Preliminary Porcine *In Vivo* Evaluation of a Telerobotic System for Transurethral Bladder Tumor Resection and Surveillance

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Abstract

Introduction: Transurethral resection of bladder tumors (TURBTs) can be a challenging procedure, primarily due to limitations in tooltip dexterity, visualization, and lack of tissue depth information. A transurethral robotic system was developed to revolutionize TURBTs by addressing some of these limitations. The results of three pilot *in vivo* porcine studies using the novel robotic system are presented and potential improvements are proposed based on experimental observations.

Materials and Methods: A transvesical endoscope with a mounted optically tracked camera was placed through the bladder of the swine under general anesthesia. Simulated bladder lesions were created by injecting HistoGel processing gel mixed with blue dye, transabdominally, into various locations in the bladder wall under endoscopic visualization. A 7-degree-of-freedom (DoF) robot was then used for transurethral resection/ablation of these simulated tumors. An independent 2-DoF distal laser arm (DLA) was deployed through the robot for laser ablation and was assisted by a manually controlled gripper for en bloc resection attempts.

Results: Lesions were created and ablated using our novel endoscopic robot in the swine bladder. Full accessibility of the bladder, including the bladder neck and dome, was demonstrated without requiring bladder deflation or pubic compression. Simulated lesions were ablated using the holmium laser. En bloc resection was demonstrated using the DLA and a manual grasper.

Conclusion: Feasibility of robot-assisted en bloc resection was demonstrated. Main challenges were lack of depth perception and visual occlusion induced by the transvesical endoscope. Recommendations are given to enhance robot-assisted TURBTs. Lessons learned through these pilot swine studies verify the feasibility of robot-assisted TURBTs while informing designers about critical aspects needed for future clinical deployment.

Keywords: transurethral resection, TURBT, robot-assisted surgery

Introduction

AMONG ALL CANCER DIAGNOSES, the incidence of bladder cancer ranks fourth in the United States¹ and seventh worldwide in males.² Approximately 75% of all bladder cancers are categorized as nonmuscle-invasive bladder cancer (NMIBC).³ Although transurethral resection of bladder tumors (TURBTs) remains the gold standard for diagnosis and treatment of NMIBC, it suffers from several limitations. A successful procedure requires complete resection of all bladder tumors with inclusion of the muscle layer for proper

pathologic staging without perforation of the bladder. In addition to poor tool dexterity that was characterized previously,^{4–6} the tumor boundaries and depth of penetration are difficult to distinguish intraoperatively. Due to risk of perforation, insufficient resection⁷ results in inadequate tissue for definitive pathologic diagnosis in as much as 51% of TURBT procedures and may delay definitive diagnosis and treatment.⁸

Furthermore, during standard TURBTs, bladder tumors (with the exception of small tumors) are typically removed piecewise, which may result in increasing the likelihood

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of recurrence.^{9–11} Piecemeal resection could result in re-seeding and reimplantation.¹² Due to under-resection and high recurrence risk, repeat procedures [restaging transurethral resection (TUR) or re-TUR] and adjuvant intravesical chemotherapy are often strongly recommended.¹³ As a result, bladder cancer has the highest overall treatment costs per patient among all cancers.^{14–16}

Several transurethral robots have been developed, mostly targeting benign prostatic hyperplasia.^{17–20} With regard to transurethral robots that can be deployed for bladder pathologies, our group developed an early proof-of-concept robot for TURBTs.²¹ In addition, there were several efforts by other groups to use robotics for surveillance of the bladder.^{22–24} These instruments facilitated bladder surveillance, but had limited reach.

Following up on our earlier concept for TURBTs,^{21,25} we developed a different transurethral robotic platform called TURBot (Fig. 1a) to overcome limitations of the earlier system. These limitations include insufficient dexterity to access the bladder neck, lack of independent laser control, lack of a robot-compatible resectoscope, and lack of proper high-level control algorithms for TURBT application.

TURBot is capable of accessing all regions of the bladder for visualization and laser ablation. Three 1.8-mm working channels of TURBot's miniature multibackbone continuum robot (MBCR) allow deployment of graspers,

custom flexible cameras, and other imaging probes to facilitate resection/ablation. In this regard, TURBot is the first endoscopic robotic system to provide full coverage of the bladder workspace for surgical intervention and surveillance and to have been evaluated in *in vivo* animal experiments.

Since the eventual deployment of the TURBot for bladder tumor resection hinges on accurate matching between the characteristics of the robot and clinical requirements, this article aims to detail our experience and lessons learned through evaluating the TURBot on three pilot *in vivo* porcine experiments. The goals of our study were (1) to evaluate the TURBot in accessing all regions of the bladder, (2) to evaluate robot-assisted resection/ablation of simulated bladder lesions, and (3) to explore the feasibility of robot-assisted en bloc resection. In this article, the results of several porcine *in vivo* experiments are presented and discussed with recommendations for future improvements.

Materials and Methods

Figure 1a shows the TURBot system. The core elements are a three-segment MBCR with three working channels (item (1) in Fig. 1a), a robot-compatible resectoscope (item (2)), and a statically balanced arm mounted on a mobile base (items (4) and (5)). In addition, a microsnake-like robot (item (6)) is deployed through one of the working channels of the

FIG. 1. (a) TURBot: a master-slave robotic system for surveillance and TURBTs, (1) three-segment MBCR, (2) custom resectoscope, (3) 10-DoF actuation unit, (4) statically balanced arm, (5) mobile base, (6) 2-DoF DLA, and (7) Omega.7 master haptic interface. (b) Animal laboratory setup: (1) TURBot slave, (2) master haptic interface, (3) surgeon monitor, (4) optical tracker base, (5) optical marker on transvesical endoscope camera, and (6) anesthetized pig. DLA = distal laser arm; DoF = degree-of-freedom; MBCR = multibackbone continuum robot; TURBT = transurethral resection of bladder tumor.

MBCR to control an ablation laser fiber (Boston Scientific Flexiva™ TracTip 200).

The three-segment MBCR (lengths 18, 20, and 15 mm) is 5 mm in diameter with three 1.8-mm round working channels used for deploying a 1.65-mm distal laser arm (DLA), a 1.6-mm fiberscope (10K pixels), and a 1.0-mm grasper. The MBCR has three actively bending segments that allow for 6 degrees of freedom (DoFs) of motion within the bladder space.²⁶

A custom-made resectoscope (item (2) in Fig. 1a) with a 3/8" external sheath was used for deployment of the robot and a 3-mm endoscope and to provide saline gravity irrigation to control bladder distension.²⁷

TURBot was designed for facilitating preclinical deployment by providing modularity and fast setup. A 5.3 kg assembly, including the actuation unit of the MBCR (item (3) in Fig. 1a) and the resectoscope, was designed with a quick-connect mechanism, allowing rapid engagement with the statically balanced arm and mobile base. This setup allowed the user to deploy the resectoscope into the urethra while monitoring for safe insertion using visualization from the endoscope. During insertion, the MBCR is retracted into the resectoscope sheath. Once inserted into the bladder space, adjustments of the insertion and the angle of approach of the resectoscope sheath can be performed manually by adjusting the mobile base and the statically balanced arm.

Figure 1b shows the operating room during the experiments. The TURBot is telemanipulated by a 7-DoF haptic device (Force Dimension Omega.7 haptic device). A foot pedal is used to switch control of the master device between the 7-DoF MBCR and the 2-DoF DLA. Visualization was provided to the surgeon using a transvesical endoscope (item (5)) and an endoscope monitor. An optical tracker (NDI Polaris Vicra, item (4)) was used to track markers attached to the robot and the transvesical camera to allow the surgeon to telemanipulate the MBCR in the endoscopic camera frame. This feature was crucial for retroflexed configurations of the MBCR.

Permission was obtained from the Vanderbilt University Institutional Animal Care and Use Committee (IACUC) for a

series of nonsurvival pilot studies. After fasting for 12 hours, the female swine (80–100 lb.) was placed under general anesthesia. It was then situated in a supine position with its hips abducted and pelvis lifted slightly to mimic a standard lithotomy position. A 10-mm blunt-tip trocar balloon port (Medtronic, Minneapolis, MN) was placed through the anterior bladder wall, similar to a suprapubic tube. A 10-mm laparoscope with a mounted camera was inserted through this port to visualize the resection/ablation process. Under endoscope guidance, a guidewire was inserted through the urethra and advanced into the bladder. Amplatz renal dilators were advanced sequentially over the guidewire to dilate the urethra and facilitate insertion of the robot resectoscope sheath. Once the sheath was in place, the guidewire was removed.

Next, the simulated bladder lesions for resection were created. HistoGel specimen processing gel (Ref HG-4000-012 Thermo Scientific), an aqueous gel composition, was liquefied in a 60°C water bath and then mixed with blue dye (toluidine or methylene blue). One to two milliliters of blue HistoGel was then injected into the bladder submucosa in multiple locations to simulate tumors. The injections were performed under direct vision from the laparoscope with 18-gauge needles generally inserted through the abdominal and outer bladder walls, thereby reducing the likelihood of puncturing the inner surface of the bladder where the liquefied gel could leak into the bladder. Lesions created on the posterior wall of the bladder necessarily had to be done by inserting the needle all the way through the anterior wall and then into the submucosa of the posterior wall. The room temperature saline irrigation in the bladder quickly cooled the HistoGel, thus solidifying it into a lesion. The lesion creation process had been previously tested and verified in bench top studies.

Next, the robot and the DLA were deployed. Initially, the bladder workspace coverage was tested by accessing various locations in the bladder. Then, robot-assisted resections of multiple lesions at different locations (except for the neck) were performed. En bloc resection was attempted as the last task.

FIG. 2. TURBot MBCR reaching the bladder: (a) right posterior, (b) anterior dome, (c) anterior neck, (d) left posterior, (e) left lateral (using only distal segment), and (f) posterior neck (using only distal segment).

FIG. 3. Reaching the bladder neck by simultaneously extending and retroflexing the MBCR. This leaves all segments unconstrained, hence more available dexterity.

Results

These experiments demonstrated deployment of the TURBot, the ability to retroflex within the bladder confines and reach all regions of the bladder, and the ability to perform en bloc resection using a combination of laser ablation and a grasper.

Figure 2 shows the MBCR reaching various regions of the bladder. The bladder dome was accessible by using the insertion stage. The bladder neck could be reached with all three segments inserted into the bladder while relying on retroflexion (e.g., Fig. 2c) or with partial insertion of MBCR segments (e.g., Fig. 2e–f). The control algorithm was designed to take into account the MBCR segments that were constrained inside the resectoscope sheath. It was found that full extension of the MBCR past the distal tip of the resectoscope sheath better preserves distal dexterity. The images in Figure 3 show the MBCR reaching the bladder neck using this method.

Figure 4 illustrates an attempt to ablate an ~10.5-mm simulated tumor at the left lateral wall (1 J at 10 Hz). This was performed only by the MBCR (DLA was not utilized). This task took ~4 minutes and 12 seconds. The change in tumor size that can be seen between images is due to motion of the transvesical camera.

The images in Figure 5 illustrate an en bloc resection attempt. First, a 1-mm grasper was extended manually to grasp the mucosal tissue (Fig. 5a, b). Then, the DLA was

telemanipulated independently to traverse around the grasped tissue while firing the laser simultaneously (Fig. 5c–h).

Discussion

TURBot could reach all aspects of the bladder, including the bladder neck. This obviated the need for suprapubic compression or adjustment of bladder distension. Resection at several bladder sites (excluding the neck) was conducted with submillimetric accuracy (the accuracy was determined based on follow-up phantom studies). Compared with the observed time for manual resections in the operating room (OR), the resection time using TURBot was higher. However, this was primarily due to limited training of the surgeon on the TURBot and the small size of the laser fiber compared with that of the electrocautery loop.

Although the overall experience with TURBot was positive and instructive, several challenges were encountered during the studies that merit attention. First, the porcine bladder size was small in comparison with the human bladder. Since the MBCR segment lengths were originally designed for potential deployment in the human bladder, this rendered robot manipulation and visualization challenging. In addition, the resectoscope-based endoscope employed in this prototype could not provide sufficient field of view and the robot body often caused visual occlusion. As a result, the

FIG. 4. Ablating a mock-up tumor of ~10.5 mm on the left lateral wall by 7-DoF MBCR (DLA is not utilized). Note the change of tumor size between snapshots is due to the camera displacement. (n) Shows postablation lesion.

FIG. 5. En bloc resection attempt: (a) reaching to grasp the mucosa tissue, (b) grasping, and (c–h) distal laser arm independent control to fire on and around the grasped tissue.

FIG. 6. Main challenges: (a) laser fiber tip sticking to the tissue, (b) laser fiber penetrating the mucosa and getting caught inside due to sticking and tissue deformation, (c) a swine bladder with a semi-conical neck, *arrows* show the neck contour, and (d) reaching a lesion with distal segment.

surgeon had to rely primarily on the transvesical anterior trocar-based endoscope for visualization. The balloon port in turn occupied a substantial portion of the small bladder, at times disrupting access and manipulation as well as posing visual occlusion in some areas. In light of these observations, the MBCR segment lengths were shortened to alleviate such challenges. However, there was substantial size variability across various porcine bladders.

Yet another challenge was that the swine bladder had a semiconical shape with a fairly acute angle at the bladder neck (Fig. 6c). Therefore, the retroflex postures could not be easily utilized to target the neck zone because of the tight space. Instead, the surgeon often pulled back the proximal and middle segments in the sheath to use the distal segment (Fig. 6d).

Another major challenge encountered was the lack of depth perception. Therefore, it was difficult to maneuver the laser tip in the plane of the tumor and sometimes it would perforate the tumor or move just over the surface. Once the laser perforated the surface of the tumor, the MBCR tip was dragged inside the tissue until the laser was pulled off, rendering the motion control challenging as shown in Figure 6b. A similar effect was caused by the fiber tip occasionally sticking to the mucosal layer surface as seen in Figure 6a.

En bloc resection was challenging since the DLA had only 2 DoFs and the grasper did not have robotic articulation. Future system designs will require independent control of the grasper and a collision avoidance algorithm to alleviate the burden of the dual-arm control of the DLA and the grasper.

A key improvement over the current system is the potential for use of stereo vision and an actively controlled camera. A simpler alternative to improve visual coverage (and not depth perception) is to use an angled endoscope (e.g., 30°) or a variable angled lens such as STORZ EndoCAMEleon® that has variable direction of view covering a range of 30°–90°. Rotation and insertion should be actively controlled by the surgeon. This could eliminate the need for the transvesical camera. A recent exploration of this concept was recently presented by Sarli and Simaan for minimizing visual occlusion.²⁸

To streamline en bloc resection/ablation and to provide sufficient maneuverability to circumscribe the targeted tissue, a DLA with more DoFs is recommended. Furthermore, motorizing the DLA insertion could be also helpful. A robotic grasper instrument would provide even more dexterity to the surgeon, further facilitating en bloc resection.

Conclusion

The outcomes and challenges of TURBTs performed with a novel robotic prototype system on several *in vivo* swine were discussed. We used the holmium laser to ablate simulated lesions in the bladder. We demonstrated early feasibility of en bloc resection. The animal studies provided insights toward enabling robotic assistance for TURBTs for clinical application. Lessons learned through this experience will inform designers of future systems for robot-assisted TURBTs.

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Author Disclosure Statement

N.S. is cofounder of a new start-up seeking to develop new technologies for robot-assisted TURBTs. In addition, he holds several patents in the area of surgical robotics. None of these patents or industry relations have been allowed to bear any impact on this research. Dr. Simaan's activity was reviewed by the Vanderbilt University conflict of interest committee and a conflict of interest management plan was set in place in accordance with PHS policy.

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Abbreviations Used

DLA = distal laser arm

DoF = degree-of-freedom

MBCR = multibackbone continuum robot

NMIBC = nonmuscle-invasive bladder cancer

TUR = transurethral resection

TURBT = transurethral resection of bladder tumor