

Evaluation of deployment capability of a novel outside-the-scope, detachable catheter system for ablation of lung lesions in ex vivo human lung models



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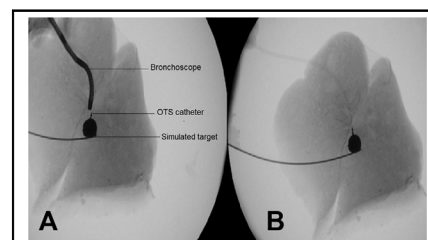
ABSTRACT

Objectives: Effective transbronchial ablation of lung nodules requires precise catheter delivery to the target lesion and freedom from the bronchoscope for safety throughout the procedure and to allow for multiple catheter insertions. A fully detachable, outside-the-scope (OTS) probe system was developed that attaches to a flexible bronchoscope. Using this system, the operator can deploy the probe in the target and completely detach it from the scope. Our aim was to demonstrate the endobronchial deployment accuracy and feasibility of an OTS, detachable, simulated ablation catheter driven to peripheral lung targets in ex vivo-ventilated human lung models.

Methods: A balloon catheter inflated with radiopaque contrast was used as a simulated peripheral target in freshly explanted lungs from lung transplant recipients. A simulated ablation catheter was positioned outside and aligned to the tip of the bronchoscope using the OTS system. Under fluoroscopic guidance, the bronchoscope and the catheter were driven toward the target in mechanically ventilated lungs. Once the catheter tip was confirmed within the target, the OTS system was released and the probe was detached from the scope. The bronchoscope was retracted and fluoroscopy was used to confirm the position of the catheter.

Results: Twelve peripheral targets were simulated. The ablation catheter was successfully deployed with its tip positioned within 5 mm from the target and confirmed stability during multiple cycles of ventilation.

Conclusions: A novel, detachable, OTS system can be successfully deployed in peripheral lung targets with potential clinical applications for multiple procedures in advanced bronchoscopy where scope freedom is advantageous. (JTCVS Techniques 2022;15:147-54)



Outside-the-scope (OTS) detachable catheter system simulating transbronchial ablation.

CENTRAL MESSAGE

A novel completely detachable outside-the-scope catheter can be deployed in peripheral lung targets. It may offer technical advantage with scope freedom for multiple advanced bronchoscopic procedures.

PERSPECTIVE

A novel, detachable, outside-the-scope catheter system can be successfully deployed in peripheral parenchymal lung targets. The initial experience with this device appears effective. The system may offer technical advantage for bronchoscopic ablative techniques and has potential implications for multiple advanced bronchoscopic procedures where device delivery with scope freedom is advantageous.

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Abbreviations and Acronyms

CT	= computed tomography
ET	= endotracheal tube
MWA	= microwave ablation
OTS	= outside the scope
PPN	= peripheral pulmonary nodule
RFA	= radiofrequency ablation

Lung cancer is one of the leading causes of cancer-related mortality worldwide,¹ and treatment options and prognosis differ according to the stage of the disease, patient comorbidities, and histologic and molecular characteristics of the tumor. Screening programs with periodic computed tomography (CT) scans of the chest have resulted in increased detection of pulmonary nodules and are showing reduction of overall and cancer-related mortality.² Surgical resection is the treatment of choice for selected patients with localized or early-stage malignancy, provided there are no significant comorbidities or limitation of cardiopulmonary function.^{3,4} In patients not amenable to undergo surgical resection, pulmonary ablative therapies can be delivered with a curative intent to accomplish local control.⁵ Furthermore, lung is not an uncommon site for metastasis, and these therapies can also be used to treat metastatic disease to the lungs as part of a multimodal treatment strategy.^{6,7}

Tumor ablation can be achieved by external radiation delivery (stereotactic body radiation therapy). However, this has limitations, particularly in patients who have received previous radiation, patients with interstitial lung disease, or if the tumor is located close to vital structures. Numerous other pulmonary ablative therapies have been used in clinical settings, such as cryotherapy, radiofrequency ablation (RFA), and microwave ablation (MWA).⁶⁻⁹ Thermal ablation induces cell necrosis by delivering extreme variations in the local temperature, either heating or freezing the tissue. Heat-based modalities include RFA, MWA, steam/vapor, and laser-induced interstitial thermotherapy, whereas cold-based modalities incorporate cryoablation. These ablative therapies can be delivered in a minimally invasive manner without significant loss of pulmonary function compared with surgical resection or radiation. Traditionally, these ablative therapies are delivered percutaneously via a transthoracic approach. However, employment of percutaneous ablative therapies requires penetration of the chest wall, parietal, and visceral pleura, and they are associated with significant and severe complications including pneumothorax, hemothorax, pyothorax, and pleural dissemination of malignancy.

To improve the safety of pulmonary ablative therapies, endobronchial technologies are rapidly evolving that enable ablation of malignant lesions in a precise fashion. The

challenge with transbronchial ablation is 2-fold: First is finding a safe, effective, and reproducible ablation modality and second is an efficient method of ablation catheter delivery. Accurate catheter delivery is imperative to the ablation procedure. The catheter not only needs to be delivered precisely to the lesion of interest, but it also needs to be free from the scope that delivers it, to allow for multiple catheter insertion and scope freedom throughout the procedure for suctioning and visualization, which is pivotal for dealing with any complications that may arise during these procedures.

This study evaluates a novel, detachable, outside-the-scope (OTS) catheter ablation system that is carried outside and along the flexible bronchoscope. Using this system, the operator can deploy the probe in the target bronchus and completely detach the scope from the probe. Our objective was to evaluate the endobronchial deployment accuracy and feasibility of an OTS, detachable simulated ablation catheter driven to peripheral lung targets in ex vivo human lung models.

METHODS**Study Design and Population**

This proof-of-concept study was conducted in a single tertiary lung cancer care center between March 2021 and June 2021. Patients on the waitlist for lung transplantation were consented to donate their freshly explanted lungs to be used for research purposes.

The Detachable OTS Catheter System

The detachable OTS catheter system (OTS Corset System; Endocision) consists of 3 main components (Figure 1): (1) a 1.7-mm (5.0-Fr), reusable simulated ablation catheter, similar in design to a cryoprobe, which is attached to the outside of a standard flexible video bronchoscope. The probe can be advanced or retracted along the side of the bronchoscope via an external working channel. (2) A rubber clip applied at the top to attach the catheter with the bronchoscope. (3) A detachable corset, made of plastic that aligns the distal end of the catheter with the tip of the bronchoscope. There are strings attached to the corset that can be pulled from the top, removing the corset from the patient to the outside and detaching the catheter from the bronchoscope. Device assembly and its utility for multiple endoscopic procedures (eg, tumor ablation, cryobiopsy, etc) are demonstrated in Video Abstract.

Procedure

Ex vivo human lung models were used to test the endobronchial deployment of the novel detachable OTS catheter ablation system. After completion of recipient pneumonectomy, explanted lungs from lung transplantation recipients were stored at 4°C and were used for experimentation within 48 hours of explantation. A Penrose drain (1 inch) was sewn to the mainstem bronchus to simulate the trachea and allow for an endotracheal tube (ET), size 9.0 Fr, to be inserted into and secured with the Penrose drain. The ET then had its balloon inflated to allow mechanical ventilation of the lungs (Figure 2). Parameters used for mechanical ventilation were respiratory rate of 15 breaths/min, tidal volume of 10 mL/kg, positive end-expiratory pressure of 5.0 cm H₂O, and fraction of inspired oxygen of 0.21.

A balloon catheter (Fogarty 14 Fr) was used as a simulated peripheral target in the lung parenchyma. The balloon catheter was inserted peripherally through a 3-mm incision in the visceral pleura and was inserted 3 cm

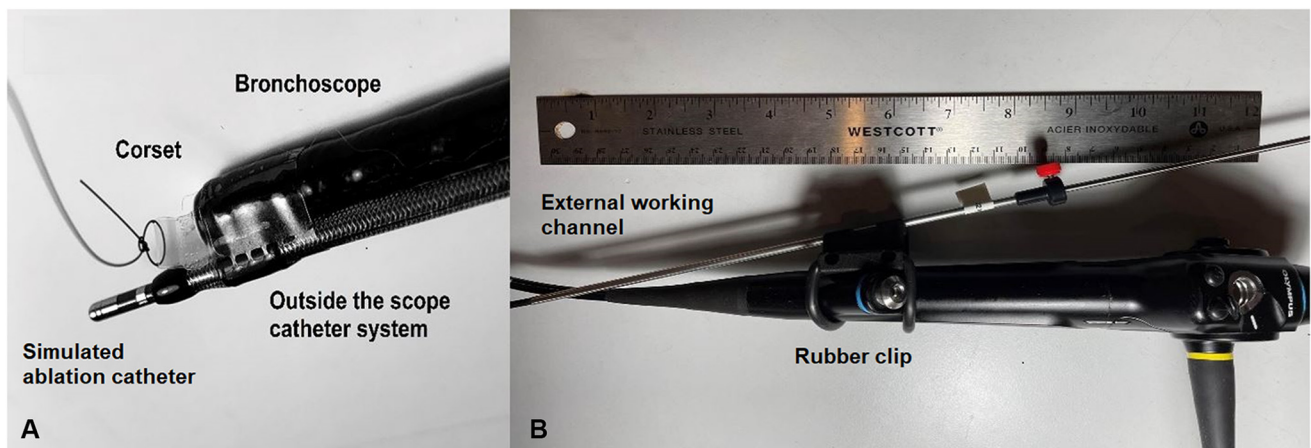


FIGURE 1. A, Outside-the-scope (OTS) detachable catheter system (OTS Corset System; Endocision) aligned at the bottom of the bronchoscope with a detachable corset. The strings attached to the corset can be pulled from the top to detach the catheter from the bronchoscope. B, OTS system with the catheter within an external working channel is attached to the bronchoscope with a rubber clip at the top.

deep from the pleural surface. The balloon was inflated with 2.0 cc of nonionic radiologic liquid contrast (Omnipaque iohexol injection, 300 mg/mL; GE Healthcare) and the catheter was attached to the lung using suture (VICRYL 2.0; Ethicon Endo-Surgery Inc). After the balloon was inflated, 3 view fluoroscopy images using a C-arm (Philips Veradius Unity; Philips Healthcare) were taken to confirm and register the position of the balloon.

A standard bronchoscope (Olympus BF P180; Olympus) with outer diameter of 4.9 mm and working channel of 2.0 mm was used and the OTS catheter system was attached to it. After adequate preparation of the system, the bronchoscope along with the OTS catheter system was introduced through the ET tube and was driven toward the target under fluoroscopy guidance. When fluoroscopy confirmed the projection of the tip of the probe within the target, the corset was released and the probe was detached from the scope. The bronchoscope was then retracted and removed from the ET tube, with the probe staying in place. Multiple bidimensional

fluoroscopy images were performed to confirm the position and stability of the probe during multiple cycles of ventilation. Once completed, the Fogarty balloon was deflated, the catheter was removed, and the pleural defect was closed with a suture line. We used bidimensional fluoroscopy for this experiment, but in an in vivo model or real-life setting standard navigational techniques such as radial probe endobronchial ultrasound, navigational or robotic bronchoscopy can be used to access the lesion. The OTS system can be used with any of the standard navigational techniques as the catheter is outside the scope in an external working channel.

Ethics

The hospital institutional review board approved this study (CR-CHUM institutional review board #: 20.220; October 16, 2020). This study was prospectively registered as a clinical trial ([clinicaltrials.gov NCT04722432](https://clinicaltrials.gov/NCT04722432)). Informed consent was obtained from lung transplant recipients before surgery, from whom the ex vivo lung models were obtained.

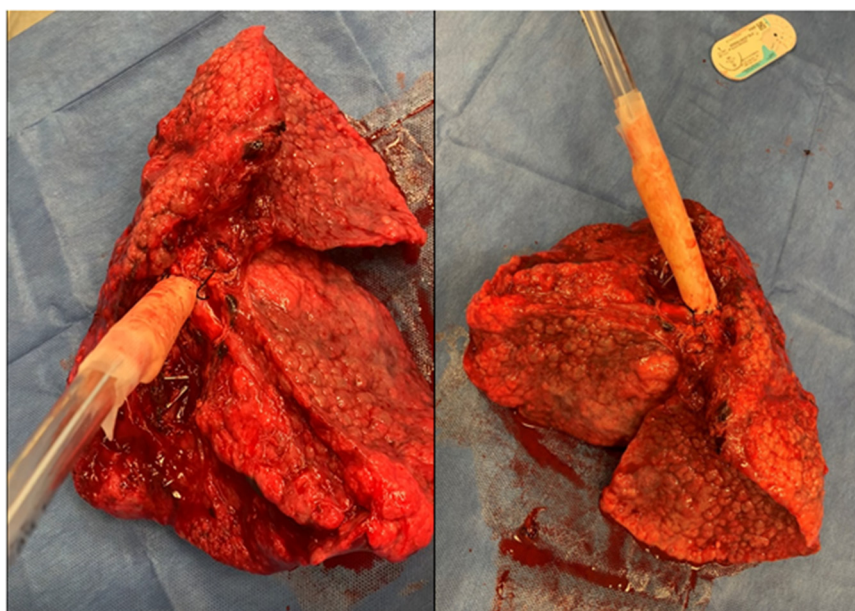


FIGURE 2. Human ex vivo explant lung stitched to a Penrose drain, which is attached to an endotracheal tube to facilitate mechanical ventilation.

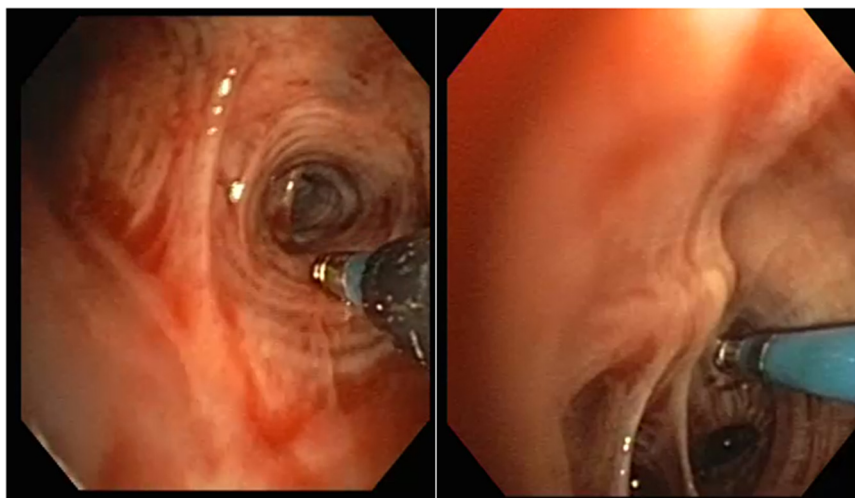


FIGURE 3. Bronchoscopic views demonstrating the attached outside-the-scope (OTS) catheter system (OTS Corset System; Endcision) approaching the target bronchial segment.

RESULTS

Four patients consented to participate in the study for their native explant lungs to be used for research purposes. Two patients had a single lung transplant and 2 had bilateral lung transplant; hence, the total number of explant lungs was 6. One patient with severe emphysema underwent bilateral lung transplant and the other 4 lungs were from patients with interstitial lung disease. We simulated a total of 12 peripheral targets in 6 explant lungs (right = 4, left = 2). All simulated nodules were injected with 2 cc of radio-opaque liquid contrast and were of similar dimensions. The target was simulated with a Fogarty balloon and subsequent OTS catheter deployment was accomplished in each lobe of the ex-vivo lung models (right upper lobe = 2, right middle lobe = 1, right lower lobe 3, left upper lobe = 3, left lower lobe = 3). Once the balloon catheter was withdrawn, the pleural defect was sealed. Depending on the lung quality and air leak, the procedure was repeated in a different segment of the same lobe.

PROCEDURE RESULTS AND FEASIBILITY

Figure 3 shows endoscopic images of the OTS catheter system approaching a bronchial segment with the simulated target. The OTS catheter system is attached to the side of the bronchoscope; its tip can be seen through the video bronchoscope and is advanced along with the bronchoscope approaching a simulated target in a subsegment in an explant lung.

The accuracy of the deployment method was measured by bidimensional (anteroposterior and lateral) fluoroscopy images (Figure 4). We successfully deployed the probe with its tip positioned at a distance less than 5 mm in both axes from the target and confirmed stability after detachment. On 4 of the 12 occasions, the catheter was not

successfully deployed in the first attempt, with a distance more than 5 mm from target or inability to detach from the bronchoscope. However, successful deployment was achieved in the subsequent attempt. After being detached from the scope, the catheter stayed in its position during multiple cycles of ventilation over 5 minutes. No device related failures were observed, such as catheter dislodgement after detachment from the bronchoscope or retained corsets in the lungs. Figure 5 shows a graphic summary of the OTS catheter system and a simulated tumor ablation.

DISCUSSION

This study reports the technical feasibility and a proof of concept for a novel, detachable, OTS catheter system for transbronchial ablation of peripheral lung nodules. We successfully deployed the catheter in 12 simulated targets in an ex vivo human lung model with no device-related failure.

CT scan-guided transcutaneous biopsies are associated with complications such as pneumothorax or hemorrhage, which have been reported to be approximately 24%.¹⁰ This is even greater for CT-guided ablation techniques, with complication rates ranging from 12.8% to 24.6% for RFA and 11.9% to 66.7% for MWA.¹¹ In patients with poor cardiopulmonary reserve and low tolerance to any complications such as pneumothorax, the best alternative treatment option is one that is least invasive and provides best possible results. There has been growing interest in endoscopic interventions in the diagnosis and treatment of peripheral pulmonary nodules (PPNs), given their safety, efficacy, and cost-effectiveness. With the advent of navigational and robotic bronchoscopy, precise access to PPNS via natural orifices is improving. Obtaining an accurate diagnosis is essential to providing treatment; bronchoscopic techniques for ablation of peripheral pulmonary nodules

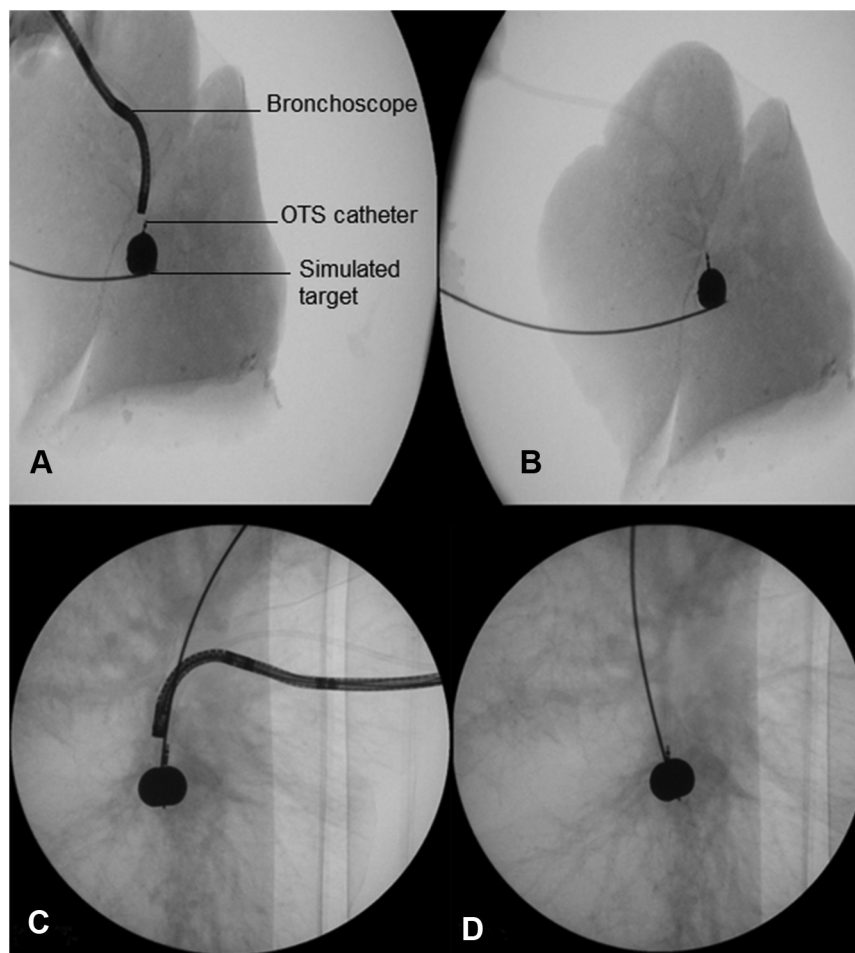


FIGURE 4. Fluoroscopic images of simulated ablation procedure. A, Anteroposterior view showing contrast filled simulated target lesion in left lower lobe, bronchoscope, and simulated catheter attached outside-the-scope (OTS) device (OTS Corset System, Endocision) are in close proximity to the target lesion. B, Bronchoscope has been retracted and simulated catheter remains in stable position. C and D, lateral views of the left lower lobe demonstrating the same procedure.

allow for diagnosis, staging, and treatment of PPNs within a single procedure, which is the panacea of lung cancer treatment. Total bronchoscopic diagnosis, staging, and treatment in a single procedure is extremely cost effective and reduces the number of invasive procedures and may potentially avoid procedure-related complications. Endoscopic techniques may pose a lower risk of radiation-induced pneumonitis and a lower risk of pneumothorax compared with percutaneous RFA.¹²

Currently, potential bronchoscopic options for treatment of peripheral lung tumors, some of which are based on the basis of preclinical research work in animals, include direct injection of intratumoral chemotherapy or gene therapies, transbronchial brachytherapy, bronchoscopy-guided RFA and MWA, placement of markers to guide real time-radiation and surgery, photodynamic therapy, heat modalities (argon plasma coagulation, electrocautery, laser phototherapy), and bronchoscopic thermal vapor ablation.^{13,14}

Previous studies have shown to achieve local control rate of 82.6% (19/23 lesions) with bronchoscopic RFA in patients with medically inoperable non-small cell lung cancer.¹² Tanabe and colleagues¹⁵ showed good results with bronchoscopic RFA in 10 patients with near-complete coagulation necrosis of the tumor and no complications. However, there was some viable tumor cells in the periphery of ablation zone. Steinfort and colleagues¹⁴ showed large areas of tumor ablation in 4 patients with near-complete necrosis in 2 of 6 patients with bronchoscopic thermal vapor ablation. Endobronchial cryotherapy is also an effective tumor ablative technique and is associated with minimal complications. There has been a suggestion that cryotherapy can stimulate the immune system to trigger antitumor effects in human lung cancer.¹⁶ The use of natural orifices to reach the lesions and provide ablation safely has been demonstrated in previous studies.^{17,18} Tsushima and colleagues¹⁹ showed that bronchoscopy-guided RFA was safe and feasible in

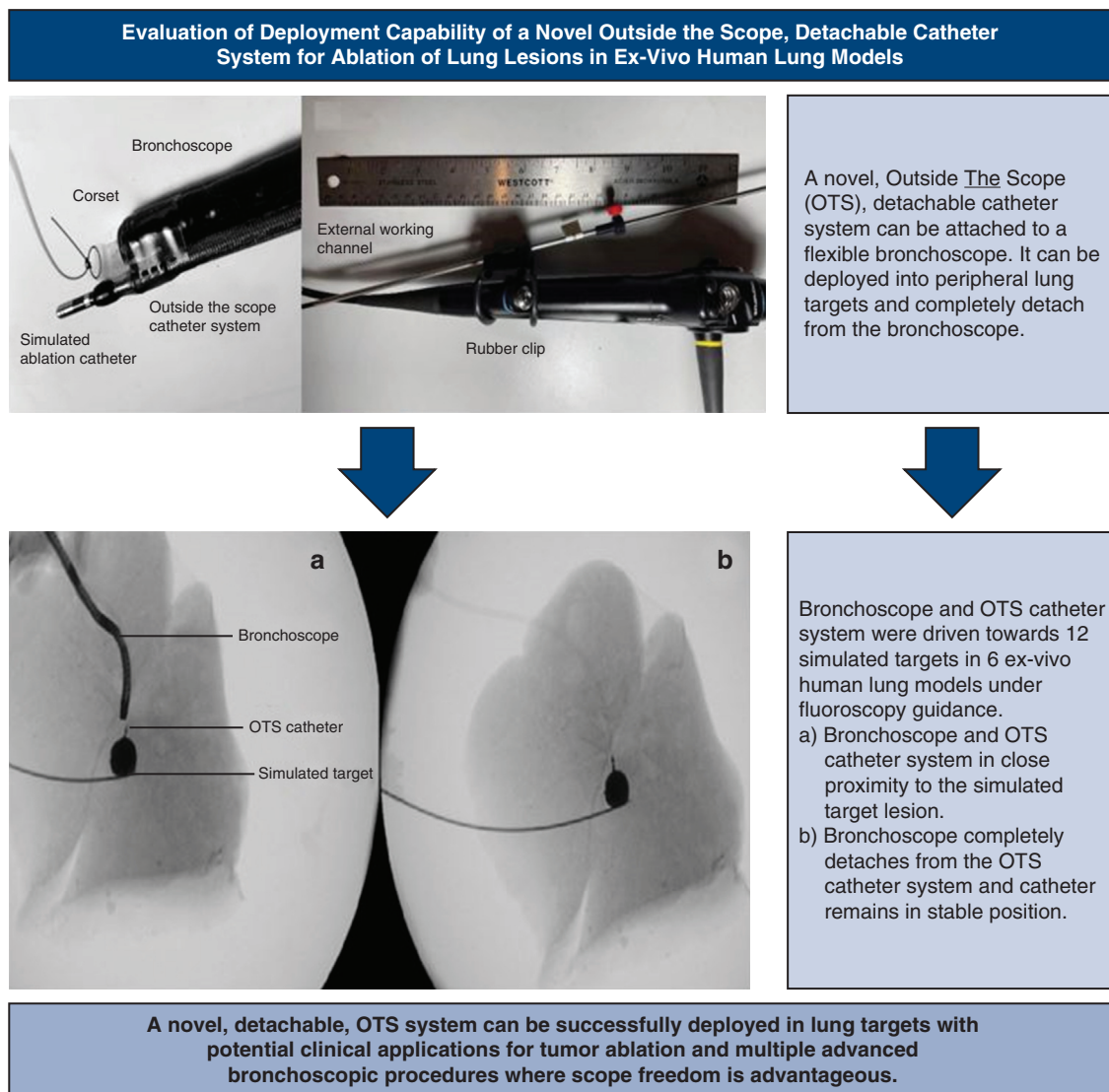


FIGURE 5. Schematic summary of the OTS catheter system and a simulated ablation procedure.

sheep lungs. Xie and colleagues²⁰ reported navigation bronchoscopy-guided RFA for peripheral pulmonary tumors with success and a decent safety profile.

To our knowledge, no previous device has been developed that allows a catheter or tool to be deployed outside the bronchoscope and allow complete freedom of the scope from the device. This is important for several reasons. First, this can be advantageous for multiple catheter deployments enabling simultaneous multiple-site treatments or multiple catheter deployments in the same target in terms of larger tumors requiring ablation in different portions of the tumor to achieve desired oncologic results. Although, with our current design, insertion of a second catheter requires withdrawing the bronchoscope and reloading another OTS catheter, it may be more time efficient overall performing simultaneous ablations given multiple catheters can be

activated at the same time for desired duration. Second, it can be useful during procedures in which the operator requires control of the scope with a free working channel and the catheter remains in place. This is particularly helpful to deal with intraprocedural complications such as local hemorrhage and desaturation. Third, these catheter probes are flexible and are easily deployed in the segmental airways, and this procedure can be performed under local or general anesthesia with a flexible bronchoscope allowing direct visualization of the OTS catheter system. Although we used a standard flexible video-bronchoscope with an outer diameter of 4.9 mm for this study and only used fluoroscopy to guide the bronchoscope into target lesion, the OTS catheter system can easily attach to smaller diameter bronchoscopes as the rubber clip and the detachable corsets used to attach the OTS system are being available in

different sizes (Figure 1). However, given it is outside the bronchoscope, it will increase the overall diameter depending on the size of the catheter. Hence, the device can be used with navigational or robotic bronchoscopy to target peripheral lesions in the smaller airways with image guidance to confirm stability of the catheter in the lesion. The OTS catheter system may offer a technical advantage with radial probe endobronchial ultrasound, given there is a free bronchoscope working channel as well as an external OTS working channel and the catheter can be advanced into the target under direct ultrasound and imaging guidance.

Future Directions

This study was a proof-of-concept experiment evaluating the feasibility of successful deployment of a simulated OTS ablation catheter system. This technology is in the early phase of clinical research; with technical developments and improvements in design, endoscopic placement will be easier, which will facilitate bronchoscopic ablation of peripheral lung tumors. The next step would be to assess the efficacy and safety in vivo of the OTS probe system to allow for successful deployment of the tool in lesion with complete scope freedom for various ablation treatments. First, we aim to use navigational bronchoscopy in an in vivo animal model to access target lesion under cone-beam CT with augmented fluoroscopy for precise localization of the lesion as well as to confirm the stability of the OTS catheter. Multiple catheters can be deployed in different lesions, which then can be ablated simultaneously with the OTS catheter system. The efficacy can be assessed histopathologically by surgical resection or by follow-up surveillance imaging. Larger multicenter trials are warranted to further assess the safety, feasibility and efficacy of the device in vivo.

In the era of robotic bronchoscopy, this device may be useful for accessing small peripheral pulmonary nodules in conjunction with image guidance. Furthermore, this device may have implications for multiple procedures where biopsy or ablation of a peripheral target can be achieved without having to remove the bronchoscope, saving time and improving accuracy and safety of the procedure.

Transbronchial cryobiopsy is an effective diagnostic tool for various forms of interstitial lung disease. It has shown to be an accurate and an alternate option to surgical lung biopsy in diagnosis of diffuse parenchymal lung diseases.^{21,22} One of the major complications during a transbronchial cryobiopsy is bleeding, which can be difficult to control endoscopically. Previous studies have reported moderate-to-severe bleeding rates of up to 39%.²³ Conventionally, a prophylactic balloon occlusion technique is used as a hemostatic measure to deal with bleeding; however, it has its own limitations, as it can interfere with bronchoscope manipulation. Other techniques such as 2-scope technique for transbronchial cryobiopsies have been employed to minimize

bleeding-related complications and achieve hemostasis.^{24,25} This involves rapidly changing the scopes with 2 operators doing the procedure. However, this still involves a time delay between changing the scopes, involves 2 operators skilled in bronchoscopy, and does not enable real-time visualization during the procedure. The current OTS catheter system may hold promise in this regard, given that the bronchoscope can stay in place, free from the probe in the airway, providing real-time confirmation of probe position, and hemostasis, which has the potential to minimize collateral damage and prevent major bleeding-related complications.

Limitations

This study has some important limitations. First, as with any developing technology, we tested the device in an ex vivo model; hence, the safety of the device in a real-world situation cannot be assessed. However, we simulated ventilation and our aim was to provide data on the feasibility and functionality in terms of detachability and device stability in lesion, which was accomplished. Second, we had a small sample size with only 12 simulated targets, and although we successfully deployed the catheter into the simulated targets, our sample size is not large enough to exclude technical complications such as deployment failure or equipment malfunction. Furthermore, there is a learning curve involved in accurately deploying the catheter system however, with increased familiarization of endoscopists with the equipment and improvement in design, this should not be a major issue as the device is intuitive and user-friendly.

CONCLUSIONS

A novel, detachable, OTS catheter ablation system can be successfully deployed in peripheral parenchymal lung targets with potential clinical applications. The initial experience with this device appears effective. The system may offer technical advantage for bronchoscopic ablative techniques and has potential implications for advanced flexible and robotic bronchoscopy with device delivery for multiple advanced bronchoscopic procedures where scope freedom is advantageous.

Conflict of Interest Statement

The authors reported no conflicts of interest.

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Key Words: tumor ablation, transbronchial ablation, peripheral lung nodules