Thulium laser resection via a flexible cystoscope for recurrent non-muscle-invasive bladder cancer: initial clinical experience

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Study Type – Therapy (case series)
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OBJECTIVE

To present our initial experience of thulium laser resection via a flexible cystoscope for recurrent non-muscle-invasive bladder cancer (ThuRBT), as transurethral resection for bladder tumour (TURBT) is regarded as the reference standard for treating this disease, but alternative laser resection or ablation is suitable especially for recurrent tumours.

RESULTS

All patients were treated successfully with ThuRBT in one session, with no bladder haemorrhage, obturator nerve reflex or vesicle perforation. Randomized biopsies taken after surgery on and adjacent to the resection surface revealed no residual tumours. The mean (range) tumour diameter was 1.5 (0.5–3) cm and the mean operative duration was 25 (15–35) min. During the first year of follow-up, local and heterotopic recurrences were found in three and six patients, respectively. The accumulated recurrence rates at 3, 6 and 12 months were 9%, 22% and 28%, respectively.

CONCLUSIONS

ThuRBT is a reliable therapy with minimal morbidity and invasiveness for selected patients with bladder cancer.

KEYWORDS

bladder neoplasm, thulium laser, flexible cystoscopy, resection

INTRODUCTION

Bladder cancer is the fifth most common cancer in men, accounting for >12 000 cancer-related deaths per year [1]; 75–85% of patients present with non-muscle-invasive (NMI) bladder cancer, which is defined as tumour confined to the mucosa (stage Ta, carcinoma in situ, CIS) and submucosal layers of the bladder (stage T1; TNM classification) [2].

Of these patients, 5–10% assessed by follow-up cystoscopy will have recurrences that are small and few [3]. Although transurethral resection of bladder tumours (TURBT) is still regarded as the reference standard in the treatment of NMI bladder cancer, it is associated with significant mortality rates and complications, e.g. bladder perforation and obturator nerve reflex. Therefore, in recent decades various laser treatment options have been developed. In patients with biopsy-confirmed recurrent NMI bladder cancer, holmium laser treatment has achieved remarkable outcomes with high patient satisfaction, although the major drawback is the lack of tissue for histological examination [4,5].

The thulium laser is a new surgical laser system in urology, with a tuneable wavelength of 1.75–2.22 µm. It might have several advantages over the holmium laser, including improved spatial beam quality, more precise tissue incision, and operation in continuous-wave/pulsed modes [6]. Recent studies have shown that the thulium laser can be used for bladder neck incision, and the characteristics are excellent [7].

In the present preliminary study, we evaluated the efficiency and safety of the thulium laser for tumour resection (ThuRBT) via a flexible cystoscope for recurrent NMI bladder cancer.

PATIENTS AND METHODS

From January 2005 to October 2005, 32 patients with early recurrent bladder tumour (recurrent within a year after TURBT) were treated with ThuRBT via a flexible cystoscope. The follow-up included urine analysis, ultrasonography and cystoscopy every 3 months.

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PATIENTS AND METHODS

From January 2005 to October 2005, 32 patients (mean age 66 years, range 53–78) underwent ThuRBT at the authors’ institution. The inclusion criteria were patients who had early recurrence (recurrent within a year after TURBT) of NMI bladder cancer, a cystoscopic papillary aspect with fewer than two tumours of <3 cm. The exclusion criterion was CIS. All patients provided written informed consent.

We used a recently developed diode-pumped solid-state laser emitting light at a wavelength of 2.0 µm (Revolix™ LISA Laser Products, Katlenburg, Germany) delivered through a silica fibre toward the endoscopic targets. The endoscope was connected to a standard camera and monitor; the laser energy was introduced through a 200 µm core diameter bare-ended silica fibre (PercuFib, LISA Laser Products) through an 18 F flexible cystoscope working channel (CYF-2, Olympus
Keymed, UK). The continuous-wave laser was operated at power levels of 5–15 W in a continuous and pulsed mode.

All patients were placed under general anaesthesia and in the lithotomy position except one who had had a artificial hip replacement 2 months earlier. Physiological saline was administered manually as an irrigating agent during the procedure. We used the 18 F flexible cystoscope to assess both the location and number of tumours. The 200 µm laser fibre was inserted into the bladder through the working channel of the flexible cystoscope. The fibre was held 2–3 mm away from the tissue and a continuous-wave of laser energy was fired at the target. Any single area of the bladder tumour or the surrounding wall was treated until there was the whitish discoloration typical of coagulation, usually after 3–4 s. It is important to treat the entire tumour bed and a 1-cm margin around the tumour. Finally, the tumour was retrieved through the flexible cystoscope working channel after grasping its reverse side with biopsy forceps. Larger tumours were removed separately by cutting them into two or three pieces. Random cold-forceps biopsies of the tumour margin, tumour base and bladder wall were taken into two or three pieces. Random cold-forceps biopsies of the tumour margin, tumour base and bladder wall were taken into two or three pieces. Random cold-forceps biopsies of the tumour margin, tumour base and bladder wall were taken routinely before the procedure was completed. The operative duration, recurrent tumours and perioperative complications were recorded. All patients were followed with a history, physical examination, urine analysis, ultrasonography and cystoscopy at 3-month intervals.

**RESULTS**

Of the 32 patients, seven had double tumours and the remaining 25 had a solitary lesion; the mean (range) tumour diameter was 1.5 (0.5–3) cm. All patients were treated successfully, with negative biopsies. The histological results confirmed TCC in all patients, of grade 1 in 26 (32 tumours) and grade 2 in six (seven tumours). The mean operative duration was 25 (15–35) min. There were no intraoperative or delayed complications; only two patients needed bladder perfusion after surgery. The catheter was removed on the following morning. Table 1 shows the recurrence rates; there were three local recurrences (9%) and six tumours (19%) recurring in untreated area of the bladder at the 1-year follow-up. The recurrent tumours were treated by another ThuRBT. Thus the accumulated recurrence rates at 3, 6 and 12 months were 9%, 22% and 28%, respectively.

**DISCUSSION**

In recent years there has been renewed interest in the use of lasers for minimally invasive treatment of urological diseases. Although TURBT remains the standard for NM1 bladder cancer, the use of lasers for treating bladder cancer has been confirmed to be safe and minimally invasive. The holmium:YAG laser has gained popularity recently, and other lasers are still in use. Noninvasive, small lesions are especially amenable to management with laser energy, and the success rates are at least as good as those of standard electrocautery resection [4,5,8]. In a randomized study, Beisland and Seland [9] reported a local recurrence rate of 7% for Nd:YAG-treated stage T1 tumours, vs 43% for similar tumours treated with standard electrocautery. Beer et al. [10] reported a similar local recurrence rate in their series of 252 consecutive patients treated with a laser for superficial lesions. Laser therapy of noninvasive tumours is usually administered on an outpatient basis and might require less anaesthesia than standard electrocautery resection. The complication rates are low; the obturator nerve will not be stimulated by laser energy, and therefore obturator spasm and its accompanying leg jerk are avoided. Tumours that overlie the ureteric orifices can be treated with apparently little risk of ureteric stricture [11]. The major drawback of laser therapy is the lack of tissue for histological examination; it is not possible to determine the level of infiltration in the wall (pT), although it is possible to determine the anaplasia grade.

The 50 W thulium laser was approved by the USA Food and Drug Administration and European Community in 2004, and came into the Chinese medical market in 2005. To the best of our knowledge, this is the first report of the thulium laser used in bladder cancer. The high-power thulium fibre laser has several potential advantages over the holmium and KTP laser. First, the central wavelength is tuneable at 1.75–2.22 µm, allowing the wavelength to exactly match the 1.94 µm water absorption peak in tissue. The higher absorption of laser radiation at the thulium wavelength results in more efficient and rapid tissue cutting. At the same time, it theoretically causes a smaller thermal damage zone in the tissue [6,12]. Second, the thulium fibre laser is diode-pumped, which allows it to be operated either in a continuous-wave or pulsed mode. The continuous-wave mode, which can offer maximum haemostasis and coagulation, is used for prostate procedures. The pulsed mode is used for applications requiring precise cutting, e.g. bladder-neck contractures and urethral strictures [13]. Third, the thulium fibre is suitable for potential use with the smallest ureteroscopes in the most challenging applications, such as access to the lower pole of the kidney for lithotripsy [13].

Because of the unique characteristics of the continuous-wave mode, ThuRBT has some advantages over holmium laser therapy. First, it is not possible to keep the holmium laser fibre tip steadily on the target during lithotripsy when in the pulsed mode. Thus a laser-fibre guide was designed to hold the laser fibre steady and guide the fibre easily to the desired location of the stone [14]. By contrast, the thulium fibre tip can be kept steadily and precisely controlled during the procedure, which decreases the risk of adjacent tissue injury. Second, rapidly expanding steam bubbles are created with holmium laser lithotripsy [13]. Contrast, the thulium fibre is suitable for potential use with the smallest ureteroscopes in the most challenging applications, such as access to the lower pole of the kidney for lithotripsy [13].

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efficient and rapid tissue cutting and a continuous-wave mode, the thulium fibre laser can be used like an ‘electric knife’ to incise tumours, apart from vaporization. In this sense, ThuRBT is a user-friendly technique requiring less expertise than with holmium laser therapy.

As the wavelength of the thulium laser is closer to the 2 μm peak of the absorption spectrum of water than that of the holmium laser, the absorption is stronger by a factor of 2.5. This leads to a reduced zone of thermal damage and to even more precise incision [7]. Thulium lasers have been assessed clinically in otolaryngology [15], ophthalmology [16,17] and neurology [18], and showed excellent incision properties. Recently, Bach et al. [7] reported excellent results at the 1-year follow-up of bladder neck incision using the thulium laser. During the thulium laser procedure, small tumours can be resected in one chip; larger tumours must be resected in fractions. First, the exophytic tumour tissue was removed, then separately the underlying bladder wall was coagulated into the muscle, and finally the edges of the resection area should also be coagulated. Therefore, the technique of ThuRBT can preserve more tissue than holmium laser therapy.

For good control of the extent of the tissue damage, a device needs to have a shallow but sufficient penetration to provide coagulation and excellent haemostasis at the same time; the thulium laser fulfil these requirements. The precise ablation and excellent haemostatic properties of the thulium laser allows bloodless tumour destruction. Excellent haemostatic properties provide surprisingly clear vision. Only two of the present patients needed bladder perfusion after surgery. The catheter was removed on the morning after surgery. Of the two tumours, one had a broad base, and the other was 2.5 cm in the diameter, indicating that ThuRBT might be not suitable for large tumours. There was no delayed bleeding in the present series. Many patients will not notice any difference in their urine, although a few will see increased urine sedimentation as the coagulated tissue sloughs.

There were no intraoperative or delayed complications in the present series. The most significant complication of laser therapy is forward scatter of laser energy to adjacent structures, resulting in perforation of a hollow, viscus organ such as overlying bowel.

This is rare but most commonly occurs with the Nd:YAG laser because of the deeper tissue penetration than with the holmium and KTP lasers [19]. If appropriate energy values are set, the risk of small bowel perforation is low. Smith [19] reported no perforation in over 200 treatments. The thulium laser only creates a minimum of 300–400 μm of peripheral thermal damage, while ablating soft urinary tissues [6]. However, caution is needed, especially when treating tumours on the bladder dome or when treating women, in whom the bladder wall can be thin; there were no perforations in the present study.

Our clinical results achieved with ThuRBT are comparable with those of electrocautery TURBT. To predict the expected number of recurrences compared with the actual number in the present series, we used the recurrence calculators designed by the European Organization for the Research and Treatment of Cancer for multivariate analyses. The scoring system is based on the six most significant clinical and pathological factors; the number of tumours, tumour size, previous recurrence rate, T category, presence of CIS and tumour grade [20]. The probability of recurrence and progression of NMI bladder cancer with standard TURBT at 1 year was 15–61% and 0.2–17%, respectively. Applying the recurrence calculator to the present series showed a likelihood of recurrence at 1 year of 21–41%, vs the actual rate of 28%. Thus, ThuRBT seems to provide good local tumour control compared with TURBT.

One of the main disadvantages is that the assessment of the depth of penetration is suboptimal, although it allows significant tissue to be procured for pathological examination. Vaporization with the holmium laser results in little or no tissue left for histological examination. By contrast, tissue was obtained in all cases with ThuRBT, but the architectural detail is distorted, so that specimens can be difficult for the pathologist to diagnose accurately, especially for stage. In the present study, tumour grade was available for every case, while the pathologist was unable to stage the tumour.

In conclusion, ThuRBT via flexible cystoscopy is a safe and effective treatment for recurrent NMI bladder tumour. This technique is easier to follow and better tolerated by patients. It is a promising treatment option due to the precise incision, low complication rate and excellent haemostasis. Long-term prospective randomized studies will be needed to confirm these promising preliminary results.

CONFLICT OF INTEREST
None declared.

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Abbreviations: NMI, non-muscle-invasive; CIS, carcinoma in situ; TURBT, transurethral resection of bladder tumour; ThuRBT, thulium laser resection of bladder tumour.