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Storz professional image enhancement system (SPECTRA A) enhancing detection of carcinoma urinary bladder by white light cystoscopy

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Abstract

Background SPECTRA A filters red light from white light through software to create contrast for better tissue visualization and light penetration. We aim to find whether the detection rate of bladder cancer is enhanced by SPECTRA A in adjunct to White Light Cystoscopy (WLC).

Methods This was a prospective observational study among 66 patients in the Department of Urology and Kidney Transplant Surgery, Tribhuvan University Teaching Hospital. All patients undergoing TURBT for suspected/diagnosed bladder tumor were evaluated with WL, followed by SPECTRA A mode, and findings were recorded using visual bladder mapping. Resection of the tumor was done on WL, margins were again reevaluated using SPECTRA A mode, and a biopsy was taken in cases of suspicious findings confirmed on SPECTRA A. Tumor detection rate (sensitivity), extra lesion detection, false positive rate, and margin status were evaluated through 2 × 2 tables, McNemar chi-square test on patient level as well as lesion level.

Results A total of 64 patients were included in the study. The mean age was 62.20 ± 13.98 with a sex ratio of M:F 4.3:1. SPECTRA A and WL had a detection rate of 95.33% and 78.80% (p = 0.001), respectively, and positive biopsy of detected lesions was 78.8% and 84.13% (p = 0.041), respectively, for SPECTRA A and WL. The false positive rate of SPECTRA A and WL was 21.19% and 15.86% (p = 0.006), respectively, whereas the false negative rate was 4% and 19.2% (p = 0.001), respectively. The number of extra lesions detected by SPECTRA A was 39, out of which 29 were histologically proven tumors.

Conclusion SPECTRA A enhances the detection rate of bladder cancer when used with WL. We can increase the detection of bladder cancer by using a combination of white light and SPECTRA A.

Keywords Bladder cancer, White light, SPECTRA A, Detection

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1 Background

Bladder cancer is the most common malignancy of urinary tract diagnosed in our part of the world and the ninth-most common cancer in the world [1]. It is the seventh-most common cancer in Nepal [2]. It is commonly found in the elderly population with hematuria [3].

Though 4/5th of patients present at non-muscleinvasive stage (Ta, T1, and CIS) and can be managed endoscopically, it has high recurrence rates of 61% at



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one year and 78% at five years [4]. Because of its high recurrence rate, bladder cancer necessitates lifelong surveillance and repeat resections, resulting in one of the highest healthcare costs of any malignancy [5].

During White Light Cystoscopy (WLC), small papillary tumors and flat Carcinoma in Situ (CIS) lesions as well as hemorrhagic lesions may not be well detected, resulting in inadequate excision of the main tumors. This leads to a significant increase in recurrence rates in the short and medium periods [6]. Trans-Urethral Resection (TUR) can result in inadequate tumor excision and misdiagnosis of bladder cancer due to blurry borders and difficult-to-see submucosal tumor margins [7]. These limitations of WLC contribute to an increased risk of cancer persistence, recurrence, and progression to metastatic fatal illness in high-grade bladder cancer [8] which emphasized the need to develop alternative endoscopic methods to increase detection of bladder lesions [9].

The Storz professional image enhancement system has just been added to the arsenal of urologists which uses software-based image enhancement method without special light source or intravesical contrast [10]. It creates contrast for better tissue imaging by filtering red light from white light (as in narrow-band imaging) using software at the point of image processing. It is a non-fluorescent optical instrument that filters WL into two narrow bandwidths of 415 and 540 nm, which correspond to blue and green light, respectively, to improve the viewing of NMIBC by enhancing visualization of vessels in the superficial mucosa and submucosa. Hemoglobin absorbs these wavelengths particularly, creating a difference between normal urothelium and abnormally vascularized tissues [11].

By filtering WL into two narrow bandwidths of 415 and 540 nm, which correspond to blue and green light, respectively, Narrow-Band Imaging (NBI) cystoscopy (which is independent of fluorescent agents) improves the visualization of Non-Muscle-Invasive Bladder Cancer (NMIBC). These endoscopic enhancing techniques may be able to increase diagnosis accuracy in early malignant lesions [12, 13].

Though there are many studies on the efficacy of narrow-band imaging, there is a scarcity of the literature on the SPECTRA A of Storz professional image enhancement; only few studies state better diagnosis by SPECTRA A [10], so we conducted a prospective observational study to observe whether professional image enhancement system (SPECTRA A) enhances bladder cancer detection in addition to white light.

2 Methods

2.1 Study design

This was a single-center, prospective observational crosssectional study done at the Department of Urology and Kidney Transplant Surgery, Tribhuvan University Teaching Hospital (TUTH), Institute of Medicine (IOM), from March 2019 to February 2020. Approval of the institutional review board was obtained with approval number as 349/ (6-11) $G^2/075/76$, as well as informed written consent was obtained from participants. All patients undergoing TURBT for suspected urinary bladder tumors based on imaging and/or white light cystoscopy were included in the study, whereas exclusion criteria were inadequate vision due to bleeding, early termination of the procedure due to surgical or anesthetic complication, and consent withdrawal.

Sample size (n) was calculated using 80% power and a 95% significance detection of carcinoma urinary bladder, 90% in SPECTRA A mode, and 70% on white light. These values were arrived at after a comprehensive literature review [14, 15]. The sample size was determined with the formula:

$$N = K \times \frac{p_1(1-p_1) + p_2(1-p_2)}{(p_1 - p_2)^2}$$

where N = sample size, p_1 = detection of bladder cancer in white light, p_2 = detection of bladder cancer in narrowband imaging (SPECTRA A), *and* K=constant which depended on the value of α and β as given below:

a	Power			
	50%	80%	90%	95%
	$\beta = 0.5$	$\beta = 0.2$	β=0.1	$\beta = 0.05$
0.10	2.7	6.2	8.6	10.8
0.05	3.8	7.9	10.5	13.0
0.02	54	10.0	13.0	15.8
0.01	6.6	11.7	14.9	17.8

A sample size of 60 was calculated using the above formula. Estimating a dropout of 10%, we decided to include at least 66.

After obtaining informed written consent, all patients with hematuria or those suspected to have bladder cancer were subjected to imaging or cystoscopy for the diagnosis. After confirmation of the diagnosis, we proceeded for TURBT. Spinal anesthesia was applied at the L3-L4 level in most cases, and few cases were performed on general anesthesia due to failed spinal or contraindication to spinal anesthesia. Patients were then kept in the lithotomy position. After painting and draping, patients were subjected to cystoscopy first under white light, and the findings were noted and recorded according to the bladder diagram. Then the light was changed to SPECTRA A mode, and findings were again noted in the bladder diagram. Any additional suspicious lesions not seen with WLC which were visible on SPECTRA A were biopsied. Then the light was changed to white light, and monopolar TURBT under 1.5% glycine irrigation was done using Karl Storz 26Fr monopolar resectoscope with 30° telescopes, and tissues were retrieved for histopathological (HPE) study. Then margins were reevaluated under SPECTRA A mode for further evaluation, and any suspicious residual lesion seen with SPECTRA A was resected. and biopsy was sent separately for HPE.

Tumors were resected from periphery to center with the stalk resected last. An additional sample of deep muscle was obtained from the tumor base, and cold-cup biopsies were taken when necessary and were sent for histopathological examination in different containers. All the required study variables (age, sex, size of tumor, complications, hospital stay, hemoglobin drop, and the presence of detrusor muscle) were recorded in proforma during the operation and in the postoperative period.

Postoperative irrigation was done with normal saline and continued till the urine became clear. The catheter was removed after 48 h in uncomplicated cases and patients were discharged.

Patients were followed up in OPD at two weeks with the histopathological report or when necessary. The histopathological findings were also recorded during follow-up.

2.2 Statistical analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 24. Tumor detection rate (sensitivity), positive histopathology rate among detected lesions (specificity), false positive rates, and false negative rate among detected lesions were calculated. Significance was determined using the McNemar chi-square test and independent sample *t* test. A *p* value of < 0.05 was considered statistically significant.

3 Results

A total of 72 patients were evaluated, out of which 68 patients were proceeded for cystoscopy and TURBT as four of them were not fit for anesthesia. Two patients were excluded because of the technical problem as spectra mode system unavailability on the day of surgery. Two patients were excluded because of extensive growth and incomplete resection. Sixty-four patients were included in the study. A total of 193 lesions were detected using both WLC and SPECTRA A, of which 145 lesions were detected by WLC only and 184 lesions were detected using SPECTRA A (Fig. 1).

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The mean age of the patients was 62.20 years. There were a total of 52 male and 12 female patients in the study. Forty-six patients had multiple tumors, whereas 18 had a single tumor. The total number of tumors detected with combined WLC and SPECTRA A was 193. The tumor size was less than 3 cm in 33 patients, whereas 31 patients had a tumor size greater than 3 cm (Table 1).

At the patient level, cystoscopy using SPECTRA A was more sensitive compared to WLC (96.87% versus 87.50%). While combining both modalities, detection rate was around 100%. When subdividing lesions detected by histological stage, SPECTRA A mode showed a higher rate of detection of NMIBC. On subdivision, difference in the sensitivity of detection was statistically significant only in Ta and CIS lesions (Table 2).

SPECTRA A cystoscopy showed a significantly higher overall diagnostic rate compared with WLC for the detection of bladder cancers (95.33% versus 78.80%) with a p value of 0.001. Similarly, SPECTRA A detected more Ta, CIS, and T1 lesions compared to WLC, but the detection rate for T2 lesions was the same for both modalities. There was also a higher number of negative histology lesions detected in the SPECTRA A group (Table 3).

Bladder cancer detection rate of SPECTRA A was significantly higher compared to WLC (96.0% vs. 80.8%), but the rate of false positive results was also higher for SPECTRA A compared with standard WLC (21% vs. 15%). Hence, the percentage of proven biopsy among detected lesions using WLC was higher compared to SPECTRA A (84% vs. 78%). More importantly, SPECTRA A missed a lower number of bladder cancer compared to WLC. On combining both modalities, sensitivity and number of positive histology increased (Table 4).

Additional tumors were detected by SPECTRA A cystoscopy in a significantly higher proportion of patients with pTa, CIS, pT1, and overall, in comparison with white light cystoscopy.

There were seven suspicious lesions detected when imaging changed to SPECTRA A after completing TURBT on white light. Further resection was done on SPECTRA A mode and sent for HPE separately, and among them, three had shown positive for malignancy: Two of them were TaLG and one lesion was CIS.

The mean hemoglobin drop was 0.78 ± 0.8 gm/dl. Detrusor muscle identification rate was 71.87%, and mean days of hospital stay were 2.53 ± 1.27 . Three patients required blood transfusion due to a significant drop in hemoglobin, and one patient required reoperation for bladder clot evacuation and hemostasis. Two patients had extraperitoneal bladder perforation and were managed conservatively.



Fig. 1 STARD flow diagram [16]

Table 1 Demographic variables

Age (years)	62.20±13.98	
Sex (M:F)	52/12	
Tumor size < 3 cm	33	
Tumor size > 3 cm)	31	
Numbers of tumors (Single/Multiple)	18/46	

Table 2 Patient detection rate

	SPECTRA A	White light	Combination	<i>p</i> Value
Global	62(96.87%)	57(87.50%)	62(96.87%)	0.03
Ta and CIS (n-24)	23(95.83%	19(79.16%)	24(100%)	0.02
T1 (n-25)	25(100%)	23(92.00%)	25(100%)	0.56
NMIBC (n-49)	48(97.95%)	38(85.71%)	49(100%)	0.04
T2 (n-11)	11	11		
Negative histol- ogy (n-4)	3	4		0.91

number of lesions

	SPECTRA A	White light	<i>p</i> Value	Total number of lesions detected combined
Global	184(95.33%)	145(78.80%)	0.001	193
рТа	63(95.71)%	52(74.28%)	0.001	66
CIS	4	1		4
pT1	63(98.43%)	56(87.5%)	0.004	64
pT2	16	16		15
Negative malignant histology	40	23		43

4 Discussion

In the last two decades, numerous strategies for enhancing bladder cancer diagnosis and therapy have been created and assessed [11, 17–19]. One of the key modalities in this is narrow-band imaging. Storz Image

	SPECTRA A	White light	Combination	<i>p</i> Value
Total no. of detected lesion (sensitivity)	184 (95.33%)	145(78.80%)	193	0.001
Total no. of biopsy-proven malignant lesions	145	122	148	0.002
The percentage of proven biopsy among the lesions detected (specificity)	78.80%	84.13%		0.041
False positive rate	39 (21.19%)	23 (15.86%)		0.006
Missed lesions	9 (4.66%)	48 (24.87%)		0.001
Positive biopsy in missed lesions	6 (66.67%)	29 (60.41%)		

Table 4 Comparison of results between SPECTRA A and white light cystoscopy

S technology is a new development that employs several light filtering techniques and integrated software to provide various forms of image enhancements, which we may toggle in and out of throughout the cystoscopy procedure. SPECTRA, the red light filtering approach of Storz Image S, processes the image so that the final image presented is similar to narrow-band imaging by filtering red light [11]. A research in otorhinolaryngology found that narrow-band imaging and SPECTRA A [20] have similar lesion detection rates, corroborating the preceding conclusion.

There are no contraindications from the patient's perspective when using SPECTRA A or NBI mode. It does not necessitate the injection of any drugs intravenously or intramuscularly. Because it comprises of a software modification to the endoscope's software, these modalities can be utilized several times, and there is no maximum duration for each treatment. Costs are cheap once the system is obtained [14, 21].

The aim of the study was to observe whether SPECTRA A cystoscopy in addition to white light enhances detection of the urinary bladder cancer. In SPECTRA A, red light is filtered by a specific software at the console during image processing, but in NBI, red light is filtered at the light source. In both systems, the essential idea of filtering red light is the same. In our work, sensitivity was 95.33% for SPECTRA A and 78.80% for white light (p=0.001). In study conducted by P Mulawakr, Spectra A had sensitivity of 91.15% and white light had 89.81% [10]. According to numerous studies, the tumor detection rate for narrow-band imaging and white light cystoscopy is 94–97% vs. 79–83%, respectively [14, 22]. When it comes to pTa and CIS lesions, the difference in detection rate is greater than when it comes to pT1 lesions. In our study, the detection rate of SPECTRA A vs. white light in pTa and CIS lesions was 95.71% vs. 74.28% (p = 0.001), and it was 98.43% vs. 87.5% (p = 0.004) in pT1 lesions. Tumor identification by NBI vs. white light for CIS ranges from 88 to 95% vs. 50 to 70%, for pTa, it ranges from 93.9 to 98.7%, and for pT1 lesions, it was 97.4 percent vs. 92.1 percent, according to the published literature [14, 22, 23], which is comparable to our results.

SPECTRA A had a significant advantage over the usual approach in terms of patient detection rate (white light). Patient detection rates in SPECTRA A and white light cystoscopy were 96.8% and 87.8%, respectively, and nine lesions were missed in SPECTRA A as none of the modalities has 100% sensitivities, and the results are comparable to other studies done by Geavlete et al. and Chen et al., which ranged from 96 to 80% vs. 87 to 89% [14, 24].

The enhanced tumor detection rate has resulted in a higher proportion of additional tumors being detected with SPECTRA A. Extra tumor detection was found in 26.6 percent of the cases in this investigation. According to various studies, a large percentage of individuals with NMIBC were diagnosed by NBI cystoscopy alone, ranging from 9.9 to 38%, and were not detected by white light [15, 23, 25] which is quite comparable to our results.

The increased sensitivity of SPECTRA A leads to higher numbers of tumors that can be detected per patient. Our study found greater number of tumor detection in SPEC-TRA A mode than white light (2.89 vs. 2.26, respectively). Herr et al. [25] reported a greater number of identified tumors visualized per patient on NBI cystoscopy (3.4) than WLC (2.3). Similar findings were seen in a study by Bryan et al. [26] which indicated that NBI identified 2.6 tumors per patient, while WLC identified only 1.9, but other studies by Chen et al. and Shen et al. have contradicting results to this by detecting a comparable number of tumor lesions between NBI and white light [24, 27].

In additional benefit, NBI has shown to offer a significantly more precise delineation of the tumor margins due to the superior visualization of the surface layer [23]. Our study found seven of the tumors had suspicious margins, and out of which three were pathologically proven to be malignant lesions. In study done by Geavlete et al., they detected about 10.3% of tumors detected by NBI in normal-appearing mucosa which was confirmed by histopathology [14].

Higher detection rate will lead to a higher false positive rate (FPR) and result in additional biopsies. In the current study, FPR between SPECTRA A and white light was 21.19 vs. 15.86% (p=0.006), respectively. Our results

revealed the percentage of positive malignant histology among detected lesions of SPECTRA A was significantly lower than WLC at per-lesion level, i.e., 78.80% vs. 84.13% (p=0.041), respectively. According to study done in spectra mode in India, it also showed false positive rate of 37.83% [10]. In the reported literatures, FPR of NBI ranged from 21.8 to 50% at per-patient level [24, 25] and ranged from 13.6 to 39.1% at per-lesion level [14, 22, 23]. Cauberg et al. [22] detected FPR of NBI was significantly higher than WLC (31.6 vs. 24.5%, p<0.01) at the perlesion level. Furthermore, a similar result was found by Tatsugami et al. [23] (29.1% vs. 13.8%, p<0.01). However, another meta-analysis by Zheng et al. [28] did not show a significant difference in that while comparing NBI and WLC (84.7% vs. 87.0%).

Our study had few limitations as cystoscopy and resections in SPECTRA A and white light were performed by different surgeons; we did not evaluate the recurrence and progressions, and this study has included pT2 lesions also in data analysis which is contrary to the other literature which might have slightly influenced the result of overall percentage.

5 Conclusions

In the case of NMIBC, SPECTRA A cystoscopy has a higher rate of tumor detection than white light cystoscopy, although white light cystoscopy has a higher rate of positive malignant histology among detected lesions. When both modalities are used together, bladder cancer detection enhances.

Abbreviations

CIS	Carcinoma in situ
NBI	Narrow-band imaging
NMIBC	Non-muscle-invasive bladder cancer
SPSS	Statistical package for social sciences
TUR	Trans-urethral resection
TURBT	Trans-urethral resection of bladder tumor
WLC	White light cystoscopy

Supplementary Information

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Supplementary material 1.

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Author contributions

DG, PRS, BDKR, SC, and PRG were involved in performance of research work (clinical work) and writing the article, whereas DG, SC, and PRG were also involved in conception of research. DG was also involved in data management

and data interpretation and analysis. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available as they have not been uploaded in public platform but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Approval of the institutional review board of Institute of Medicine, Tribhuvan University Teaching Hospital, was obtained with approval number as $349/(6-11) G^2/075/76$, as well as informed written consent was obtained from participants.

Consent for publication

The consent for publication was obtained from the participants.

Competing interests

The authors declare that they have no competing interests.

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