# Thulium laser *en bloc* resection versus conventional transurethral resection of urinary bladder tumor: A comparative prospective study

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Abstract Background: Transurethral resection of bladder tumors (TURBT) is the standard management for urinary bladder tumors; however, new techniques as Thulium laser *en bloc* resection of bladder tumors (TmLRBT) have been introduced as a substitute to TURBT.

**Objectives:** In this study safety, efficacy, and tumor recurrence after TmLRBT and TURBT were prospectively compared in patients with primary (<4 cm) bladder tumors.

**Patients and Methods:** Between August 2019 and May 2021, patients with primary (<4 cm) bladder tumors were enrolled. Patients were randomized between the two procedures. All perioperative data were collected prospectively. Pathological specimen findings and recurrence rates were reported during follow-up visits. **Results:** Sixty patients underwent TURBT, and another 60 had TmLRBT. No significant differences were detected in patient demographics or preoperative tumor characteristics between the two groups. Operation time was less (28.2 vs. 38.9 min, P < 0.001), and rate of bladder perforation was lower with TmLRBT compared to TURBT (3.3% vs. 15.0%, P = 0.027). In the TmLRBT group, higher rate of muscle detection (95.0% vs. 78.3%, P < 0.001) in the pathological specimen, and lower rate of tissue destruction (0.0% vs. 21.6%, P < 0.001) were obtained compared to TURBT. Recurrence rate in cases of nonmuscle invasive bladder cancer was lower with TmLRBT (6.7% vs. 33.0%, P < 0.001).

**Conclusion:** In this study, TmLRBT showed reduced operative time with lower perforation rates. Higher detection of detrusor muscle and less tissue destruction in the pathological specimen were obtained with TmLRBT, as well as lower rates of tumor recurrence. These findings suggest that TmLRBT is a safe and efficacious substitute to TURBT in tumors <4 cm.

Keywords: *En bloc* resection, nonmuscle invasive bladder cancer, TmLRBT, transurethral resection of bladder tumors, urothelial carcinoma

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# **INTRODUCTION**

Urothelial carcinoma ranks second among genitourinary tumors.<sup>[2]</sup> Conventional transurethral resection of

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Quick Response Code:	Quick Response Code: Website:			
	www.urologyannals.com			
	<b>DOI:</b> 10.4103/ua.ua_59_22			

bladder tumors (TURBT) still has the upper hand in the management of primary bladder tumors.<sup>[1]</sup> However, TURBT has its shortages such as obturator nerve reflex,

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**How to cite this article:** Badawy A, Sultan SM, Marzouk A, El-Sherif E. Thulium laser *en bloc* resection versus conventional transurethral resection of urinary bladder tumor: A comparative prospective study. Urol Ann 2023;15:88-94.

and tissue charring that affects detrusor muscle detection and proper pathological specimen staging. Furthermore, recurrence rates are thought to be high after TURBT due to incise and scatter resection technique.<sup>[2]</sup> Thulium LASER *en bloc* resection was introduced as a substitute to TURBT proposed to overcome its shortages.<sup>[3]</sup> In this study, the two techniques were prospectively compared regarding safety, efficacy, and recurrence rates.

# PATIENTS AND METHODS

This study was conducted between August 2019 and May 2021. Patients presenting with primary urinary bladder tumors were selected. Patients were randomized to have either conventional TURBT or TmLRBT. The two procedures were done by the same surgeon. All patients were counseled about the study and signed an informed written consent. The study was approved and registered with our local university ethical committee.

Patients with tumors that are more than 4 cm in size, have broad bases [Figure 1a], or situated in the anterior wall or bladder dome were excluded. Furthremore, recurrent cases and cases with advanced stage in computed tomography were excluded.

Thulium LASER with a 2-micron continuous wavelength (Revolex Duo 2 micron) and a 550 nm laser fiber (LISA LASER products, Lindau–Katlenburg– Germany) were used in the TmLRBT group. Laser settings were energy: 1.5 joules, pulses: 20 hertz, and the resultant power was 30 watts (W). A 26 Fr. resectoscope was used

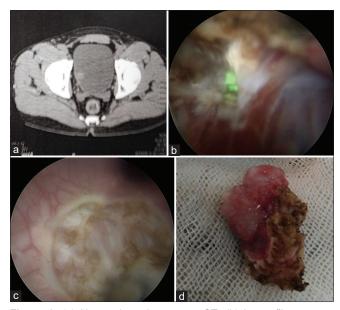


Figure 1: (a) Narrow-based tumor on CT. (b) Laser fiber cutting through muscle fibers. (c) Tumor bed after *en bloc* resection. (d) *En bloc* resected bladder tumor

to introduce the laser fiber and resection starts with circular incision surrounding the tumor leaving a safety margin of 0.5 cm to the tumor. After the completion of the incision, dissection of the mucosa was done bluntly from the deeper layers by elevating the mucosal patch toward the bladder lumen leaving the bladder-facing part of the specimen intact. After that, the remaining adhesions between the dissected mass and the bladder were removed with the laser [Figure 1b and c]. The tumor was delivered outside the bladder endoscopically as one piece using the ELIKE evacuator with small-sized tumors or using a grasper for larger tumors [Figure 1d]. Any bleeding is coagulated by laser. Two cold-cup biopsies were taken from the tumor base. Conventional TURBT was done using 26fr continuous resectoscope with a cutting loop electrode (STORZ. Tuttlingen, Germany). The cutting and coagulation power were set to 150 W and 100 W, respectively. Resection started from the lateral side of the tumor and done in pieces till reaching the muscle with safety margin of about 1-1.5 cm. Random biopsies were taken if necessary. Complete resection of the tumor was done on all patients in both procedures. Intravesical injection of Doxorubicin (50 mg) was given to all patients within 6 h postoperatively except in cases with suspected perforation or gross hematuria despite continuous bladder irrigation where injection was delayed till hematuria subsided.

Second look is done 2–6 weeks in some patients according to the European Association of Urology guidelines to check complete resection and get detrusor muscle if not obtained in the first resection.<sup>[2]</sup> Patients were followed up to detect tumor recurrences for 12 months. According to the risk stratification of the International Bladder Cancer Group, we performed revision cystoscopy every 3 months in intermediate and high-risk tumors and at 3 and 12 months in low-risk tumors.<sup>[2]</sup>

#### Statistical analysis

Data were collected, tabulated, and statistically analyzed using an IBM-compatible personal computer with Statistical Package for the Social Sciences (SPSS) version 23 (SPSS Inc. Released 2015. IBM SPSS statistics for windows, version 23.0, Armonk, NY: IBM Corp.). Qualitative data were expressed as Number (N), percentage (%), while quantitative data were expressed as mean (x), standard deviation, and range (minimum-maximum).

Two tests were used to analyze data. Student's *t*-test (*t*) is a test of significance used for comparison of quantitative variables between two groups of normally distributed data, while Mann–Whitney's test (U) was used for comparison of quantitative variables between two groups of not normally distributed data. Chi-square test ( $\chi 2$ ) was used to study the association between qualitative variables. Whenever any of the expected cells were <5, Fischer's Exact test was used. Significant test results were quoted as two-tailed probabilities. The significance of the obtained results was judged at the 5% level (P > 0.05).

#### RESULTS

A total of 120 patients were enrolled in the study; 60 patients had conventional TURBT, while the other 60 had TmLRBT. Males were 112, while only 7 patients were female. There were no significant differences in mean patient age, sex, residence, comorbidities, or smoking history between the two groups [Table 1]. All patients had one mass except two patients in the TmLRBT group and five patients in the conventional TURBT group (P = 0.439). Mean tumor size and tumor locations were not significantly different between the two groups [Table 2].

Operation time was shorter in TmLRBT (28.2  $\pm$  6.1 vs. 38.9  $\pm$  8.0 min, P < 0.001). Obturator jerk occurred in 13 cases in the TURBT cohort, while it was not seen with TmLRBT (21.6% vs. 0.0%, P < 0.001). In addition, bladder perforation (15% vs. 3.3%, P = 0.027) and perioperative

Table 1: Comparison between laser *en bloc* resection and conventional method (transurethral resection of bladder tumors) in urothelial carcinoma regarding socio-demographic and past medical history

	Laser <i>en bloc</i> resection ( <i>n</i> =60), <i>n</i> (%)	Conventional method (TURBT) ( <i>n</i> =60), <i>n</i> (%)	Test of significance $(\chi^2)$	Р
Sociodemographic characteristics				
Age (years)				
Mean±SD	64.53±8.48	61.83±7.67	<i>t</i> =1.830	0.070
Range	45-85	32-76		
Age groups (years)				
<65	31 (51.7)	37 (61.7)	1.222	0.269
≥65	29 (48.3)	23 (38.3)		
Sex				
Male	55 (91.7)	57 (95.0)	FE=0.536	0.717
Female	5 (8.3)	3 (5.0)		
Residence				
Rural	34 (56.7)	39 (65.0)	0.870	0.349
Urban	26 (43.3)	21 (35.0)		
Medical history				
Past medical history				
DM	22 (36.7)	21 (35.0)	3.57	0.312
HTN	5 (8.3)	12 (20.0)		
DM and HTN	7 (11.7)	5 (8.3)		
No	26 (43.3)	22 (36.7)		
Smoking				
Yes	26 (43.3)	34 (56.7)	2.130	0.144
No	34 (56.7)	26 (43.3)		

 $\chi^2$ : Chi-square test, FE: Fischer's exact test, *t*: Student *t*-test, Range: Minimum–maximum, SD: Standard deviation, TURBT: Transurethral resection of bladder tumors, DM: Diabetes mellitus, HTN: Hypertension

Table 2: Comparison between laser en bloc resection and conventional method (transurethral resection of bladder tumors)	in
urothelial carcinoma regarding tumor details	

Tumor details in CT	Laser en bloc resection (n=60), n (%)	Conventional method (TURBT) (n=60), n (%)	Test of significance	Р
Number				
1 mass	58 (96.7)	55 (91.7)	FE=1.365	0.439
2 mass	2 (3.3)	5 (8.3)		
Size of 1 <sup>st</sup> mass (cm)				
Mean±SD	1.85±0.49	1.81±0.58	<i>t</i> =0.410	0.684
Range	1.5-3.0	1.0-3.0		
Size of 2 <sup>nd</sup> mass (cm)				
Mean±SD	1.25±1.06	1.40±0.65	<i>U</i> =0.203	0.839
Range	0.5-2.0	0.5-2.0		
Site				
Basal	18 (30.0)	25 (41.7)	$\chi^2 = 8.49$	0.075
Right lateral	20 (33.3)	8 (13.3)		
Left lateral	20 (33.3)	23 (38.4)		
Basal and right lateral	2 (3.3)	2 (3.3)		
Basal and left lateral	0	2 (3.3)		

 $\chi^2$ : Chi-square test, FE: Fischer's exact test, t: Student's t-test, Range: Minimum–maximum, U: Mann–Whitney test, SD: Standard deviation, TURBT: Transurethral resection of bladder tumors, CT: Computed tomography

bleeding (6.4% vs. 0.0%, P = 0.042) rates were significantly higher with conventional TURBT. [Table 3]

Postoperatively, length of hospital stays  $(1.0 \pm 0.2 \text{ vs.} 1.2 \pm 0.4 \text{ days}, P = 0.002)$  and catheter time  $(3.1 \pm 0.5 \text{ vs.} 3.7 \pm 0.9 \text{ days}, P < 0.001)$  were shorter in the TmLRBT group. Tissue destruction in pathology specimen was not present with TmLRBT (0.0% vs. 51.7%, P < 0.001). This was associated with higher detection rates of detrusor muscle in the pathological specimen in the TmLRBT group (95.0% vs. 73.0%, P = 0.001) [Table 4].

One hundred and six cases were staged as nonmuscle invasive bladder cancer: 54 in the TmLRBT cohort, and 52 in the conventional TURBT cohort. Follow-up of these cases for 12 months revealed a lower rate of early tumor recurrence in the TmLRBT group compared to the conventional TURBT group (6.7% vs. 33.3%, P < 0.001). The site of tumor recurrence (P = 711) and time to recurrence (P = 914) were not significantly different between the two groups [Table 5]. Tumor recurrence was seen in intermediate and high-risk tumors, but not in low-risk ones (P < 0.001) [Table 6].

## DISCUSSION

Urothelial carcinoma of the urinary bladder is common. Till now, conventional TURBT is the gold standard

Table 3: Comparison between laser en bloc resection and conventional method (transurethral resection of bladder tumors) in
urothelial carcinoma regarding operative data, intraoperative and postoperative complications

	Laser en bloc resection (n=60), n (%)	Conventional method (TURBT) (n=60), n (%)	Test of significance (FE)	Р
Operative time (min)				
Mean±SD	28.25±6.11	38.90±8.09	t=8.133	< 0.001
Range	19.0-40.0	23.0-55.0		
Perforation				
Yes	2 (3.3)	9 (15.0)	4.90	0.027
No	58 (96.7)	51 (85.0)		
Bleeding				
Yes	0	4 (6.7)	4.140	0.042
No	60 (100)	56 (93.3)		
Obturator jerk				
Yes	0	13 (21.7)	14.579	< 0.001
No	60 (100)	47 (78.3)		
Catheter time (days)				
Mean±SD	3.13±0.50	3.77±0.98	t=4.451	< 0.001
Range	3.0-5.0	3.0-5.0		
Hospital stay (days)				
Mean±SD	1.07±0.25	1.28±0.45	U=3.110	0.002
Range	1.0-2.0	1.0-2.0		

FE: Fischer's exact test, SD: Standard deviation, TURBT: Transurethral resection of bladder tumors

Table 4: Comparison between laser en bloc resection and conventional method (transurethral resection of bladder tumors) in
urothelial carcinoma regarding tumor pathology

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	Laser en bloc resection (n=60), n (%)	Conventional method (TURBT) (n=60), n (%)	Test of significance (χ <sup>2</sup> )	Р
Tumor pathology				
Tissue				
destruction				
Yes	0	31 (51.7)	41.798	< 0.001
No	60 (100)	29 (48.3)		
Muscle presence				
Yes	57 (95.0)	44 (73.3)	10.568	0.001
No	3 (5.0)	16 (26.7)		
Staging				
Ta	18 (30.0)	24 (40.0)	1.393	0.498
T1	34 (56.7)	30 (50.0)		
Invasive TCC	8 (13.3)	6 (10.0)		
Grading				
Low grade	15 (25.0)	24 (40)	3.094	0.213
High grade	37 (61.7)	30 (50)		
Invasive TCC	8 (13.3)	6 (10)		
Risk grouping				
High	25 (46.3)	32 (61.5)	2.520	0.284
Intermediate	8 (14.8)	5 (9.6)		
Low	21 (38.9)	15 (28.8)		

TURBT: Transurethral resection of bladder tumors, TCC: Transitional cell carcinoma

	Laser <i>en bloc</i> resection ( <i>n</i> =60), <i>n</i> (%)	Conventional method (TURBT) ( <i>n</i> =60), <i>n</i> (%)	Test of significance $(\chi^2)$	Р	
Outcome of TCC					
Invasive					
Radical cystectomy	4 (6.7)	6 (10)	0.440	0.803	
Radio and chemotherapy Noninvasive	2 (3.3)	2 (3.3)			
Follow-up	54 (90.0)	52 (86.7)			
Risk grouping					
High	25 (46.3)	32 (61.5)	2.520	0.284	
Intermediate	8 (14.8)	5 (9.6)			
Low	21 (38.9)	15 (28.8)			
Follow-up					
Free	50 (83.3)	32 (53.3)	14.590	< 0.001	
Recurrent	4 (6.7)	20 (33.3)			
Site of recurrence					
At the old site of resection	2 (50)	12 (60.0)	0.140	0.711	
Out of the old site of resection	2 (50)	8 (400)			
Time of recurrence					
After 3 months	2 (50)	8 (40.0)	0.180	0.914	
After 6 months	1 (25)	7 (35.0)			
After 12 months	1 (25)	5 (25.0)			

Table 5: Comparison between laser *en bloc* resection and conventional method (transurethral resection of bladder tumors) in urothelial carcinoma regarding recurrence follow-up

TURBT: Transurethral resection of bladder tumors, TCC: Transitional cell carcinoma

Tab	le 6:	Relation	between	risk	and	recurrence	( <i>n</i> =24)
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Risk grouping	<b>Recurrence</b> ( <i>n</i> =24), <i>n</i> (%)	No recurrence ( <i>n</i> =96), <i>n</i> (%)	Test of significance ( $\chi^2$ )	Р
High	15 (62.5)	16 (16.7)	28.02	< 0.001
Intermediate	9 (37.5)	31 (32.3)		
Low	0	49 (51.0)		

management option for urinary bladder tumors. However, new modalities have been developed to overcome the drawbacks of conventional TURBT. One of these new modalities is the Thulium laser *en bloc* resection (TmLRBT).<sup>[2]</sup> Thulium laser has a tunable wavelength of  $1.75-2.22 \,\mu$ m, which is much closer to the water absorption peak value (1.94  $\mu$ m). Its thermal damage depth was theoretically calculated as only 0.2 mm and its penetration in water is 250  $\mu$ m.<sup>[4]</sup> Due to these characteristics, thulium laser has higher vaporization and cutting efficiency with excellent hemostasis due to continuous energy output which make a thin layer of eschar on the surface of the wound with clear cutting depth identification.

In this study, we prospectively compared two groups of patients, one underwent conventional TURBT, while the other had TmLRBT. Clinical results of the study indicated the superiority of TmLRBT over conventional TURBT in terms of operative time, obturator jerk occurrence, perioperative bleeding rate, bladder perforation rate, and catheterization and hospitalization times. In addition, lower tissue destruction and higher detrusor muscle detection in the pathological specimen were in favor of TmLRBT over conventional TURBT. Finally, TmLRBT group had lower early (<12 months) tumor recurrence rate.

Previous studies using Thulium laser found that obturator jerk occurs more with conventional TURBT than with Thulium laser *en bloc* resection.<sup>[5-7]</sup> This is due to the absence of electric current in LASER resection and the shallow penetration of LASER. Monopolar *en bloc* resection would not obviate obturator jerk as reported by Yang *et al.* when obturator jerk occurred in nine out of 26 patients.<sup>[8]</sup> Our study confirms the superiority of TmLRBT in avoiding obturator jerk and reduction of bladder perforation risk. In addition, we could report advantage of TmLRBT in hemostasis after bladder tumor resection. Similar findings were reported by Liu *et al.* and Long *et al.*<sup>[9,10]</sup>

In our study, we found that the operative time is shorter with TmLRBT. This may be explained by the papillary characteristic of the tumor with narrow base which makes *en bloc* resection easier. Furthermore, smaller tumor size in our cohort (<4 cm), surgeon experience, and better hemostasis offered by laser are contributing factors. Li *et al.* reported similar results.<sup>[11]</sup> In contrast to these findings, Xu *et al.* found nonsignificant difference between laser *en bloc* resection and conventional TURBT in operative time in their retrospective study.<sup>[6]</sup> However, the operative time for *en bloc* resection was shorter than conventional TURBT, but the small number of *en bloc* resection cohort (n = 26) may have affected the statistical significance. Additional benefits of TmLRBT are the shorter hospitalization and catheterization times. This could be owing to better hemostasis, and the lower rates of obturator jerk and bladder perforation. Liu *et al.* found the same advantage in their work comparing TmLRBT and conventional TURBT.<sup>[9]</sup>

The technique of TmLRBT is done by making a circular incision around the tumor with safety margin 5 mm. After that laser energy is introduced through this circular incision in the deep layer of muscle, then the resectoscope is used to dissect the muscle fibers smoothly with laser being used only for hemostasis and cutting attached fibers resistant for dissection. Laser is known to have smooth cutting surface and shallow thermal damage. These all contribute to good pathological specimen retrieval and preservation of detrusor muscle with no thermal damage. In our study, higher rates of detrusor muscle detection with less tissue charring and destruction could be observed with TmLRBT as compared to conventional TURBT. Wolters et al. stated that detrusor muscle is found in 100% of en bloc resection specimens.<sup>[12]</sup> Migliari et al. compared TmLRBT with monopolar resection and reported that detrusor muscle is found in all cases who had TmLRBT. Furthermore, he found that all 58 cases who underwent TmLRBT were negative for malignancy in biopsies taken from old tumor site after 90 days, but seven of 61 cases who underwent TURBT were positive for malignancy and 3 of them were upstaged.<sup>[13]</sup> Similarly, Kramer et al. conducted a study in 90 patients using TmLRBT and found that biopsies from the old site of resection were negative of tumor in all cases.<sup>[14]</sup> In our study, only two of 54 TmLRBT cases were positive for malignancy after 90 days, but 8 of 52 TURBT cases were positive.

TmLRBT is done using continuous energy output with high vaporization and cutting efficacy. Furthermore, tumor base and detrusor muscle are cut under vision with a good safety margin but in conventional TURBT tumor is cut in pieces (incise and scatter technique) with more dispersal of tumor cells.<sup>[15]</sup> We report lower rate of early tumor recurrence after TmLRBT in comparison to conventional TURBT. Wu et al. conducted a meta-analysis in 886 patients to compare TmLRBT and conventional TURBT regarding the efficacy and feasibility of both techniques and they reported that recurrence is less with TmLRBT.<sup>[16]</sup> Many studies were conducted on LASER en bloc resection and reported that LRBT is better than conventional TURBT in recurrence-free rate.[5,17-19] Other studies found no difference in recurrence rates.<sup>[9,10]</sup> In our study, there are four cases recurrent in TmLRBT group, two were at the old resection site, and two were outside the site of resection. Recurrence at tumor site in TmLRBT is not common and previous studies reported that most of the recurrences in TmLRBT are outside the tumor site which could represent tumors that were small and undetected at first resection.<sup>[20,21]</sup>

Limitation of the current study is the inclusion of small tumors with narrow bases only. Furthermore, tumors in the anterior wall and bladder dome were excluded as they are challenging to be resected *en bloc*. The small number of cases and short follow-up are other limitations. However, strengths of the study are inclusion of a large number of a homogeneous population of primary bladder tumors, and the prospective design of the study. This allowed the conclusion of the superiority of TmLRBT over conventional TURBT in cases of small, narrow-based primary bladder tumor situated in the lateral walls and base of the urinary bladder.

## CONCLUSION

In cases of primary small (<4 cm) urinary bladder tumors situated in the lateral walls or bladder base TmLRBT is superior to conventional TURBT in terms of operative time, hospitalization time, catheterization time, complication rate, pathological specimen acquisition, and tumor recurrence rate.

# Financial support and sponsorship Nil.

Conflicts of interest

There are no conflicts of interest.

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