

# Narrow band imaging (NBI) cystoscopy and assisted bipolar TURBT: A preliminary experience in a single centre

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**Summary** *Objective: The aim of this study was to compare, in order to increase our ability to detect bladder cancer, the predictive power of narrow band imaging (NBI) versus white light cystoscopy (WL).*

*The secondary objective was to evaluate how the preoperative use of NBI cystoscopy can increase the ability to detect bladder lesions in terms of status, multi-focality and dimensions. Materials and methods: Between June 2010 and April 2012, 797 consecutive patients, 423 male and 374 female, affected by suspected bladder cancer lesions, underwent to WL plus NBI cystoscopy and subsequently to WL Bipolar Gyrus PK (Olympus, Tokyo, Japan) transurethral resection of bladder tumour (WL-TURBT). The average follow-up was 24 (16-38) months. Mean age was 67.7 yrs. (range 46-88).*

*All the patients underwent by same surgeon to WL resection (WL-TURBT) of the previously identified lesions by same surgeon. All the removed tissue was sent separately for histological evaluation after mapping the areas of resection on a topographic sheet.*

*Results: In our study we considered 797 patients that matched our inclusion criteria. Through the use of WL cystoscopy, we identified 603 patients (75.53%) with suspicious lesions, instead, with the use of light NBI, we found 786 patients with suspicious lesions (98.49%). The use of NBI cystoscopy increases by approximately 30% the specific ability to detect lesions not otherwise visible with WL cystoscopy (OR 21.9 and RR 1.30), in particular for patients with lesions size < 3 cm (OR 24.00; RR 1.40), unifocal (OR: 22.28; RR 1.47) and recurrent (OR 58.4; RR 1.34). Pathology demonstrated the presence of cancer in 512 (64.2%) patients, of whom 412 (51.8%) were visible both with WL cystoscopy and NBI cystoscopy.*

*In our experience, only 11 (1.38%) lesions were only positive at WL cystoscopy (negative at NBI cystoscopy) thus 501 (62.8%, OR 10.13; RR 1.21) patients showed bladder oncological lesions positive at NBI cystoscopy. In these patients, the use the NBI Cystoscopy has better highlighted a recurrence ( $p < 0.005$ ; OR 22.8, RR 1.23; 95% CI-1.13 to 0.24) or a lesion < 3 cm ( $p < 0.05$ ; OR 11.4, RR 1.30; 95% CI-0.18 to 0.29) or a unifocal lesion ( $p < 0.005$ ; OR 10.38, RR 1.34, CI 0.18 to 0.30).*

*Conclusions: The use of NBI cystoscopy, significantly increases by approximately 30% our predictive power to identify neoplastic lesions, especially unifocal or < 3 cm or recurrent lesions. Following WLTURBT, stage, dimension and focality are statistically significant determinants ( $p < 0.001$ ) of the bladder oncological lesions detected by NBI cystoscopy rather than by WL cystoscopy.*

**KEY WORDS:** Bladder cancer; Narrow band imaging (NBI); Cystoscopy; Bipolar TURBT.

Submitted 15 August 2017; Accepted 18 August 2017

## INTRODUCTION

Bladder cancer is a very common malignant genitourinary tumour and transitional cell carcinoma accounts for almost 90% of all primary bladder tumours. The standard method used to diagnose bladder cancer and monitor patients in the follow-up is *white light* (WL) cystoscopy. Unfortunately, this method may not be able to detect small papillary lesions and *carcinoma in situ* (CIS) lesions (1). Tumours not detected in the course of TURBT will appear later as a relapse, and some of them may become invasive. This calls for the development of better endoscopic methods, namely fluorescence (2-4), and *narrow banding imaging* (NBI) cystoscopy (5). NBI is a technique for improving optical images. It is designed for endoscopy and its purpose is to increase the contrast between mucosal surfaces and microvascular structures without resorting to dyes. This technique is based on a phenomenon by which the depth of light penetration into the mucosa increases as the wavelength increases. In NBI, the tissue surface is illuminated with narrow band light, with wavelengths in the blue and green light spectra (415 nm and 540 nm respectively) (6). The primary objective of this study was to assess the ability of NBI to increase the detection rate of lesions not visible with WL cystoscopy. The secondary objective was to evaluate how the preoperative use of NBI cystoscopy can increase the ability to detect bladder lesions in terms of status, focality and dimensions after TURBT, as opposed to WL cystoscopy.

## MATERIALS AND METHODS

From June 2010 to April 2012, 797 consecutive patients (pts.), 423 male and 374 female, affected by primary (461 pts, 57.8%), recurrent (336 pts, 42.1%), unifocal (491 pts., 61.6%), multifocals (306 pts., 38.3%), < 3 cm (570 pts., 71.5%) and > 3 cm (227 pts., 28.4%) suspicious non-muscle invasive bladder tumours, underwent WL plus NBI cystoscopy and WL plus NBI Bipolar TURBT with a Bipolar Gyrus PK Scalpel in saline (TURis). The mean follow-up was 24 (16-38) month. Indication of suitability for TURBT was provided on the basis of the *EAU Guideline* 2010. All patients provided written informed consent prior to the study.

All procedures were carried out initially by performing a cystoscopy with white light. The characterization of the sites, including the number, size and appearance of the neoplasms, were recorded on a topographic bladder map.

No conflict of interest declared.

Subsequently a cystoscopy with NBI was carried out to confirm what had been seen by white light examination, and to report other suspicious areas at NBI light. These, too, were recorded on the topographic bladder map. All endoscopic resections were performed with an Gyrus PK scalpel, bipolar generator (*Olympus, Tokyo, Japan*), in saline, with optics at 30 degrees. Resection of each lesion was carried out with white light by the same surgeon who had performed cystoscopy and all histopathological evaluations were performed by the a single pathologist on the basis of 2004 WHO classification.

In order to evaluate the efficacy of NBI vs WL cystoscopy, we conducted a hypothesis test to determine whether the difference between the two proportions of positive results obtained by WL and by NBI ( $p_{wl}$  and  $p_{nbi}$ ) was significant. The two-proportion z-test was administered on the overall sample and, after TURBT, on the histologically positive set of patients. The appropriate test assumes a model for matched pairs (7).

The analysis was carried out in relation to status (primitive and recurring), focality and dimension of detected lesions. All Z-scores (before and after TURBT) were largely below the selected significance level ( $\alpha = 0.05$ ).

The related confidence intervals were also calculated.

In addition we estimated *odds ratio* (OR) and *relative risk* (RR) to quantify how strong is the difference between NBI and WL results. Logistic regression was applied to predict which lesions were in fact malignant after NBI cystoscopy. Multiple linear regression analyses tested the association between different prognostic variables and their impact on the ability to identify bladder lesions following NBI cystoscopy.

## RESULTS

In our study we considered 797 patients that matched our inclusion criteria. WL cystoscopy was used to identify 603 patients (75.5%) with suspicious lesions, while the use of NBI following WL allowed identifying a total of 786 patients (98.49%).

A total of 1,571 suspicious lesions were identified in 797 patients, some of whom had multifocal lesions. Of these lesions, 496 (50.6%) were single lesions and 1,075 (49.3%) multiple lesions. Of these 1,571 lesions, 1,337 (85.11%) were identified by WL cystoscopy alone. The subsequent use of NBI light allowed finding 234 lesions (14.89%), not visible otherwise with WL, reaching a total of 1,571 suspicious lesions. The use of NBI cystoscopy increases by approximately 30% the ability to detect lesions not otherwise visible with WL cystoscopy alone (OR 21.9 and RR 1.30), particularly in patients with lesion size < 3 cm

**Table 1.**  
WL and NBI cystoscopy results (before TURBT).

All cases	Yes	No	Total	Odds	Odds ratio	Absolute risk	Relative risk
NBI positive	786	11	797	66.14		0.985	
WL positive	603	194	797	3.087	21.9	0.755	1.304
<b>Primitive</b>							
NBI positive	452	9	461	45.10		0.978	
WL positive	354	107	461	3.26	13.79	0.785	1.27
<b>Recurrent</b>							
NBI positive	334	2	336	167.0		0.994	
WL positive	249	87	336	2.86	55.34	0.741	1.341
<b>Unifocal</b>							
NBI positive	481	10	491	43.6		0.978	
WL positive	325	166	491	1.95	22.28	0.662	1.47
<b>Multifocal</b>							
NBI positive	305	1	306	305.0		0.997	
WL positive	277	29	306	9.55	31.93	0.905	
<b>&lt; 3 cm</b>							
NBI positive	560	10	570	56.0		0.982	
WL positive	399	171	570	2.33	24.00	0.700	1.404
<b>&gt; 3 cm</b>							
NBI positive	226	1	227	22.6		0.991	
WL positive	203	24	227	8.45	13.3	0.894	1.108

(OR 24.00; RR 1.40), unifocal (OR: 22.28; RR 1.47) and recurrent lesions (OR 58.4; RR 1.34) (Table 1).

All 797 patients were subjected to bipolar TURBT with Gyrus PK (*Olympus, Tokyo, Japan*). The final histology results demonstrated the presence of cancer in 512 (64.2%) patients (Table 2), of whom 412 (51.8%) were visible both with WL cystoscopy and NBI cystoscopy.

In our experience, 501 (62.8%) patients showed bladder oncological lesions positive in NBI cystoscopy thus only 11 (1.38%) lesions were only positive at WL cystoscopy. Totally, 1,571 cancer lesions were identified as suspicious, 1,051 lesions (66.85%) were positive for malignancy and 520 (33.14%) negative for malignancy.

The histology after WLTURBT showed the ability of NBI cystoscopy to identify, in more than 20%, a lesion oncologically significant than was not evident at WL cystoscopy (Table 2).

**Table 2.**  
WL and NBI cystoscopy results (histologically positive after TURBT).

All cases	Yes	No	Total	Odds	Odds ratio	Absolute risk	Relative risk
NBI positive	501	11	512	41.6		0.977	
WL positive	412	100	512	4.12	10.1	0.805	1.21
<b>Primitive</b>							
NBI positive	317	9	326	31.6		0.969	
WL positive	263	63	326	4.17	7.57	0.807	1.20
<b>Recurrent</b>							
NBI positive	184	2	186	92.0		0.989	
WL positive	149	37	186	4.02	22.84	0.801	1.235
<b>Unifocal</b>							
NBI positive	290	10	300	26.2		0.963	
WL positive	215	85	300	2.5	10.38	0.717	1.344
<b>Multifocal</b>							
NBI positive	211	1	212	211.0		0.995	
WL positive	197	15	212	13.3	16.06	0.929	1.071
<b>&lt; 3 cm</b>							
NBI positive	309	10	319	30.9		0.989	
WL positive	223	85	319	2.70	11.40	0.730	1.326

Thanks to use of the NBI light we identified 500 patients with lesions NBI positive oncologically significant (62.7%; OR 10.13; RR 1.21). In particular, NBI cystoscopy improved bladder neoplasms detection rate of WL cystoscopy in recurrent (OR 22.8 vs 7.5; RR 1.23 vs 1.20), < 3 cm (OR 11.4 vs 7.4; RR 1.30 vs 1.06) and unifocal tumours (OR 10.38 vs 16.06; RR 1.34 vs 1.07). The difference in detection rate is not so high as in recurrences in primitive lesions (RR 1.23 vs 1.20). In 512 patients with tumors detected after WL TURBT, the use of the NBI cystoscopy has more frequently demonstrated a recurrent injury ( $p < 0.005$ ; 95% CI-1.13 to 0.24) or a lesion < 3 cm ( $p > 0.05$ ; 95% CI-0.18 to 0.29) or an unifocal lesion ( $p < 0.005$ ; CI 0.18 to 0.30). It is clear that with the NBI cystoscopy, compared to WL cystoscopy alone, we could identify a statistically significantly greater number of neoplastic lesions, in relation to pathological stage and grade ( $p < 0.005$ , IC-95% 0.13- 0.21 and  $p < 0.005$ ; 95% CI-0.14 to 0.24, respectively). In particular, we highlighted an higher number of CIS lesions ( $p < 0.005$ , IC-95% from 0.48 to 0.92) and HG lesions ( $p < 0.005$ ; CI-95%. In our experience we identified in the group of 512 patients with bladder cancer confirmed after WLTURBT, 88 patients who had bladder neoplastic lesions detected only through the use of NBI cystoscopy (WL cystoscopy negative) with an adjunctive detection rate (ADR) of 11.4%.

The overall false positive detection rate was 33.14% (521 lesions) and after NBI cystoscopy this rate was 39.44%. Using the logistic model, we observed that the use of NBI cystoscopy significantly increases our predictive power to identify lesions not visible with WL cystoscopy: primitive lesions (95% CI 2.97-1.095;  $p < 0.02$ ), multifocal (95% CI 0.06-0.12;  $p < 0.0001$ ), and < 3 cm (95% CI 0.05-0.13;  $p < 0.001$ ). It is interesting to note that HG (high-grade) neoplasms (95% CI 0.14-0.24;  $p < 0.001$ ) tend to reach a value very close to significance compared to papillary urothelial neoplasms of low malignant potential (PUNMP) (95% CI 0.004-0.04;  $p < 0.005$ ) and low grade neoplasms (low-grade) (95% CI 0.10-0.21;  $p < 0.001$ ).

Using NBI cystoscopy, the likelihood of identifying patients with a primitive tumour, compared to patients with a relapse, reached approximately 80% (point estimate 1.790, 95% CI 1.095-2.927). In a patient with a unifocal tumour, the likelihood of having a bladder tumour detected by NBI cystoscopy increases by about seven times compared with those a multifocal tumour (point estimate 0.153, 95% CI 0.060-0.390).

NBI cystoscopy has also proved to be very useful in CIS. By comparing the sensitivity, specificity, positive predictive value and negative predictive value (NPV) of NBI versus WL cystoscopy for CIS lesions, we noticed that sensitivity and NPV were the statistically significant values (100%, 95% CI,  $p < 0.05$ , and 80.62%, 95% CI, 100%, 95% CI,  $p < 0.05$ , and 78.35%, respectively). NBI cystoscopy increases the likelihood of detecting a CIS lesion by about one and a half times compared to a patient with a pTa lesion ( $p < 0.001$ ).

## DISCUSSION

Bladder cancer is considered the most expensive tumour both in terms of costs for patients per year and in terms

of operating costs per patient. Up to 70% of patients with NMIBC will develop a recurrence after TURBT (8).

Photodynamic diagnosis with Hexaminolevulinat blue light cystoscopy has made significant advances in terms of rates (9) of diagnostic accuracy and recurrence for the detection of CIS lesions (10), as well as pTa and pT1 tumours (11).

However, some questions have been raised as regards the cost-effectiveness of this approach.

Numerous studies have demonstrated the ability to display improved images of the surface layers of the various apparatuses using NBI (10, 12-18). NBI is a diagnostic imaging technique that improves the contrast between mucosal surfaces and microvascular structures, based on the wavelength-dependent increase in the depth of light penetration into the mucosa, without additional costs to conventional cystoscopy and without lengthening the operating time.

In our experience, using WL and NBI cystoscopy together, we have identified 234 lesions (14.1%) that WL cystoscopy alone would not have otherwise been able to identify. However, the essential result is not so much the number of lesions that can be identified using NBI as opposed to the number of those visible with WL alone, but rather how many of these are neoplasms. Of these 234 lesions identified with NBI alone, as many as 127 were bladder tumours (12.17%) in 88 patients (11,4%). Comparing our experience with the data available in the literature, we were able to find some interesting data.

The experience of *Bryan et al.* (5) showed a greater capacity to identify lesions ( $\Delta = -7.15\%$ ) compared to our results, while our technique showed an improvement ( $\Delta = +3.81\%$ ) compared to the results of *Herr et al.* (19)

In fact, we detected 12.17% of lesions not otherwise detectable, by WL cystoscopy, thus placing our experience between the two aforementioned studies.

To better understand the diagnostic efficacy of the NBI compared to WL cystoscopy an analysis of the odds ratio was performed (positive results against the negatives for each type of investigation). The two methods of cystoscopy did not change the state of the patient on which they were performed. Therefore 797 cases can be considered as a sample to which two different but non-interacting methods were administered.

The odds ratio, measuring the frequency of success of a technique respect to another, in our case highlights the success of NBI. In fact a value greater than 1 indicates greater effectiveness of NBI in the detection of lesions against the non-detection. If we consider all the cases, the calculated value of OR = 21.90 (Table 1) shows a strong prevalence of NBI identification of lesions. A more intuitive interpretation of the results is made up of the relative risk. In fact, this index relates the absolute risk (ratio of successes and the total number of cases) of the two methods. In this way it is possible to assess with greater immediacy the effectiveness of the method NBI compared to WL.

The use of NBI cystoscopy has therefore allowed improving our ability to overall detect lesions not otherwise visible with WL cystoscopy alone (ADR= +30%) in terms of focality (unifocals: OR 22.28; RR 1.47) as well as dimensions < 3 cm, OR 24.00; RR 1.40) and status (recurrences: OR 58.4; RR 1.34).

Following WL TURBT, we observed 500 pts with NBI bladder oncological lesions, with a ADR of 20%. The use of NBI cystoscopy, significantly increases our predictive power to identify lesions not visible with WL cystoscopy, especially for unifocal lesions ( $p < 0.005$ , IC-95% 0.18-0.30), those  $< 3$  cm ( $p < 0.005$ , IC-95% 0.18-0.29) and recurrent lesions ( $p < 0.005$ , IC-95% 0.13-0.24).

Similarly, through the use of NBI light, we observed that, as regards pathologic stage and grade, we registered an overall increase in bladder lesion detection rate ( $p < 0.005$ , IC-95% 0.13-0.21 and  $p < 0.005$ ; IC-95% 0.14-0.24, respectively).

In our experience, the use of NBI cystoscopy significantly increased the ability to detect both CIS lesions ( $p < 0.0001$ ) and HG ( $p < 0.005$ ) (Table C: d-e) compared to WL cystoscopy. The relative risk (RR) to identify a bladder tumour with NBI TURBT is 3 times greater in the case of a pTa LG lesion and about 8 times greater if the lesion is a CIS. In our experience, as well as in Herr's experience (19), the use of NBI cystoscopy in comparison to WL cystoscopy was particularly useful in the identification of CIS lesions, showing a sensitivity and NPV of 100% vs. 80.62% and 100% vs. 78.35% ( $p < 0.05$ ) respectively.

By contrast, we recorded a non-significant specificity and PPV. In our experience, the overall false positive detection rate was 33.14% (521 lesions) and after NBI cystoscopy this rate amounted to 39.44%. These data overlap with other international experiences.

## CONCLUSIONS

This is the first study in the literature in which the ability of NBI cystoscopy to increase the ability to detect suspicious bladder lesions was compared with the use of WL cystoscopy alone in the same patient. The use of NBI cystoscopy, significantly increases our predictive power to identify lesions not visible with WL cystoscopy, especially for unifocal lesions, those  $< 3$  cm and recurrent lesions. Following WL TURBT, status, dimension and focality are statistically significant determinants in order to detect bladder oncological lesions by NBI cystoscopy rather than WL cystoscopy.

In conclusion, NBI is an effective method for the identification of bladder lesions and can be useful in supporting WL cystoscopy.

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