

Tm:YAG laser en bloc mucosectomy for accurate staging of primary bladder cancer: early experience

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Abstract

Introduction Exact pathological staging of bladder cancer is crucial for determination of further treatment. One limiting factor is the surgical ‘incise and scatter’ technique that might contribute to tumour recurrence. En bloc resection techniques are an emerging issue. We present initial results with Thulium:YAG (Tm:YAG) en bloc resection of bladder tumours for treatment and accurate staging of solitary transitional cell carcinoma of the bladder.

Materials and methods From June through October 2010, six patients were treated by TmLRBT (Thulium laser resection of bladder tumour). Inclusion criteria were solitary lesions, treatment naive patients and tumour localisation of

the lower bladder wall and trigonum. En bloc resection was applied on all of the tumours. Two cold-cut biopsies from the tumour base were extracted. On five of the six patients, a re-resection was performed after 6 weeks.

Results Pathological evaluation revealed 1 patient with pTa G1, 2 patients with pTa G2 and 3 patients with pT1 G3. All of the resected specimens provided detrusor muscle, and all biopsies were positive for muscle cells. No intra-, peri- or post-operative complications were observed. Bladder irrigation was mandatory in only 50% of the patients. All patients were negative for residual TCC in re-resection 6 weeks after initial treatment.

Conclusion TmLRBT has been proven safe and effective for both, treatment and pathological staging of primary TCC of the bladder. Tm:YAG en bloc resection therefore could be an appropriate tool for accurate staging with possibly lower scattering potential for the assessment and treatment of patients with TCC.

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Introduction

The gold standard for the treatment of non-muscle invasive bladder cancer (NMIBC) has been transurethral resection. However, the technique harbours some serious disadvantages, e.g., thermal damage of adjacent tissue, the use of the ‘incise and scatter’ technique that causes fragmentation of the tumour and leads to a high amount of exfoliated cancer cells that are suspicious of causing out-of-field recurrences as well as the difficulty of accurate pathological evaluation of fragmented tissue [1, 2].

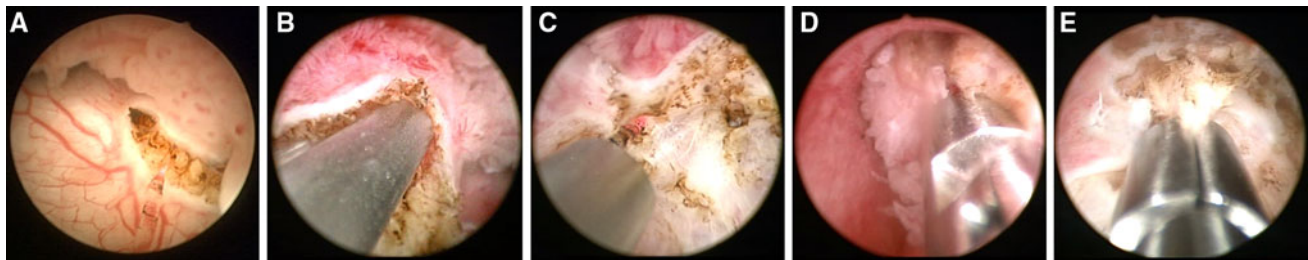


Fig. 1 **a** Circumferential incision of the tumour with a 2-mm safety margin, **b** Blunt dissection of the bladder mucosa from the deeper layers and lifting of the mucosal patch towards the bladder lumen,

c Separation of remaining adhesions with laser energy, **d** Extraction of the tumour in one piece with a grasper, **e** Cold-cut biopsies from the tumour ground

Lasers have been reported for the treatment of non-muscle invasive bladder tumours. However, most reports focused on recurrent tumours as the resection technique has been in a developing process [3, 4]. Several groups could show successful en bloc resection of NMIBC using Holmium YAG (Ho:YAG) and Thulium YAG (Tm:YAG) lasers [5, 6]. A comprehensive review addressing this topic can be found within this issue [7].

Endoscopic submucosal en bloc dissection with high-frequency current has been used for the diagnosis and treatment for early gastrointestinal tumours of the oesophagus, stomach, duodenum and colon and has been introduced to the urological field for bladder cancer, recently [8–10]. Various publications could show its feasibility with a low complication rate even when applied on patients under anticoagulants [11–13].

The aim of this study was to show the feasibility of Tm:YAG en bloc resection of urothelial bladder tumours for accurate pathological staging. Furthermore, we analysed the safety and efficacy of this method.

Materials and methods

Since June 2010, six patients have been treated by Tm:YAG en bloc resection. Inclusion criteria were solitary papillary lesions, treatment naive patients and localisation of the tumour on the lower bladder wall and trigonum. An incision into the circumference of the tumour with a macroscopical safety margin of 0.5 cm to the tumour was carried out with a 550 nm laser fibre (RigiFibTM, LISA laser products, Katlenburg, Germany) that was advanced through the working element of a 26 F continuous-flow resectoscope (Karl Storz GmbH, Tuttlingen, Germany). The 2,013 nm Tm:YAG laser (RevolixR, LISA laser products, Katlenburg, Germany) was used at the power level of 10–15 W. At first, the tumour was circumferential incised with the aid of the Tm:YAG laser with a safety margin of 2 mm (Fig. 1a). Then, the bladder mucosa was bluntly dissected

from the deeper layers by lifting the mucosal patch towards the bladder lumen with the beak of the resectoscope leaving the bladder facing part of the specimen intact (Fig. 1b). Remaining adhesions were cut with laser energy (Fig. 1c). Bleeding vessels were punctually coagulated. The tumour was endoscopically extracted in one piece with a grasper (Fig. 1d). At the end of the procedure, two cold-cut biopsy specimens were taken from the tumour ground (Fig. 1e). Finally, the tumour ground was adequately coagulated using laser energy.

Bladder perforation, uncontrollable bleeding and prolonged hospital stay were considered as major complications.

Results

Six patients (5 men, 1 woman) with a mean age of 64 years (range 57–80) were treated by Tm:YAG laser en bloc resection. Patient's characteristics are shown in Table 1. All patients signed a written informed consent prior to the operation. The mean duration of the procedure was 36 min (range 14–60). All patients had solitary superficial bladder tumours located on the lower bladder wall or trigonum. Neither intraoperative nor peri- or post-operative complications, as defined above, occurred.

Pathohistological classification and the depth of tumour infiltration (T stage) were provided by the Institute of Pathology, Medical School Hanover, Germany. The tumours were graded according to the 2004 WHO and the 1973 classification. Pathological evaluations revealed 1 patient with pTa G1, 2 patients with pTa G2 and 3 patients with pT1 G3. Table 1 lists the pathological results. Each of the obtained urothelial lesions were confined to the mucosa and did not show invasive areas. All specimens included upper layers of muscle cells, all cold biopsies taken from tumour ground were positive for detrusor muscle. Figure 2 shows the histological section of the resected specimens (Fig. 2). The re-resection after 6 weeks of initial treatment revealed no residual TCC.

Table 1 The characteristics for Tm:YAG laser en bloc resection of primary papillary bladder tumours of 6 patients

No.	Age (years)	Gender (m/f)	Operation time (min)	Histological analysis	En bloc resection	R0 resection	Muscle layer in cold-cut biopsies	Pathological findings in re-resection (6 weeks after operation)
1	73	m	35	pTaG1	Yes	Yes	Yes	No re-resection performed
2	57	m	50	pT1G3	Yes	Yes	Yes	No
3	60	m	60	pTaG1	Yes	Yes	Yes	No
4	57	m	14	pTaG2	Yes	Yes	Yes	No
5	57	m	26	pT1G3	Yes	Yes	Yes	No
6	80	f	35	pT1G3	Yes	Yes	Yes	No

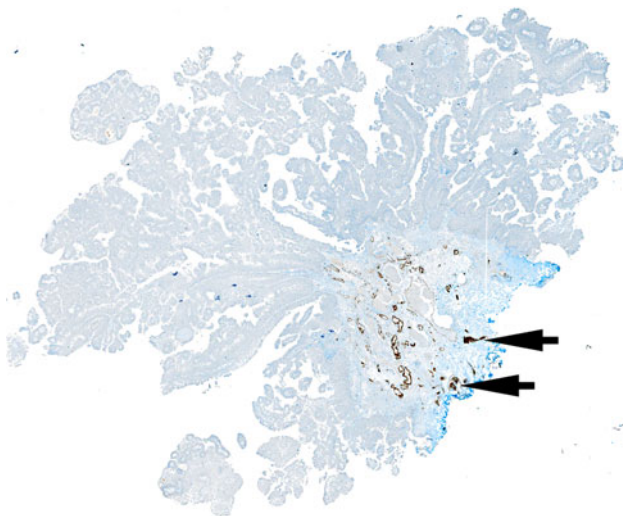


Fig. 2 Resection specimen 1: Histologic examination shows well-preserved structure of this papillary urothelial carcinoma resection specimen. Overall, papillary architecture can be easily appreciated, also the inked (*blue*) resection margins at the right bottom. This desmin immunoperoxidase stain shows superficial bundles of the detrusor muscle (*arrows*). Desmin immunoperoxidase, flatbed scan, original magnification $\times 7$

Discussion

The well-established ‘incise and scatter’ resection technique that is used by TURB contradicts oncological principles [1]. To solve this matter, various groups developed en bloc resection methods within the last two decades. Ukai and colleagues used a short curved needle electrode to make a circular incision around the malignant lesion, thus making it possible to lift the entire tumour [14]. A similar technique was reported by Kawada and colleagues [15]. Saito was the first to pass on this technique to Ho:YAG en bloc resection of bladder tumours in 2001 [5]. From 35 patients, he could retrieve sufficient material for pathological evaluation. More recent studies by Zhu et al. and Xishuang

et al. proved superiority of laser treatment in terms of safety and efficacy compared to conventional TURB [16, 17]. They observed fewer bladder perforations, had fewer incidences of obturator nerve reflex and reported of fewer post-operative bleedings.

In other medical fields, en bloc resection of possibly tumorous lesions has been applied successfully. Especially in Japan, mucosectomy of oesophageal lesions is currently a widespread surgical method [11, 13, 18]. Using en bloc resection, the rate of recurrence has been decreased and the quality of life of treated patients has been improved [11, 13]. The vast majority of published manuscripts describing en bloc mucosectomy of gastrointestinal lesions describe low complication rates among which clinically relevant bleeding was observed in only a limited number of patients [8, 9, 13].

Our preliminary data on a small cohort of patients indicate the feasibility of endoscopic en bloc resection of NMIBC as an efficient and safe procedure. All tumours could safely be resected and removed in toto. The complication rate was negligible. The major advantage, however, is the preservation of the entire lamina propria and the en bloc resection. Detrusor muscle was preserved in all of the resected tumours thus giving the pathologist the opportunity of correct staging regarding invasiveness. Above, by using en bloc resection, we potentially limited the amount of tissue scattering. This stays in contrast to conventional TURB in which tissue samples are often difficult to analyse due to tissue shrinkage and fragmentation. Especially, the feature of ordered or disordered architecture of the papillae that is a parameter of the classification algorithm of papillary urothelial tumours suggested by the 2004 edition of the WHO classification (ISBN 9283224124) is obscured by tissue fragmentation. Due to preservation of the entire histological structures, especially on the edges of the specimen, the adequacy of the resection can be very well confirmed at the deep and lateral margins. This might contribute to a reduced need for unnecessary re-TURBs, reducing patient and socioeconomic burden. Five of the six analysed

patients underwent re-TURB after 6 weeks of the initial TURB. In none of the patients, remaining in-field (former resection area) and out-of-field TCC was identified.

The limitation of the current study is clearly the small number of patients that were analysed. Furthermore, all of the resected tumours were <3 cm and solitary, papillary lesions at the trigonum or on the lower bladder wall that limits the number of patients that can be treated with this technique. We decided to perform this procedure only at the above mentioned areas from a safety point of view. However, we could show that the application of Tm:YAG laser as well as en bloc resection is an efficient approach to treat small urothelial carcinomas of the bladder. None of the patients experienced post-operative bleeding, although one patient was under full anticoagulation with a low-molecular-weight heparin (LMWH) at time of surgery. Only 50% of the patients needed bladder irrigation overnight. Furthermore, all indwelling catheters could be removed the day after treatment. None of the patients experienced delay in hospitalisation. However, it has to be mentioned that two of the six patients experienced prolonged surgery with 50- and 60-min operation time. We saw a steep learning curve and believe that the average operation time can be decreased to that of conventional TURB.

Larger prospective, randomized studies with an extended follow-up period will be necessary to determine the hypothetical advantage of lower scattering and therefore lower likelihood of tumour cell spillage with consecutively lower recurrence rates. Furthermore, future studies need to investigate whether en bloc resection is feasible for all locations within the bladder.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Wilby D, Thomas K, Ray E, Chappell B, O'Brien T (2009) Bladder cancer: new TUR techniques. *World J Urol* 27(3):309–312. doi:10.1007/s00345-009-0398-9
2. Bach T, Herrmann TR, Cellarius C, Geavlete B, Gross AJ, Jecu M (2009) Bipolar resection of the bladder and prostate—initial experience with a newly developed regular sized loop resectoscope. *J Med Life* 2(4):443–446
3. Syed HA, Biyani CS, Bryan N, Brough SJ, Powell CS (2001) Holmium:YAG laser treatment of recurrent superficial bladder carcinoma: initial clinical experience. *J Endourol* 15(6):625–627. doi:10.1089/089277901750426427
4. Jonler M, Lund L, Bisballe S (2004) Holmium:YAG laser vaporization of recurrent papillary tumours of the bladder under local anaesthesia. *BJU Int* 94(3):322–325. doi:10.1111/j.1464-410X.2004.04882.x
5. Saito S (2001) Transurethral en bloc resection of bladder tumors. *J Urol* 166(6):2148–2150
6. Zhong C, Guo S, Tang Y, Xia S (2010) Clinical observation on 2 micron laser for non-muscle-invasive bladder tumor treatment: single-center experience. *World J Urol* 28(2):157–161. doi:10.1007/s00345-010-0532-8
7. Kramer MW, Bach T, Wolters M, Imkamp F, Gross AJ, Kuczyk MA, Merseburger AS, Herrmann TR (2011) Current evidence for transurethral laser therapy of non-muscle invasive bladder cancer. *World J Urol*. doi:10.1007/s00345-011-0680-5
8. Coda S, Trentino P, Antonellis F, Porowska B, Gossetti F, Ruberto F, Pugliese F, D'Amati G, Negro P, Gotoda T (2010) A Western single-center experience with endoscopic submucosal dissection for early gastrointestinal cancers. *Gastric Cancer* 13(4):258–263. doi:10.1007/s10120-010-0544-5
9. Probst A, Pommer B, Golger D, Anthuber M, Arnholdt H, Messmann H (2010) Endoscopic submucosal dissection in gastric neoplasia—experience from a European center. *Endoscopy* 42(12):1037–1044. doi:10.1055/s-0030-1255668
10. Nagele U, Kugler M, Nicklas A, Merseburger AS, Walcher U, Mikuz G, Herrmann TR (2011) Waterjet hydrodissection: first experiences and short-term outcomes of a novel approach to bladder tumor resection. *World J Urol*. doi:10.1007/s00345-011-0653-8
11. Ono H (2005) Endoscopic submucosal dissection for early gastric cancer. *Chin J Dig Dis* 6(3):119–121. doi:10.1111/j.1443-9573.2005.00206.x
12. Ono S, Fujishiro M, Niimi K, Goto O, Kodashima S, Yamamichi N, Omata M (2009) Technical feasibility of endoscopic submucosal dissection for early gastric cancer in patients taking anti-coagulants or anti-platelet agents. *Dig Liver Dis* 41(10):725–728. doi:10.1016/j.dld.2009.01.007
13. Oyama T, Tomori A, Hotta K, Morita S, Kominato K, Tanaka M, Miyata Y (2005) Endoscopic submucosal dissection of early esophageal cancer. *Clin Gastroenterol Hepatol* 3 (7 Suppl 1):S67–S70
14. Ukai R, Kawashita E, Ikeda H (2000) A new technique for transurethral resection of superficial bladder tumor in 1 piece. *J Urol* 163(3):878–879
15. Kawada T, Ebihara K, Suzuki T, Imai K, Yamanaka H (1997) A new technique for transurethral resection of bladder tumors: rotational tumor resection using a new arched electrode. *J Urol* 157(6):2225–2226
16. Xishuang S, Deyong Y, Xiangyu C, Tao J, Quanlin L, Hongwei G, Jibin Y, Dongjun W, Zhongzhou H, Jianbo W, Lina W, Lin Y (2010) Comparing the safety and efficiency of conventional monopolar, plasmakinetic, and holmium laser transurethral resection of primary non-muscle invasive bladder cancer. *J Endourol* 24(1):69–73. doi:10.1089/end.2009.0171
17. Zhu Y, Jiang X, Zhang J, Chen W, Shi B, Xu Z (2008) Safety and efficacy of holmium laser resection for primary nonmuscle-invasive bladder cancer versus transurethral electroresection: single-center experience. *Urology* 72(3):608–612. doi:10.1016/j.urology.2008.05.028
18. Kuwano H, Mochiki E, Asao T, Kato H, Shimura T, Tsutsumi S (2004) Double endoscopic intraluminal operation for upper digestive tract diseases: proposal of a novel procedure. *Ann Surg* 239(1):22–27. doi:10.1097/01.sla.0000103381.32956.7c