent additional postoperative procedures and 17% of patients received more appropriate treatment because of

Table 1
Summary of key trials evaluating BLC in NMIBC.

Author	Year	Location	Patients	Design	Study arms	Outcomes
Jichlinski et al. ^[6]	2003	Europe	n = 52	Within-patient comparison (WLC then BLC)	-	Detection: 96% sensitivity for BLC vs. 73% for WLC
Schmidbauer et al. ^[13]	2004	Europe	n = 286	Within-patient comparison (WLC then BLC)	-	Detection: BLC identified 28% more patients with CIS than WLC alone
Jocham et al. ^[14]	2005	Europe	n = 162	Within-patient comparison (WLC then BLC)	-	Detection: 96% sensitivity for BLC vs. 77% for WLC
Grossman et al. ^[15]	2007	North America	n = 311	Within-patient comparison (WLC then BLC)	-	Detection: Ta: 95% for BLC and 83% for WLC T1: 95% for BLC and 86% for WLC
Stenzl et al. ^[16]	2010	North America	n = 814	Detection: within-patient Recurrence: comparison of 2 groups	Group 1: WLC plus TURBT Group 2: WLC plus BLC plus TURBT	Detection: In 16% of patients with ≥ 1 Ta or T1 tumor, at least one tumor was seen with BLC only Recurrence (9 mo): 47% in BLC group vs. 56% in WLC group
Hermann et al. ^[17]	2011	Europe	n = 233	Comparison of randomized groups	Group 1: WLC plus TURBT Group 2: WLC plus TURBT, then BLC plus TURBT	Detection: BLC detected residual tumor after WLC TURBT in 49% of patients Recurrence (12 mo): 30.5% in BLC group vs. 47.3% in WLC group

BLC = blue-light cystoscopy; NMIBC = nonmuscle invasive bladder cancer; TURBT = transurethral resection of bladder tumor; WLC = white-light cystoscopy.

the addition of BLC.^[14] They suggested that the use of BLC might reduce the need for aggressive treatments such as radical cystectomy due to decreased risks of recurrence and progression after complete tumor resection.

The use of BLC has been associated with a decrease in cancer recurrence. Stenzl et al.^[16] enrolled patients at increased risk for recurrence due to the presence of more than one initial or recurrent papillary tumor or recurrence within 12 months of a prior bladder cancer. At 9-month follow-up, disease recurred in 47% of patients in the BLC group and 56% of patients in the WLC group ($p < 0.05$), which corresponded to a 16% relative reduction in recurrence with use of BLC.^[16] Similarly, Hermann et al.^[17] reported 12-month recurrence rates of 47.3% after WLC alone and 30.5% after WLC plus BLC ($p = 0.05$). A 2013 meta-analysis of 9 randomized clinical trials (RCTs) found significantly lower recurrence rates at 12 months with BLC (34.5%) as compared with WLC (45.4%; relative risk [RR], 0.761; $p < 0.05$).^[11] Similarly, a 2021 meta-analysis of 12 RCTs found reduced recurrence rates with BLC at 12 months (RR, 0.73; 95% CI, 0.68–0.88) and 24 months (RR, 0.75; 95% CI, 0.62–0.91).^[19]

Overall, the results of these RCTs and meta-analyses provide substantial evidence of the benefit of BLC in the detection of NMIBC. In addition, several studies have shown decreased rates of recurrence after BLC, likely due to more complete TURBT and more appropriate risk stratification and treatment.

3.1.2. Disease progression While research supports the benefits of BLC for detection and recurrence of NMIBC, evidence regarding disease progression has been less clear. Theoretically, BLC could result in decreased disease progression due to a more complete TURBT resulting in less residual disease and improved treatment strategies.^[5] However, changing definitions of disease progression for bladder cancer have hindered consistent reporting of research results. Disease progression was historically defined as progression to muscle-invasive disease. However, the International Bladder Cancer Group published new definitions of progression in 2016.^[20] According to these new definitions, disease progression can be defined by an increase in either disease stage or grade. Regarding stage, progression includes development of or increase in stage due to lamina propria invasion (Ta to T1 or CIS to T1), muscle invasive disease (T2 or higher), or lymph node or distant metastasis (previously N0 and/or M0).^[20] In terms of grade, progression is defined as an increase from low- to high-grade disease.

Stenzl et al.^[16] noted a nonsignificant trend toward decreased risk of progression to muscle invasive bladder cancer when using BLC compared with WLC. After 4.5 years of additional follow-up, they found a trend toward decreased progression after BLC, with progression to T2 or higher disease occurring in 6.1% of WLC and 3.1% of BLC patients ($p = 0.06$).^[21] Kamat et al.^[22] reanalyzed these data in 2016 using the new International Bladder Cancer Group definition of progression, finding a trend toward a decrease in progression, with progression occurring in 17.6% of WLC patients and 12.2% of BLC patients ($p = 0.085$).

A 2016 meta-analysis by Gakis and Fahmy^[23] analyzed the results of 4 randomized studies and 1 retrospective review to determine the impact of BLC on disease progression. Defining disease progression as muscle-invasive disease, they found a significantly lower risk of progression using BLC (6.8%) compared with WLC (10.7%) after a median follow-up of 28 months ($p < 0.05$).^[23] Although these results reached statistical significance, because their study used the previous definition of disease progression, additional prospective randomized research is needed to determine the true benefit of BLC in terms of disease progression.

3.2. Expanding use: Office-based blue-light flexible cystoscopy for surveillance of NMIBC

Given the high risk of recurrence in NMIBC, patients typically require surveillance office-based cystoscopy every 3–6 months. However, this has historically been performed using white-light flexible cystoscopy (WLFC), which has been demonstrated to miss a significant proportion of malignant lesions.^[8] Therefore, research has increasingly focused on the use of blue-light flexible cystoscopy (BLFC) for office-based surveillance.

The phase III trial by Daneshmand et al.^[8] examined the use of BLFC during surveillance for detection of recurrent bladder cancer. Patients at high risk for recurrence were randomized to WLFC with or without BLFC, and those with suspicious lesions were referred to the operating room for WLC and BLC with biopsy or resection. The primary end point was the percentage of patients with malignancy detected only by BLFC. Among patients with recurrence, 20.6% were detected only by BLFC ($p < 0.05$).^[8] In the operating room, 34.6% of patients diagnosed with CIS were identified only by BLC.^[8] The authors concluded that in-office BLFC improves detection of recurrent bladder cancer.

Blue-light cystoscopy was initially Food and Drug Administration approved in 2010 for the detection of NMIBC in patients who have or are suspected to have lesions.^[7] In 2018, after the results of this new trial, the Food and Drug Administration approved a new drug application for extension of indications for BLC to include flexible cystoscopy and use in ongoing surveillance.^[24]

The 2018 study by Daneshmand et al.^[24] also led to an American Urologic Association (AUA) consensus statement on the use of blue-light in-office-based cystoscopy. Consensus statement recommendations, summarized in Table 2, include: use of BLFC at 3-month follow-up for patients at high or intermediate risk of recurrence, use of BLFC at 3 months, 6 months, and then every 6 months for 2 years for patients at high risk of recurrence, use of BLFC before intravesical therapy if residual disease after TURBT is a concern, and use of BLFC at the time of office fulguration and/or biopsy for low-grade tumors.^[24] They also noted that BLFC may have a role in evaluating patients with positive cytology

Table 2
2018 AUA consensus recommendations for use of BLFC for surveillance.

Recommendation number	Factor	Recommendation
1	Likelihood of recurrence	Strong recommendation for value of BLFC at initial 3-mo cystoscopy for patients at high risk or intermediate risk of recurrence
2	Frequency of use	BLFC at 3 and 6 mo and then every 6 mo for patients at high risk of recurrence in the first 2 yr
3	Residual disease	Use before intravesical therapy if residual disease after TURBT is a concern
4	Biopsy/fulguration	Use at time of office fulguration and/or biopsy for low-grade tumors
5	Positive cytology and normal WLC and equivocal lesions with negative WLFC	May have a role in evaluating patients with positive cytology and normal WLC or equivocal lesions on WLFC with negative cytology

Reprinted from Lotan et al.^[24] This is an open access article distributed under the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>).
AUA = American Urologic Association; BLFC = blue-light flexible cystoscopy; TURBT = transurethral resection of bladder tumor; WLC = white-light cystoscopy; WLFC = white-light flexible cystoscopy.

and normal WLC or equivocal lesions on WLC with negative cytology.

Following the 2018 AUA consensus statement, Lotan et al.^[24,25] studied a cohort of 190 patients who underwent office-based BLFC for surveillance of NMIBC. They found that BLFC detected additional cancers in 33% of patients with positive WLC and BLFC.^[25] In their group, there were 26 cystoscopies (8%) with negative WLC but positive BLC findings. Eight of these patients had CIS (30.8%), 8 had high-grade Ta (30.8%), and 3 had low-grade Ta (11.5%), while 3 had benign findings (11.5%).^[25] In patients who had negative WLC and positive BLC, cytology was positive in only 3 of 16 (18.8%).

A recent retrospective review examined the utility of BLC specifically for the surveillance of patients who had undergone treatment with bacillus Calmette-Guérin (BCG). They found that WLC alone missed 13% of high-grade recurrences within the first year after BCG treatment, and 88% of these missed recurrences had CIS present.^[26]

3.3. Patient-reported outcomes

A 2019 study by Smith et al.^[27] examined the impact of office-based BLFC on patient pain and anxiety, as well as their opinions on the test's value and their willingness to pay. They administered the Patient-Reported Outcomes Measurement Information System "Anxiety," "Pain," and "Was it Worth it" questionnaires at baseline, after surveillance BLFC, and after operating room resection.^[28] They found that pain levels were low, patient anxiety decreased after BLFC, and 76% of patients undergoing BLFC were willing to pay out of pocket. Ninety-four percent of patients found BLFC worthwhile, and 91% of patients would recommend it to others.

3.4. Safety

Typical adverse events reported by patients undergoing BLC are the same as those usually associated with standard cystoscopy, including postoperative pain, hematuria, abdominal pain, urinary retention, and dysuria.^[6,13,15,21] Studies have reported no relevant changes in laboratory safety values or vital signs.^[13] When comparing WLC and BLC, Stenzl et al.^[16] found similar levels of adverse events in both groups, which were mostly mild and moderate in intensity. A meta-analysis revealed no difference in adverse effects with BLC compared with WLC.^[29] Overall, rates of adverse events after either WLC or BLC are between 22.5% and 80.5%, with less than 2.4% of these events being attributed to use of HAL in cystoscopy.^[30]

Several studies have evaluated the safety of repeated use of HAL cystoscopy.^[30,31] Apfelbeck et al.^[31] reported adverse effects associated with HAL, including allergic reactions, urinary tract infections, skin photosensitization, and changes in blood pressure. In 80 patients who underwent an average of 4 HAL TURBT procedures, no allergic reactions were reported, and minor adverse effects included urinary tract infection, dysuria, pollakiuria, and bladder spasm, all of which were present in a similar proportion of patients before the procedure.^[31] In a similar study, Lane et al.^[30] found no difference in rates of adverse events in patients who underwent BLC once versus those who underwent the procedure 2 or more times.

3.5. Cost-effectiveness

Bladder cancer carries a significant economic burden, with lifetime cost estimates per patient with NMIBC ranging from \$96,000 to \$230,000.^[32] Part of this expense is due to the need for frequent surveillance and potentially repeat TURBT, each of which costs \$2900 to \$6000. While the use of BLC may carry higher up-

front costs, its potential to decrease recurrence and progression has been hypothesized to decrease overall costs associated with bladder cancer.^[2] Garfield et al.^[33] analyzed the cost-effectiveness of detection with BLC versus WLC over 5 years. They found that costs at 5 years were 15% lower for patients initially undergoing BLC (\$25,921) compared with WLC (\$30,581).^[33] Patients in the BLC group spent less time managing disease recurrence and progression over the 5-year period compared with those in the WLC group. A similar cost analysis in Sweden found that incorporation of HAL into cystoscopy during TURBT would be cost-neutral or cost-saving over a 5-year period due to reduction in disease recurrence and progression.^[34]

A 2022 clinical and cost-effectiveness analysis examined the budget impact on practices that use BLFC for surveillance in the clinic setting.^[32] They reported that over a 2-year period, BLFC identified 9 additional recurrences compared with WLC alone, and use of BLFC increased cost by only \$0.76 per cystoscopy.^[32] Despite this marginal increase in up-front cost, the benefits of BLFC for detection, recurrence, and progression might decrease overall costs for patients with NMIBC.

3.6. Professional recommendations and ideal uses

Recent society guidelines regarding BLC are summarized in Table 3. The AUA/Society of Urologic Oncology joint 2016 guidelines recommend "In a patient with NMIBC, a clinician should offer BLC at the time of TURBT if available to increase detection and decrease recurrence."^[4] The European Association of Urology 2016 guidelines also state that fluorescence-guided biopsy and resection are more sensitive compared with traditional white light for the detection of malignant tumors, particular CIS (evidence level 2a).^[35] Lastly, the National Comprehensive Cancer Network 2021 guidelines state that enhanced cystoscopy may be helpful in identifying lesions not visible using WLC and recommend considering enhanced cystoscopy, if available, for initial evaluation or when urine cytology is positive.^[36]

Based on evidence and professional recommendations, it is recommended to use BLC, if available, for all patients at initial TURBT to increase detection and reduce recurrence.^[37] In addition, BLC may be useful in patients with positive urine cytology but normal WLC.^[7] Other possible uses of BLC include patients suspected of having high-risk bladder cancer, patients with a history of CIS, patients with multiple low-grade tumors, and follow-up surveillance cystoscopy after BCG treatment.^[26]

It is extremely important to use BLC in combination with WLC. While BLC improves the detection of malignant lesions, Schmidbauer et al.^[13] found that 2% of CIS was detected by WLC and not by BLC. Similarly, Grossman et al.^[15] found that in 10% patients with Ta tumors, at least one more tumor was detected by WLC than BLC.

3.7. Adoption of BLC

While the use of BLC during TURBT is supported by evidence and recommended by recent AUA/Society of Urologic Oncology and European Association of Urology guidelines, a recent study found that it may be underutilized in practice.^[38] This database study examined TURBT procedures in the US between 2011 and 2020 and found that BLC was used in only 1.2% of procedures.^[38] Further research is needed to determine what barriers exist to adoption of this technique at both the hospital and provider level.

3.8. Ongoing trials and future directions

There are several ongoing trials investigating the use of BLC. The Blue Light Cystoscopy with Cysview Registry is a registry study, which aims to gather additional information on current usage of

Table 3**Society recommendations for use of BLC.**

Society	Year	Recommendation	Strength of recommendation
AUA/SUO	2016	In a patient with NMIBC, a clinician should offer BLC at the time of TURBT, if available, to increase detection and decrease recurrence.	Moderate recommendation evidence strength grade B
AUA/SUO	2016	In a patient with a history of NMIBC with normal cystoscopy and positive cytology, a clinician should consider prostatic urethral biopsies and upper tract imaging, as well as enhanced cystoscopic techniques (BLC, when available), ureteroscopy, or random bladder biopsies.	Expert opinion
NCCN	2021	Enhanced cystoscopy may be helpful in identifying lesions not visible using WLC.	-
NCCN	2021	Consider enhanced cystoscopy (if available) for initial evaluation or when positive urine cytology.	-
EAU	2016	Fluorescence-guided biopsy and resection are more sensitive than conventional procedures for the detection of malignant tumors, particularly for CIS	Evidence level 2a

AUA = American Urologic Association; BLC = blue-light cystoscopy; CIS = carcinoma in situ; EAU = European Association of Urology; NCCN = National Comprehensive Cancer Network; NMIBC = nonmuscle invasive bladder cancer; SUO = Society of Urologic Oncology; TURBT = transurethral resection of bladder tumor; WLC = white light cystoscopy.

BLC in urology practices.^[39] The researchers are collecting data on detection, recurrence, and progression with use of BLC. PHOTO, a randomized trial assessing clinical and cost-effectiveness, is also underway in the United Kingdom.^[40] This study seeks to determine whether BLC is clinically more effective than WLC, measured by time to recurrence, and whether it is cost-effective, measured as incremental cost per recurrence avoided and cost per quality-adjusted life per year gained.

Future research should include prospective randomized trials to evaluate the true benefit of blue light in terms of disease progression. Additional clinical and cost-effectiveness studies are also needed given the recent adoption of blue-light in-office flexible cystoscopy. Given the underutilization of BLC found in the 2020 database study by Lewicki et al.,^[38] future research should also seek to understand barriers to adoption of this technique for hospitals as well as individual providers.

4. Conclusions

Blue-light cystoscopy is a valuable enhancement to traditional WLC for the detection and surveillance of NMIBC. Evidence from several clinical trials shows improvements compared with WLC in detection of NMIBC, especially CIS, as well as reduced risk of recurrence at 12 months. Research also supports the use of BLC to reduce progression of disease. Overall, BLC is a safe, effective method of enhanced imaging used in the diagnosis and surveillance of bladder cancer. Future research directions include obtaining additional prospective data to clarify the benefits of BLC in terms of disease progression, as well as studies on cost-effectiveness of this modality, especially for office-based surveillance.

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Statement of ethics

Not applicable.

Conflict of interest statement

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Author contributions

All authors participated in the writing and revising of this article.

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