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Microwave Ablation for Malignant Central Airway Obstruction: A Pilot Study

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Keywords

Airway obstruction · Bronchoscopic treatment · Interventional bronchoscopy · Lung cancer · Microwave ablation · Tracheobronchial obstruction · Tumor ablation

Abstract

Background: Malignant central airway obstruction (CAO) is a debilitating complication of primary lung cancer and pulmonary metastases. Therapeutic bronchoscopy is used to palliate symptoms and/or bridge to further therapy. Microwave ablation (MWA) heats tissue by creating an electromagnetic field around an ablation device. We present a pilot study utilizing endobronchial MWA via flexible bronchoscopy as a novel modality for the management of malignant CAO. ***Methods:*** Therapeutic bronchoscopy with a flexible MWA probe was performed in 8 cases. We reviewed tumor size, previous ablative techniques, number of applications, ablation time, amount of energy delivered, rate of successful recanalization, complications, and 30-day follow-up. ***Results:*** Successful airway recanalization was achieved in all cases. No complications were noted. In 1 case, tumor ingrowth within a silicone stent was ablated with no damage to the stent. ***Discussion:*** Endobronchial MWA is a novel technique for tumor destruction while maintaining an airway axis. The oven effect and air gap around a tumor allow for safe and effective tissue devitalization and hemostasis without a thermal effect on structures surrounding the airway.

Introduction

Malignant central airway obstruction (CAO) is a debilitating complication of primary lung cancer and pulmonary metastases occurring in up to 30% of patients [1]. Patients with CAO often have significant respiratory symptoms and impaired quality of life in addition to a poor overall prognosis [2]. The goal of therapeutic bronchoscopy is to recanalize an airway to palliate symptoms, bridge to further cancer therapy, and improve survival [3]. Thermal modalities such as electrocautery, argon plasma coagulation (APC), and laser are widely used for the management of CAO and utilize a spectrum of tem-

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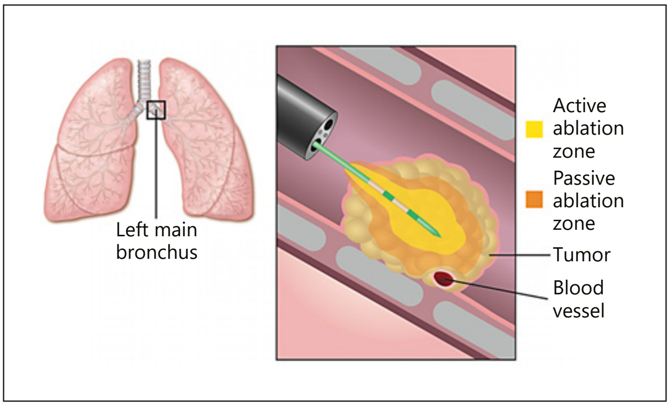

Fig. 1. Characteristics of MWA with ablation zones, oven effect, and thermal sink effect.

peratures to achieve hemostasis and devitalize tissue prior debridement [4].

The thermal effects of electrosurgery on tissue depend on the temperature reached as well as the rate and duration of tissue heating. Based on tissue conductivity and duration of heating, either reversible or irreversible changes can occur at temperatures between 40 and 50°C. Protein denaturation occurs above 60°C and cellular changes become irreversible. Regardless of the technology, tissue is heated by both active and passive means, thus creating active and passive ablation zones (Fig. 1). Tissue conductivity ultimately determines the results of the thermal procedures. The water content of a particular type of tissue affects the tissue conductivity. High-water-content tissues such as blood, muscle, and kidney offer less resistance to current flow than tissue with less water content (soft tissue, bone, mesentery, etc.). The tissue behaves as a resistor, and as its temperature rises above 60°C, protein denaturation accentuates heating effects and creates a passive ablation zone while avoiding a thermal effect beyond this boundary. Air gaps already present or created by microwave ablation (MWA) as a tumor shrinks as well as airway cartilage play a role in the preservation of the surrounding structures. An analogy is a microwave oven. When food inside an oven is heated, the outside environment remains intact and unaffected; this is called the "oven effect" (Fig. 1) and can be useful when debulking a large amount of tissue utilizing longer ablation times.

MWA is a field-based technology that heats tissue by creating an oscillating electromagnetic field around an ablation device [5]. The existing polar molecules in the tissue (mostly H_2O) are forced to continuously move back and forth billions of times per second, causing friction and resulting in temperature elevation. MWA has been used regularly for the ablation of liver tumors, particularly hepatocellular carcinoma, and is increasingly used for peripheral lung tumor ablation [6]. It has multiple advantages which make it a safe, effective modality for endobronchial tumor ablation. The oven effect, together with limited "thermal sink effect," makes MWA suitable for ablation around larger vascular structures (Fig. 1) [7]. Another advantage of MWA is that the wavelength of the microwave energy elongates as the denaturing protein changes the tissue's dielectric constant. This causes a comet-shaped ablation zone, which is particularly important in nonuniformly shaped airways. In this paper, we present a pilot study of 8 cases utilizing MWA via flexible bronchoscopy as a novel modality for the endobronchial management of malignant CAO. We demonstrate that MWA can be safely utilized for the ablation of obstructing endobronchial disease. Additionally, we hope this study fuels future endeavors to determine the ideal dosimetry of microwave energy needed to achieve endobronchial devitalization of tissue.

Methods

We report eight endobronchial MWAs of obstructing central airway tumors using a flexible MWA probe performed at the University of Mississippi Medical Center between January 1, 2019, and June 30, 2020. IRB approval was obtained as well as informed consent prior to each bronchoscopy. We included patients 18 years and older with endobronchial or endotracheal lesions obstructing at least 50% of the affected airway lumen. Two interventional pulmonologists (M.S. and G.E.A.) performed the procedures under general anesthesia, while patients were intubated, ventilated, and oxygenated via a rigid bronchoscope or tracheoscope (Karl Storz, Tuttlingen, Germany). A tumor permittivity feedback control MWA system (PulsaBlade™ MedWaves Inc.) was used in a temperature control mode with a set target temperature range between 80 and 90°C. When powered on, the system began to deliver microwave energy at a maximum power until the probe reached the target temperature range. The power (10–32 W) and the frequency (902–928 MHz) of the delivered microwave energy were continuously automatically adjusted by the generator, reflecting the ever-changing conditions within the ablation zone to maintain a target temperature of 80°–90°C at the microwave probe active tip. The system reported the amount of energy delivered in kilojoules (kJ), ablation duration, reflected power, set and actual tissue temperature, and alerts of unsafe system conditions.

A 1.7-mm, 1-cm active tip, 123-cm length microwave probe was used in each session to deliver variable amounts of energy during each application. After connecting the flexible MWA probe to the microwave generator (MedWaves Inc., AveCure ®), the probe was inserted into the working channel of a flexible therapeutic bronchoscope (Olympus BF 1T1180). The tip of the MWA probe was in-

Table 1. Patient and tumor characteristics, complications, and follow-up

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Tumor location	LMS bronchus	LSM bronchus	RMS bronchus	Trachea	LMS bronchus	RMS bronchus	RMS bronchus + trachea	LMS bronchus
Size, mm	35 × 13	30 × 15	20 × 14	20 × 18	20 × 14	34 × 12	25 × 11	35 × 15
Prior endoscopic therapies	APC, stent placement ×2	APC, PDT	None	Y stent	None	None	None	None
Setting	Outpatient	Outpatient	Outpatient	Inpatient	Inpatient	Inpatient	Outpatient	Outpatient
Adjunctive intervention	None	None	SEM stent placed	None	APC for hemostasis	None	Y-stent placed	None
Pathology	Metastatic neuroendocrine tumor	Metastatic renal cell carcinoma	Lung adenocarcinoma	Metastatic synovial sarcoma	Metastatic rectal carcinoma	Large cell carcinoma	Adenocarcinoma	Non-small cell, NOS
Clinical/pathological stage	IV	IV	IV	IV	IV	IV	IIIB	IIIA
Treatment within 30 days postablation	Chemotherapy	Immunotherapy	Immunotherapy	Unknown	Hospice	None[2]	None[2]	None[3]
Preprocedure mMRC dyspnea grade	3	3	4	4	4	4	4	3
mMRC dyspnea grade at follow-up	2	3	Unknown	Unknown	Unknown	2	2	0
24-h postablation AE	None	Fluid-responsive hypotension	None	None	None	None	None	None
30-day severe AE[1]	None	None	None	Unknown	None	None	None	None
Overall survival, days	58	>90	84	35	39	>90	>90	>90

APC, argon plasma coagulation; RMS, right main stem; LMS, left main stem; PDT, photodynamic therapy; SEM, self-expanding metallic; NOS, not otherwise specified; mMRC, modified Medical Research Council; AE, adverse event. [1] Severe AE includes the change in clinical status requiring a higher level of care, readmission to hospital, massive hemoptysis, acute changes in mental status, acute respiratory failure requiring invasive or noninvasive positive pressure ventilation, cardiovascular event, and death. [2] Immunotherapy initiated >30 days postprocedure. [3] Surgical resection performed >30 days postprocedure.

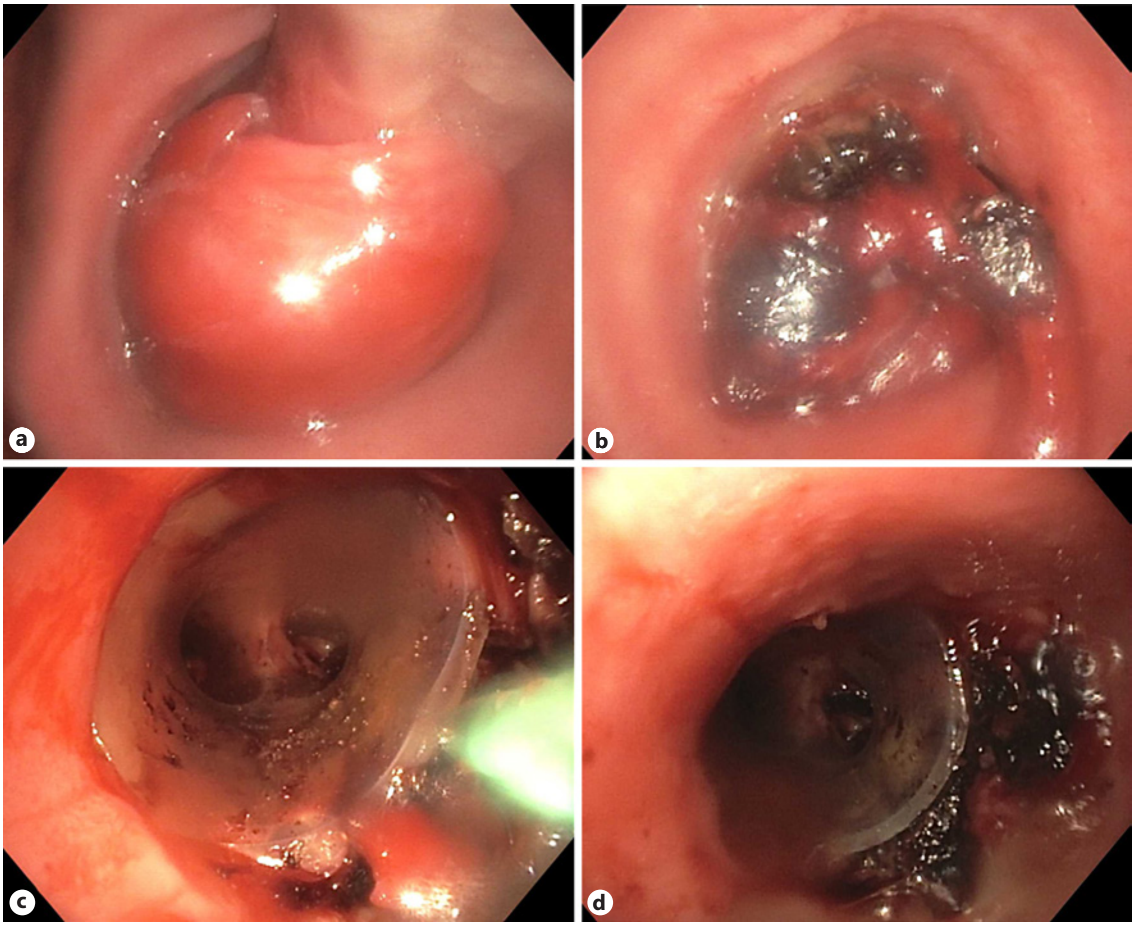

Fig. 2. MWA of a tracheal tumor completely obstructing a silicone stent. **a** Ball valve tracheal tumor completely obstructing the proximal end of a silicone stent. **b** Partial ablation of tracheal tumor, revealing tumor inside and outside of the stent. **c** Tumor inside stent has been ablated. MWA catheter inside tumor between stent and airway wall. **d** Postablation of tumor inside and outside of silicone stent.

serted into a visible part of the endobronchial tumor. Multiple MWA applications were delivered from different angles. The duration of each application was chosen based on visible changes of the tissue as well as the degree of hemostasis. The tumor was removed by mechanical means after each ablation. APC straight fire probe (pulsed, 40 W, 0.8 L) was used if further hemostasis was needed after tumor debulking. Lesion location, size, and involvement of the surrounding structures were determined from a diagnostic CT or PET/CT scan performed prior to the procedure. Sizing of each lesion was performed by combining airway lumen diameter and CT measurements of the lesion. All tissue removed was sent for pathological examination based on clinical indication. Unless lost to follow up or in a hospice care, all patients were followed up clinically postprocedure. Due to the palliative nature of the procedure, patients were subjected to repeat bronchoscopy only if indicated. Pre- and postprocedural assessment of dyspnea was done using the modified Medical Research Council (mMRC) dyspnea scale.

After the first 8 cases, we retrospectively reviewed tumor measurements, previous ablative techniques, number of microwave energy applications, time of each application, total time of MWA, amount of energy delivered, set temperature during ablation, rate of successful ablation, need for other ablative techniques, adjunctive interventions, other treatment received within 30 days postablation, complications, and 30-day follow-up. We calculated the mean time, mean energy delivered, and standard deviations of ablative applications per case. Energy delivered per mm^3 tumor volume was calculated as total energy delivered (kJ) divided by the estimated tumor volume based on the measured diameters and the ellipsoid volume formula.

Results

Eight patients with CAO were treated with endobronchial MWA. Table 1 summarizes the characteristics of the tumors, procedural details, change in mMRC, and overall survival. We achieved successful airway recanalization in all cases, defined as at least a 50% improvement

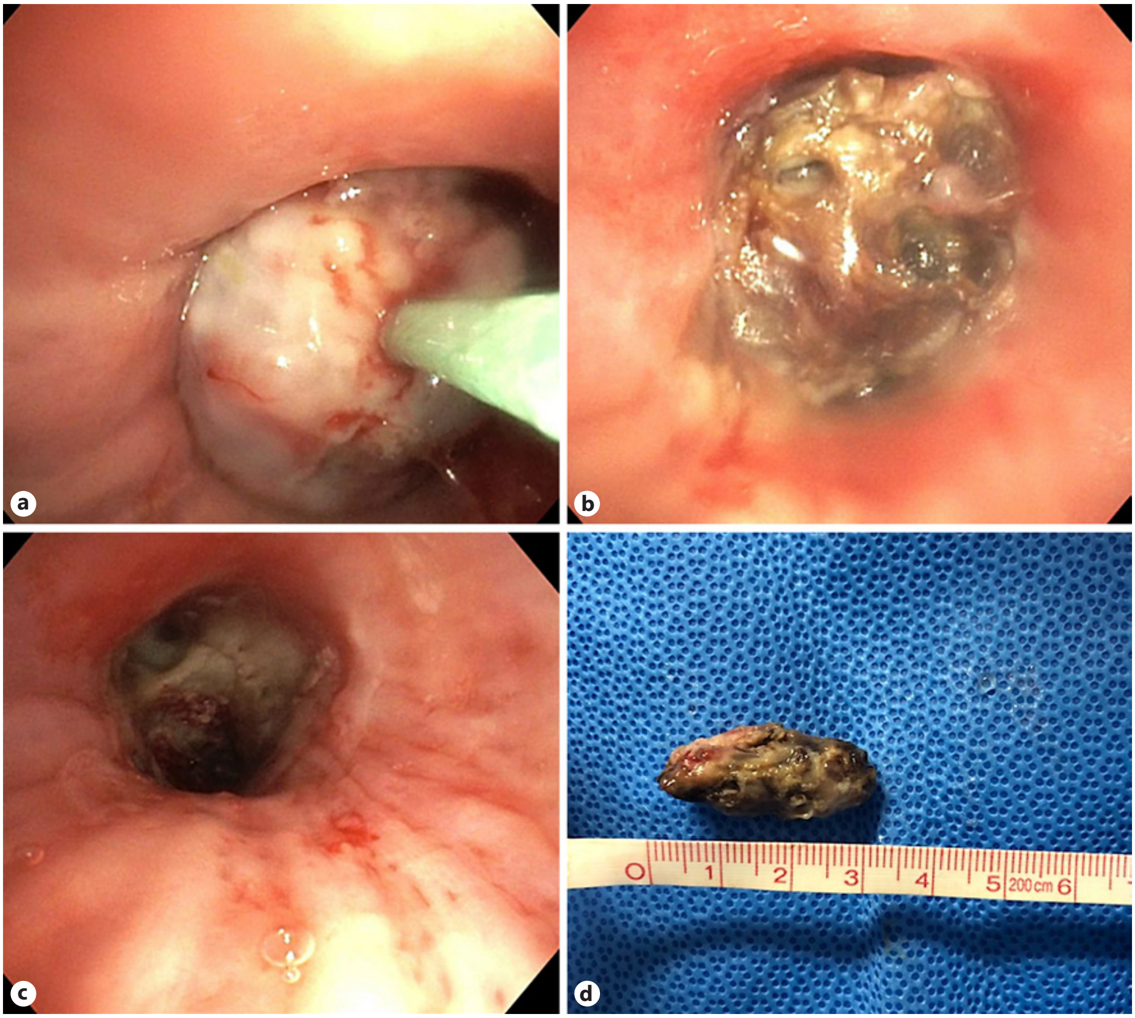

Fig. 3. MWA of a LMS bronchus tumor. **a** Tumor completely obstructing the LMS bronchus with a microwave catheter placed in the center. **b** Postablation of LMS tumor. Notice an air gap between the tumor and airway mucosa. **c** Patent LMS bronchus after ablation and tumor removal. **d** LMS tumor cored out in one piece. LMS, left mainstem.

in airway lumen size as measured visually pre- and postprocedure. No immediate complications were noted. One patient experienced postprocedural fluid-responsive hypotension and was admitted for observation after the procedure. This was ultimately attributed to anesthesia effect. There were no severe adverse events reported within 30 days postprocedure in 7 cases. No information about postoperative course beyond first 24 h was available in case 4 as the patient was lost to follow up. All patients were alive at 30 days. Four cases received no additional treatment within 30 days postprocedure. Of those 4 cases, 1 patient died in hospice care and 3 patients who underwent further cancer treatment were alive past 90 days postprocedure. In 1 case, we ablated tumor ingrowth within a silicone stent and restored airway patency with no damage to the stent (Fig. 2). We observed the previously described "oven effect" during all ablations. As the tumor was centrally ablated, we noticed that the borders of the tumor moved further away from the surrounding structures creating or increasing an air gap. This was particularly useful during ablations with less clear airway axes as well as during ablation around the silicone stent. It also allowed us to remove ablated tumor in one or two large pieces in the majority of the cases (Fig. 3). We biopsied underlying mucosa posttumor removal in 1 case. Pathological examination showed no tu-

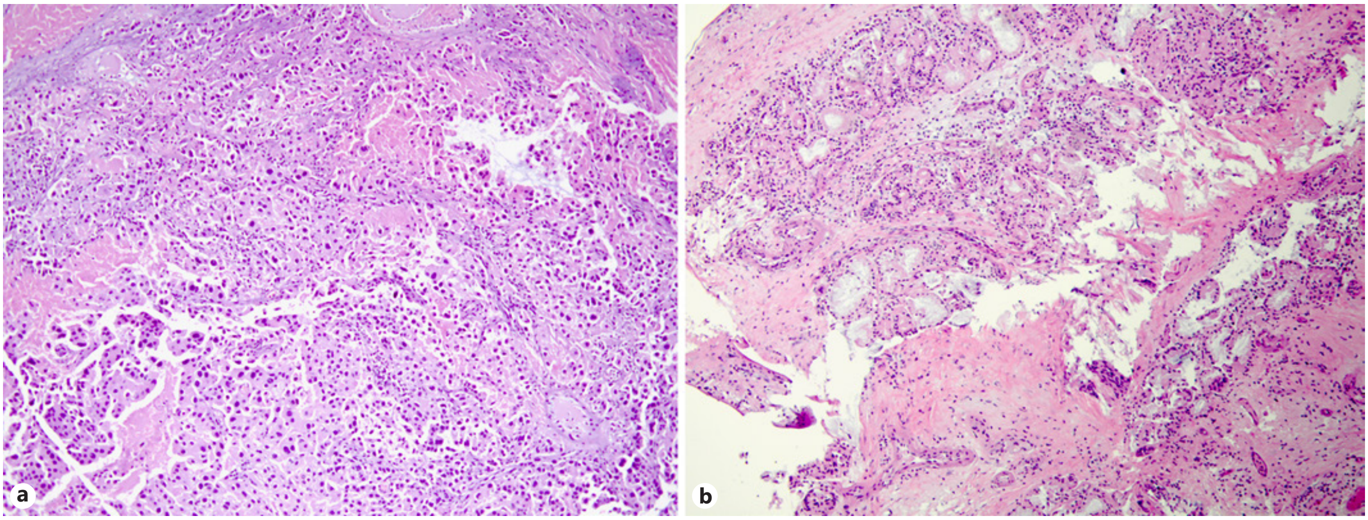

Fig. 4. a Endobronchial biopsy of right mainstem bronchus tumor. H&E, ×200: Sheets of malignant cells with hyperchromatic nuclei and dense cytoplasm, and foci of necrosis. **b** Postablation endobronchial biopsy of right mainstem bronchial wall. H&E, ×200: fragments of unremarkable bronchial wall with submucosal glands. No malignancy identified.

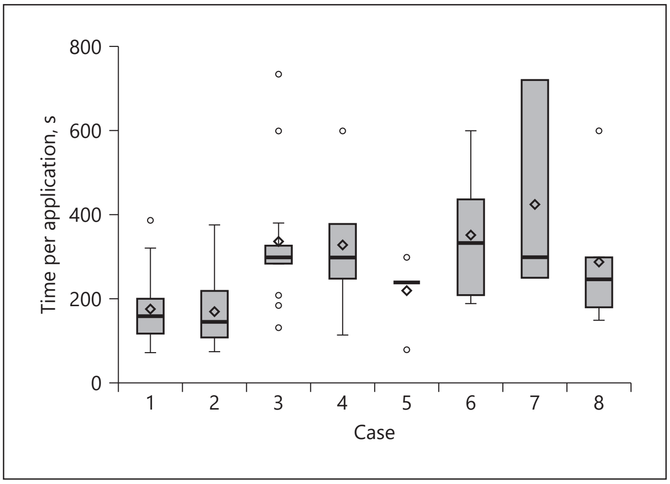

Fig. 5. Distribution of energy application times in each ablation case.

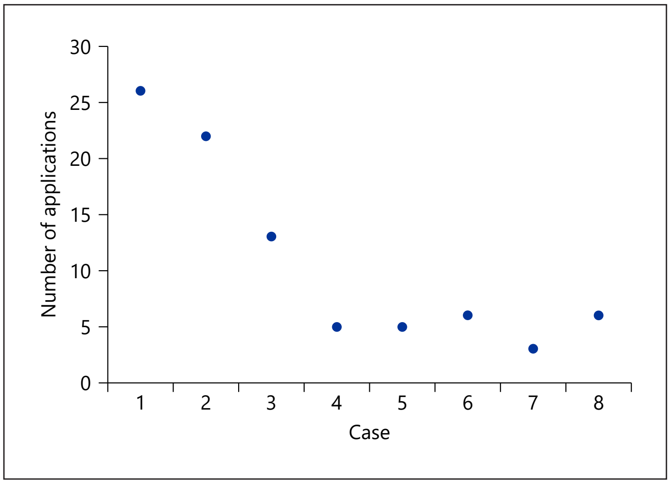

Fig. 6. Number of microwave applications in each ablation case.

mor present and preserved normal airway mucosa (Fig. 4). Two patients underwent repeat bronchoscopy for stent revision; we observed no macroscopic delayed effects of MWA on the adjacent airway wall in either case. We observed that as the operator became more familiar with endobronchial MWA, the duration of each ablation application increased (Fig. 5), while the total number of applications decreased (Fig. 6). Table 2 outlines the technical aspects of MWA applications.

Discussion

In this study, we describe eight successful cases of endoluminal MWA of obstructing tracheal and bronchial tumors. In all cases, MWA aided complete airway recanalization with no MWA-related complications. One patient experienced postprocedural, fluid-responsive hypotension for which the patient was admitted to the hospital, observed, and discharged the following day. This

Table 2. Microwave ablation procedural characteristics

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
MWA applications, *n*	26	22	13	5	5	6	3	6
Total energy delivered, kJ	58.0	76.5	93.1	31.7	19.2	43.7	18.4	31.2
Mean (std. dev.) energy per application, kJ	2.2 (0.9)	3.5 (1.8)	7.2 (2.6)	6.3 (2.9)	3.8 (1.1)	7.3 (3.0)	6.1 (2.8)	5.2 (2.3)
Total time of energy delivery, min	75.9	62.4	73.0	27.4	18.3	35.1	21.2	28.7
Mean (std. dev.) time per application, min	2.9 (1.3)	2.8 (1.4)	5.6 (2.7)	5.5 (3.0)	3.7 (1.4)	5.8 (2.7)	7.1 (4.3)	4.8 (2.7)
Energy per tumor volume, kJ/mm^3	18.7	21.6	45.4	9.3	9.4	17.0	11.6	7.6
Target temperature, °C	80	90	90	90	80	90	90	90

°C, Celsius; kJ, kilojoules; MWA, microwave ablation; s, seconds; Std. Dev., standard deviation.

patient had undergone 4 previous bronchoscopic procedures for airway debulking, none of which used MWA, and experienced postprocedural hypotension each time, attributed to anesthesia effect. We therefore attribute this patient's hypotension again to anesthesia effect and not as a complication of MWA.

To our knowledge, this is the first description of this type of approach to airway recanalization. Trigiani and colleagues [8] describe a series of 7 cases of airway stenosis from extrinsic compression for which they applied MWA via a rigid needle placed through the airway wall. They, however, do not describe endobronchial ablation of obstructing intrinsic tumor using an MWA catheter [8].

We observed that as operator familiarity with the procedure improved, in general the duration of each MWA application increased, while the total number of applications decreased. Additionally, we found that we delivered higher amounts of total energy (kJ) and energy per tumor volume (kJ/mm^3) as well as had longer total ablation times in the first 3 cases due to the initial learning curve. Endobronchial MWA ablates tumor from the inside outward, which contrasts with all other traditional thermal ablation techniques. As we learned the visual signs indicating adequate ablation, we found that total ablation time and amount of energy delivered both decreased. Longer ablation times did occur if there was intralesion hemorrhage, likely due to some aspect of the "heat sink" effect, where energy applied to a target tissue is dispersed due to the presence of surrounding blood vessels or bleeding. However, we did not halt MWA in any case due to bleeding, and ultimately, MWA caused coagulation and hemostasis in all cases. We visually observed a significant tissue contraction during endobronchial MWA, which has been described previously in the liver and the lung parenchyma with both RFA and MWA. In ex vivo lung tissue, MWA has been shown to contract ablated tissue by nearly 50%. Protein denaturation, cellular dehydration, and collagen contraction are all thought to play a part in this process [9].

Both RFA and MWA are ablative technologies that have been used in the treatment of liver and peripheral lung tumors. MWA is an electromagnetic, field-based technology and is not reliant upon an electrical conductive path as is the case with RFA; thus, MWA can more effectively ablate tissue with low conductivity. RFA requires tissue conductivity, which can be impaired at temperatures above 95°C. These elevated temperatures result in water evaporation, tissue desiccation, and charring, consequently raising impedance and limiting the effectiveness of RFA. MWA does not rely on conductivity and can penetrate tissue with low water content such as lung or charred soft tissue [10]. These properties make RFA more susceptible to the "heat sink" phenomenon, which leads to unpredictable sizes and shapes of the total RFA ablation zone. In contrast, MWA has a larger, more homogeneous, and more predictable ablation zone that is less susceptible to "heat sink." MWA additionally requires less ablative time than RFA [11, 12]. These characteristics inherently make MWA a potentially safer, more reliable means of ablating tissue surrounded by large blood vessels. The "oven effect," as described earlier, is also a useful property of MWA, especially when debulking a larger amount of endobronchial tissue utilizing longer ablation times as it accentuates the passive heating zone and preserves underlying mucosa. All of these properties of MWA make it a technology suited for endobronchial destruction of tissue.

When compared to tools that are widely used to manage malignant CAO such as APC and Nd:YAG laser, we see several differences with MWA. Tumor ablation and devitalization both occur starting at the center of the tumor and extend to the periphery, whereas ablation with conventional methods begins on the external surface of the lesion. Using MWA, tissue contraction allows maintenance of airway axis visibility and the enlarging air-gap minimizes the risk of the thermal injury to surrounding tissue or structures, including devices such as stents. Given the mechanism of action, there is no need for decreased oxygen administration during the ablation, which is a significant advantage in patients requiring high oxygen content. It also avoids the potential for the rare but serious complication of airway fire seen using traditional electrosurgical tools. Grounding, which is required for electrocautery devices, is not needed with MWA due to its unique mechanism of energy delivery. Additionally, the time required to perform mechanical debulking post-MWA is much shorter as most of the obstructing tumors can be removed in large pieces without causing hemorrhage. In comparison, APC due to its shallow depth of penetration is often used repeatedly during mechanical debulking to devitalize the exposed parts of a tumor and to control bleeding. Finally, there is no risk of gas embolism with MWA as exists with APC and Nd:YAG laser [13].

As we have shown in this pilot study, endobronchial MWA is an effective means of achieving tissue devitalization and subsequent airway recanalization. It should be studied further to assess ideal ablation settings and to confirm its safety profile. In further trials, we suggest treating lesions with >75% airway obstruction and/or where the airway axis is unclear using 2-5 5-min applications with the target temperature of 80°C. The MWA probe should be repositioned to different areas of a tumor between individual applications. We also suggest using visual improvement in the airway axis due to tumor contraction as the metric by which total ablation time is determined rather than macroscopic thermal changes such as tissue charring.

Conclusion

Malignant CAO may have serious consequences, such as severe respiratory symptoms resulting in decreased quality of life and increased mortality. Therapeutic bronchoscopy plays a key role in the management of these cases by recanalizing airways in a variety of manners. Different thermal ablative technologies are available and can be used endobronchially to achieve airway patency. MWA is a field-based technology used reliably in the treatment of liver and peripheral lung parenchymal tumors. It confers an excellent safety profile and produces reliable active and passive ablation zones due to various inherent technological factors, including improved tissue conductivity and decreased "heat sink" effect as compared to RFA. We report the first series of MWA used endoluminally in cases of intrinsic tracheal and bronchial obstruction. In this series, MWA was both safe and effective in achieving airway recanalization. We recommend further studies of endobronchial MWA to further characterize proper dosimetry settings as well as duration and number of applications needed to adequately ablate endoluminal airway tumors.

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Statement of Ethics

This research complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Studies involving human subjects. Informed consent was obtained prior to each procedure. Institutional Review Board of University of Mississippi Medical Center approved the study protocol (IRB File #2020-0185).

Conflict of Interest Statement

M.S. has been a scientific consultant for Medtronic Inc., MedWave Inc., and Optellum Inc. G.E.A. has been a scientific consultant for AstraZeneca. E.F. has been a scientific consultant for Boston Scientific, Medtronic, and Cook. E.F. has received an institutional grant from Intuitive Surgical. C.L.O., W.B.H., and I.A. have nothing to disclose.

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Author Contributions

M.S., C.L.O., G.E.A., W.B.H., and E.F. are the guarantors of the entire manuscript as they had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. M.S., C.L.O., G.E.A., W.B.H., I.A., and E.F. contributed substantially to the study design, data analysis, interpretation, and writing of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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