

## Early detection of urinary bladder tumors with narrow band imaging

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### Abstract

**Background:** Early diagnosis at the incipient stages of bladder tumors is one of the current issues discussed in modern urology. Although the main method of diagnosis remains cystoscopy, new methods of visualization and detection of bladder tumors have been proposed over the last decade. The purpose of the study was to determine the impact of narrow band imaging (NBI) cystoscopy in the detection of non-muscular invasive bladder tumors in relation to white light (WL) cystoscopy.

**Material and methods:** 57 patients with bladder tumor pathology were diagnosed within the Urology Clinic of Nicolae Testemitanu State University of Medicine and Pharmacy during February 2016 – March 2018. All patients underwent white light cystoscopy, followed by narrow band imaging cystoscopy. The obtained data were comparatively analyzed.

**Results:** Out of the total number of 57 patients diagnosed with bladder tumors, 49 (86%) patients were diagnosed via WL cystoscopy and NBI cystoscopy performed after WL; tumor pathology was also detected in other 8 (14%) patients. The quantitative assessment of tumor lesions revealed 102 lesions, of which 75 (73.5%) were determined through WL and 27 (26.5%) tumor lesions were identified by using the NBI method.

**Conclusions:** Narrow band imaging cystoscopy determines more favorable results in the early diagnosis of non-muscular invasive bladder tumors compared to white light cystoscopy.

**Key words:** narrow band imaging cystoscopy.

### Cite this article

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### Introduction

Bladder cancer is the 11<sup>th</sup> most common malignancy worldwide and one of the most common cancers of the urinary tract. There are two types of bladder cancer: about 75% is non-muscle-invasive bladder cancer (NMIBC), the remaining 25% is muscle-invasive bladder cancer (MIBC) [1].

In the Republic of Moldova, bladder cancer ranks second after prostate cancer, according to the nosological structure of tumors of the urogenital system. Over 15 years, cancer morbidity has almost doubled. Since 2000, due to the implementation of new diagnostic methods, the number of patients detected at the early stages has increased, which allows the improvement of treatment results and the quality of life of patients [2].

The initial treatment of all bladder tumors includes an accurate transurethral resection of the tumor, which is commonly performed by white light (WL) cystoscopy. Full resection of all visible tumors with the histological examination is the standard medical care that must be performed. However, white light cystoscopy may fail to detect flat and small lesions [3]. A small, flat lesion that was, in fact, a tumor or carcinoma *in situ* (CIS) and that was missed at the time of primary diagnosis and surgery can result in recurrence [4]. These overlooked flat lesions have the chance to

recur: about 61% in the 1<sup>st</sup> year and 78% within the 5<sup>th</sup> year, which may even progress into invasive bladder cancer: approximately 17% in the first year and 45% during the 5<sup>th</sup> year [5, 6]. Because of these great rates of recurrence and prevalence, bladder cancer is a large burden on the economy and medical insurance [7].

To optimize the therapeutic and diagnostic approach of NMIBC narrow band imaging (NBI) cystoscopy has been introduced into the medical practical use. NBI is an optical image enhancement technique that uses wavelengths in the blue – 415 nm and green – 540 nm zone of the electromagnetic spectrum. These specific wavelengths are strongly absorbed by hemoglobin and vascular structures, such as tumors and areas of carcinoma *in situ*, making them appear dark brown or green against a pink or white normal mucosal background, without the use of any dye [8]. NBI is useful in endoscopy detection of early stages of gastrointestinal cancer that is, therefore, expected to play a significant role in the diagnosis of NMIBC [9].

The aim of the study is to determine the impact of narrow band imaging cystoscopy in the detection of non-muscular invasive bladder tumors if compared to white light cystoscopy.

## Material and methods

The study was conducted on 57 patients, diagnosed with bladder tumor pathology within the Department of Urology and Surgical Nephrology of *Nicolae Testemitanu* State University of Medicine and Pharmacy, in *Timofei Mosneaga* Republican Clinical Hospital during February 2016 – March 2018. A transversal descriptive study was performed. The patients were selected from all amount of bladder tumor patients treated in our department by cystoscopy with transurethral resection of the bladder tumors, according to the following criteria. The patients inclusion criteria were primary non-muscular invasive bladder cancer, patients aged over 18 and the Eastern Cooperative Oncology Group (ECOG) score 0-2. The exclusion criteria were identified as follows: other non-urothelial tumors, severe comorbidities, ECOG score  $\geq 3$ , and pregnancy. White light cystoscopy was performed in all patients, followed by narrow band imaging cystoscopy; the obtained data were comparatively analyzed. Descriptive statistics was applied. The results of the study are presented as absolute and relative values.

## Results

The demographic data of the patients with NMIBC are presented in table 1.

Of the 57 patients included in the study, based on gender distribution, 48 (84%) were men and 9 (16%) were women. The age ranged between 24-85 years old, the mean age was 65.4 years. The number of patients, included in the 18- 30-year-old age group was 4 (7%), confirming that bladder cancer is an older age-related disease. In 17 (30%) of the patients included in the research, age varied from 31 to 60 years. However, the most common study age group was over 60, which consisted of 36 patients (63%). Another important risk factor for the development of bladder cancer is tobacco smoking. 24 (42%) patients out of 57 are tobacco users.

Tumor analysis showed that the majority of the patient's single bladder tumor was detected in 36 (63%) cases. 2 tumors were discovered in 9 (16%) cases and multiple tumors – 3 cases and more – in 12 (21%) patients. According to bladder tumor volume, 49 (86%) patients included in the study had up to 3 cm size, and massive tumors of over 3 cm were recorded in 8 (14%) cases.

The results of the histopathological examination after the T stage showed that stage Tis was observed in 3 (5%) cases, stage Ta was detected in the majority of the patients that made up 35 (61.5%) cases and stage T1 was in 19 (33.5%) cases.

According to the WHO/ISUP 2004 classification: PUNLMP – papillary urothelial neoplasm of low malignant potential was detected in 3 (5%) cases, low-grade papillary urothelial carcinoma – in 25 (44%) patients and high-grade papillary urothelial carcinoma – in 29 (51%) cases of patients included in research.

Out of the total number of 57 patients, diagnosed with

Table 1

### Patient and tumor demographics

Parameters	Categories	Patients (n=57)
Gender:	Men, n (%)	48 (84%)
	Women, n (%)	9 (16%)
Age, years	Mean age (CI 95%)	65.4 (26-83)
Age group:	18-30 years, n (%)	4 (7%)
	31- 60 years, n (%)	17 (30%)
	60 years and more, n (%)	36 (63%)
Tobacco/Smoking	Yes, n (%)	24 (42%)
Tumor size:	< 1 cm, n (%)	22 (38.5%)
	1-3 cm, n (%)	27 (47.5%)
	> 3 cm, n (%)	8 (14%)
Number of tumors:	Single tumors, n (%)	36 (63%)
	2 tumors, n (%)	9 (16%)
	> 2 tumors, n (%)	12 (21%)
T stage:	Tis (CIS), n (%)	3 (5%)
	Ta, n (%)	35 (61.5%)
	T1, n (%)	19 (33.5%)
Histopathology grade:	PUNLMP, n (%)	3 (5%)
	Low-grade, n (%)	25 (44%)
	High-grade, n (%)	29 (51%)

Note: CI — Confidence Interval, Tis (CIS) — Carcinoma *in situ*, “flat tumor”, Ta — Noninvasive papillary tumor, T1 — Invades subepithelial connective tissue, PUNLMP — papillary urothelial neoplasm of low malignant potential, Low-grade — Low-grade papillary urothelial carcinoma, High-grade — High-grade papillary urothelial carcinoma.

Table 2

### Detection of tumor lesions during white light cystoscopy and narrow band imaging

Characteristics	White light cystoscopy (WL)		Narrow band imaging cystoscopy (NBI)		Total	
	n	%	n	%	n	%
Tumor lesions	75	73.5%	+27	+26.5%	102	100%
Number of patients	49	86%	+8	+14%	57	100%

bladder tumors (tab. 2), this diagnosis was established by WL cystoscopy in 49 (86%) patients, and by NBI cystoscopy performed after WL; the tumor pathology was detected in 8 (14%) patients. The quantitative assessment of tumor lesions revealed 102 lesions, of which 75 (73.5%) were determined through WL and 27 (26.5%) tumor lesions were identified using the NBI method. Of CIS lesions, 1 lesion was detected during WL and other 2 with NBI.

### Discussion

Despite being introduced within a urologic setting more than 10 years ago, NBI is still not being routinely utilized in the detection of NMIBC. Nevertheless, some researches have shown that NBI is more efficient in detecting NMIBC than WL. Bryan et al., who first introduced NBI in the urologic setting, found that 15 additional urothelial carcinomas were detected in 12 of 29 patients (41%) [10].

The proposal of a new cystoscopy visualization technique, should meet at least two requirements: first, it must improve the diagnostic precision in the detection of bladder cancer and second, the implementation of the technique in the transurethral treatment should be capable to decrease the risk of progression and/or recurrence. Different studies have demonstrated an improvement in the diagnostic rate of bladder tumors using NBI, but it remains unclear whether the increase of detection rate is due to the second accurate examination of the bladder only [11].

According to the data of the specialized literature, compared to WL, NBI can detect more tumors in 9%-56% additional patients [3, 10, 12-16]. In our study, NBI discovered additional pathologies in extra 14% of patients.

According to the acknowledged superiority of NBI in the detection of extra tumors, as well as in our research, NBI has revealed additional 26.5% of tumor lesions. However, the site of the resection with NBI control in the transurethral resection algorithm remains to be clearly determined [17].

However, it has been observed that visibility during NBI was restricted due to inflammation and bleeding, making it hard to reveal and resect tumor lesions. It may be the case because wavelengths during NBI are actively absorbed by free hemoglobin, which occurs in bleeding [14].

In the detection of additional tumors, NBI cystoscopy is superior to WL cystoscopy. NBI is not perfect for the primary resection of multiple and large tumors due to poor visualization. However, NBI can influence the finding of residual or missed tumors after initial resection under WL. It may be right to propose the adage "NBI to detect, WL to resect" for future use [18].

### Conclusions

Narrow band imaging cystoscopy determines more favorable results in the early diagnosis of non-muscular-invasive bladder tumors compared to white light cystoscopy. Only adequate equipment is required to perform the NBI

cystoscopy. The technique is easy to apply, just pushing on a single button, without using additional medical substances. In our research, NBI was able to detect additional pathologies in 8 (14%) patients and detected 27 (26.5%) additional tumor lesions.

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#### Authors' contribution

IV and AP acquired, interpreted the data, drafted the first manuscript, GS performed most of the analyzed interventions, VG designed the trial and revised the manuscript critically. All the authors revised and approved the final version of the manuscript.

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#### Ethics approval and consent to participate

The research was approved by the Research Ethic Board of *Nicolae Testemitanu* State University of Medicine and Pharmacy (protocol No 4 of December 16, 2019). Written informed consent was obtained from all participants in the study.

#### Conflict of Interests

The authors have no conflict of interests to declare.

