Endobronchial therapy with a thulium fiber laser (1940 nm)

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Background: Nd:YAG laser (1064 nm) is standard in bronchology. The thulium fiber laser (1940 nm) has a nearly 1000-fold increased absorption in water, enabling precise tissue ablation with a small margin of coagulation, whereas 1064-nm laser light penetrates deeper into tissue with less controllable effects.

Objectives: To assess the safety, feasibility, and versatility of endobronchial thulium laser therapy in an observational cohort study.

Methods: Endobronchial treatment with the thulium fiber laser was performed in a cohort study of 187 bronchoscopies on 132 consecutive patients with 135 endobronchial lesions amenable to laser resection.

Results: The thulium fiber laser produced superficial, precise, and rapid tissue ablation. Eighty-one lesions were completely vaporized; 82 lesions were treated by deep tissue destruction by inserting the fiber into tissue followed by mechanical resection. Tumor bleeding was coagulated with rapid and sustained hemostasis ($n = 28$). Nitinol stents were removed after resection of severe granulation tissue overgrowth ($n = 10$). Intact stents were maintained after ablation of in-stent tissue ($n = 47$). In 11 cases, bleeding occurred during laser treatment ($n = 11$ of 187). Power settings between 5 and 20 W were found to be safe.

Conclusions: Endobronchial therapy with the thulium laser at 1940 nm seems to be safe, feasible, and highly versatile for treatment of airway stenosis and stent obstruction caused by tissue ingrowth. Further studies are warranted. (*J Thorac Cardiovasc Surg* 2014;147:1827-32)

Video clip is available online.

The Nd:YAG laser emitting at a wavelength of 1064 nm has been used in interventional bronchoscopy for decades.^{1,2} The principles of its use have been described by Dumon and colleagues.³ The efficacy of this wavelength for endobronchial application via flexible devices has been explored in large case series.^{4,5}

The interaction between light and tissue depends on the wavelength of the light and the optical parameters of the tissue. The optical penetration depth as well as the resulting effects are wavelength dependent for a specific tissue.⁶ The

Nd:YAG laser beam travels deeply into pale tissue, whereas dark tissue colors (eg, blood or charring) result in high absorption and limited penetration. The extent of deep laser-induced damage within the target tissue is difficult to predict. Laser energy deposition can increase the temperature in deeper layers of the tissue to higher than the boiling point of water. Rapidly expanding pockets of steam can explode and erupt through the tissue surface (popcorn effect), obscuring the operating field and causing tissue perforation and hemorrhage.

The diode pumped thulium fiber laser (TmFL) emits light at a wavelength of 1940 nm in continuous mode. This wavelength coincides with a local maximum in the absorption spectrum of water⁷⁻⁹ (Figure 1), leading to a nearly 1000-fold increased absorption coefficient in water compared with the 1064 nm wavelength.¹⁰ Although for light at 1064 nm, water and other tissue chromophores are potential absorbers, light at 1940 nm is mainly absorbed by tissue water and therefore has a specific target. Because of its high absorption, the optical penetration depth into tissue is low and the energy is mainly absorbed near the tissue surface, enabling precise and predictable tissue ablation.

Clinically, the thulium laser wavelength was first introduced in urology for prostate resection,¹¹⁻¹⁴ and is currently under study for in laparoscopic partial nephrectomy,^{10,15-17} It has also been used in otorhinolaryngology,¹⁸⁻²¹ ophthalmology,^{22,23} and neurology.^{24,25} These studies characterize the device as a precise cutting tool with well-defined thermal damage ensuring hemostasis.

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Abbreviation and Acronym

TmFL = thulium fiber laser

Considering its physical properties and the experience in other medical specialties, it was hypothesized that the use of thulium laser light in bronchoscopy would improve clinical laser application with respect to some side effects induced by the gold standard Nd:YAG laser. To show safety and feasibility and to explore the clinical potential of this new wavelength, an observational cohort study was performed, reporting the first experience using a TmFL in interventional pulmonology.

MATERIALS AND METHODS

In a referral center for interventional pulmonology (Asklepios-Fachkliniken Munich-Gauting, Germany) from September 2011 to January 2013, consecutive patients with endobronchial lesions amenable to laser-assisted tissue resection²⁶ were treated with the TmFL. Patients gave written informed consent before the intervention. The study was approved by the Ethical Committee of Ludwig-Maximilians-University of Munich (project no. 410/10).

Procedures were performed using rigid bronchoscopy under general anesthesia and jet ventilation as described elsewhere.¹ During bronchoscopy, the type of endobronchial lesion (exophytic tissue, extrinsic compression, or stricture) and degree of airway stenosis before and after the procedure (no stenosis, lumen reduction $\leq 25\%$, 26%-50%, 51%-75%, 76%-90%, or 91%-100%) were assessed according to a recently proposed classification.²⁷ During laser light application, the fraction of inspired oxygen (Fio₂) was reduced to less than 40%.

Laser treatment was performed using a TmFL (Vela, StarMedTec, Starnberg, Germany) emitting at 1940 nm in continuous mode. The power emission was set from 5 to 50 W at increments of 1 W. The light energy was transported via a flexible quartz bare fiber (core diameter 365 μm) introduced through the working channel of a flexible videobronchoscope (BF-1T180, Olympus, Hamburg, Germany; Figure 2). Initially, the power setting was restricted to 5 W. During the early case series, laser power was titrated upward in increments of 5 W according to the observed effect and risk; the most intuitive risk of high energy levels is laser-induced fire, because interventional bronchoscopy works in an oxygen-rich environment. Other endobronchial treatments were applied as needed.

Individual patients with endobronchial lesions amenable for laser intervention by bronchoscopy were recorded. Every bronchoscopy with endobronchial laser application was evaluated as a separate case.

TmFL procedure-related adverse events were documented; for example, bleeding, popcorn effect, perforation of airway wall, laser-induced fire defined as persistent burning of carbonized tissue, laser fiber, or the flexible bronchoscope.

As the focus of the study was on feasibility and short-term effects, there was no formal follow-up of the patient cohort. Follow-up bronchoscopies were only performed as indicated by the clinical course of the patients during the study period.

Data are shown as means $\pm$ standard deviation.

RESULTS**Patient Cohort and Lesions**

One hundred thirty-two patients (mean age 64.5 ± 12.1 years; range, 22-88 years; 82 male, 50 female) underwent

187 bronchoscopies with laser application (1 bronchoscopy, $n = 103$, 2 bronchoscopies, $n = 14$; 3 bronchoscopies, $n = 10$, 4 bronchoscopies, $n = 2$; and 5, 6, and 7 bronchoscopies, each $n = 1$). The 55 repeat laser bronchoscopies were performed because of insufficient effect of the first bronchoscopy ($n = 6$; $\Delta t = 4.8 \pm 2.9$ days; range, 1-10 days) or recurrence of the endobronchial lesion ($n = 49$; $\Delta t = 174.9 \pm 146.4$ days; range, 11-636 days).

One hundred thirty-five different endobronchial lesions were treated; 97 (71.9%) were malignant and 38 (28.1%) benign. Diagnoses are shown in Table 1.

The type of airway stenosis was judged to be exophytic in 73 (39%) cases, a combination of exophytic tissue and extrinsic compression in 82 (44%) cases, and a benign stricture in 30 (16%) cases. In an additional 2 cases without stenosis, laser light application was used for hemostasis (1%).

In exophytic and combination stenosis, the exophytic part of the lesion was regarded as polypoid in 35 (22.6%) cases and broad based in 120 (77.4%) cases. The localization of the treated lesions is shown in Table 2.

Procedure

The mean procedure time was 44.6 ± 29.4 minutes (range, 12-200 minutes), mean laser-on time was 6.3 ± 7.1 minutes (range, 1-41 minutes). The initial power setting of 5 W induced tissue ablation but the hemostatic effect was not sufficient in all cases. The laser output power could safely be increased up to 20 W. At power values larger than 20 W, progressive emission of sparks from the treated tissue was observed. Suspecting an increased risk of laser fire, the use of these high-power settings was avoided. The optimal power setting was found to be 10 W with a sufficient combination of ablative and hemostatic effects.

With endobronchial treatment using the TmFL, superficial, rapid, and precise tissue ablation began immediately on activation of the laser at the lowest possible power setting of 5 W. Vaporization of tissue produced smoke, which was easily removed by suction through the flexible bronchoscope. Otherwise the operating field stayed clean during the procedure.

Frequently, TmFL resection was combined with other endobronchial treatment modalities ($n = 104$), such as stenting ($n = 52$) of residual compression stenosis after laser resection of exophytic tissue, dilation ($n = 23$), cryorecanalization ($n = 20$) for the extraction of large exophytic tumors,²⁸ tamponade with swabs ($n = 5$), argon plasma coagulation ($n = 2$) for hemostasis in large bleeding surface areas, and resection with the electrosurgical snare ($n = 2$) for the removal of pedunculated lesions.

In cases of early follow-up bronchoscopy, the laser-treated area showed a thin layer of fibrin deposit and necrosis. Debridement was not required at the site of the previous intervention in any patient.

FIGURE 1. Absorption coefficient of water⁷⁻⁹ and position of the thulium fiber laser (1940 nm) and the Nd:YAG laser (1064 nm).

Immediate Airway Reconstitution

Before laser treatment, significant airway stenosis defined as a degree of stenosis of 50% or more was diagnosed in 145 cases. Immediate reconstitution of a patent airway (<50% stenosis) was possible in 123 cases (85%) as shown in Figure 3. Recanalization failed because of complex pathology with exophytic tissue and extrinsic compression and multilocular involvement down to the segmental level in the remaining 22 patients.

Effects With Respect to Type of Lesion

Eighty-one small exophytic lesions in 65 patients were treated by complete vaporization. The TmFL was used in noncontact mode with a power setting of 8.1 ± 3.5 W and 4.7 ± 1.4 minutes laser-on time.

Eighty-two bulky lesions in 72 patients were treated by deep tissue destruction followed by immediate mechanical resection. The activated laser fiber was inserted into the exophytic intraluminal tissue as tangentially to the airway wall as possible with a power setting of 8.6 ± 2.7 W and 9.2 ± 8.0 minutes laser-on time. By covering the whole volume of an exophytic lesion via multiple entry points on the surface, lesions were coagulated and carbonized.

FIGURE 2. Introduction of the laser fiber and the flexible bronchoscope through the rigid instrument.

TABLE 1. Diagnosis for 135 lesions treated with endobronchial thulium fiber laser light application and corresponding type

Diagnosis	n	Type of lesion (n)*		
		Exophytic	Mixed	Stricture
Malignant disease (n = 97)				
Non-small cell lung cancer	48	16	32	
Small cell lung cancer	11	3	8	
Endobronchial metastasis	26	12	14	
Renal cell carcinoma	7	3	4	
Esophageal carcinoma	5	2	3	
Sarcoma	4	3	1	
Colonic carcinoma	3	1	2	
Thyroid carcinoma	3	2	1	
Anal carcinoma	1		1	
Endometrium carcinoma	1		1	
Laryngeal carcinoma	1	1		
Penile carcinoma	1		1	
Low grade malignancies	12	9	3	
Typical carcinoid	7	7		
Adenoid cystic carcinoma	4	1	3	
Mucoepidermoid carcinoma	1	1		
Benign disease (n = 38)				
Granulation tissue	21	16	3	2
Due to a stent	17	12	3	2
Due to a tracheotomy tube	4	4		
Scar stricture	7			7
Subglottic stenosis in Wegener disease	3			3
Post-tracheotomy stenosis	3			3
Stenotic anastomosis after lung transplantation	2		1	1
Lipoma	1	1		
Bleeding after biopsy	1			

*Mixed, a combination of exophytic tissue + extrinsic compression; pure extrinsic compression is not part of this study as lesions of this type are not amenable to laser resection.

The destructed tissue was then removed mechanically in the same procedure. Using this technique, the silica fiber tip comes in direct contact with the heated tissue, resulting

TABLE 2. Location of treated endobronchial lesions in 187 cases (52% of cases showed complex lesions involving more than 1 site giving a total >187 and >100%)

Location	n	%
Upper third of trachea	33	17.6
Middle third of trachea	15	8.0
Lower third of trachea	25	13.4
Right main stem bronchus	67	35.8
Right upper lobe bronchus	35	18.7
Intermediate bronchus	43	23.0
Middle lobe bronchus	18	9.6
Right lower lobe bronchus	17	9.1
Left main stem bronchus	65	34.8
Left upper lobe bronchus	25	13.4
Left lower lobe bronchus	26	13.9

FIGURE 3. Degree of airway stenosis before and after the procedure, assessed according to a recently proposed scale.²⁷

in relatively fast deformation with improper laser energy emission, requiring frequent renewing and cleaving. Nevertheless, this laser energy application technique allows rapid debulking.

In 30 cases (18 patients) with a stricture or hourglass-shaped stenosis, accurate incision of the lesion was achieved by moving the activated laser fiber repeatedly across the tissue either in contact or at 2 mm distance (Video 1). By mechanical dilation of the incised lesion, immediate airway patency was achieved in all cases. As a result of recurrence of the lesion, the procedure had to be repeated once in 2 patients, twice in 2 patients, and 6 times in 1 patient (power setting, 7.5 ± 2.5 W; laser-on time, 3.6 ± 5.5 minutes).

In 28 cases (26 patients), TmFL was used to achieve hemostasis. Spontaneous tumor bleeding occurred in 18 cases, whereas 10 episodes of bleeding occurred after endobronchial measures (after biopsy $n = 2$, after mechanical resection $n = 8$). Light application was performed in noncontact mode to achieve superficial coagulation of a large surface area at a power setting of 8.7 ± 2.2 W and laser-on time of 3.8 ± 3.5 min. In most cases, rapid and sustained hemostasis was achieved. In 3 cases, however, laser application had to be combined with tamponade and/or stenting to achieve complete hemostasis.

Lesions Within Airway Stents

In 57 cases (31 patients), the TmFL was applied within preexisting airway stents originally placed in 15 patients for benign lesions and in 16 patients for malignant lesions. To minimize the risk of ignition, the power setting was restricted to 5 W in these situations.²⁹

In 10 cases, partially covered nitinol stents (Ultraflex [Boston Scientific, Natick, Mass], $n = 4$; Leufen ECO-Stent [Micro-Tech, Nanjing, China], $n = 6$) were removed after laser resection of severe tissue overgrowth (granulation tissue, $n = 6$; tumor tissue, $n = 4$). The stents were

uncovered by superficial ablation of overgrowing tissue without deep damage to the airway wall. Direct contact of the laser probe with nitinol struts produced flashing phenomena but no fire or emission of sparks was observed. Some struts were cut accidentally by direct laser energy application, but the stents remained adequately intact to be extracted with rigid forceps. The location of the stents that were removed was trachea ($n = 2$), bifurcation ($n = 1$), right main stem bronchus ($n = 3$), left main stem bronchus ($n = 2$), and intermediate bronchus ($n = 2$). In 5 cases, a new stent was placed during the same procedure using a fully covered metallic stent ($n = 4$) or silicone stent ($n = 1$). Attempts to remove a metallic stent failed in 2 cases. Overall, the laser-on time for tissue removal from tissue-covered stents was 13.2 ± 11.8 minutes.

In 47 cases, preexisting stents (silicone stents, $n = 13$; metallic stents, $n = 34$) remained intact and were retained after laser-assisted ablation of in-stent tissue (Video 2). Laser-assisted tissue removal was performed close to the stent wall without relevant damage to the stent material. The laser-on time for these procedures was 5.1 ± 5.5 minutes.

Complications

Bleeding from tumor tissue was induced by laser treatment in 5.8% ($n = 11$ of 187). During these procedures, the laser fiber was introduced into exophytic malignant tissue to achieve deep tissue destruction. Five bleeding episodes were minor, requiring no specific action. A further 5 episodes were moderate necessitating temporary tamponade of the bleeding airway with swabs. In 1 case of a bleeding carcinoid tumor of the right upper lobe, a covered metal stent was placed over the lobar orifice to achieve permanent hemostasis. No other prespecified or unexpected complications were observed in this study.

DISCUSSION

Endobronchial laser treatment is well established in interventional bronchology. Although the Nd:YAG laser is most commonly used, we report our results of endobronchial laser therapy using a TmFL. Because the TmFL wavelength of 1940 nm shows high absorption in tissue water, a well-defined laser effect with a high degree of accuracy can be achieved. Laser-induced coagulation effects ranged within 1 to 2 mm instead of uncontrollable deep tissue coagulation.

Summarizing the clinical experience of this study, the following principles of endobronchial treatment with the TmFL were established:

1. Vaporization: small lesions can be completely vaporized ($n = 81$).
2. Deep tissue destruction followed by mechanical resection: theoretically, the superficial action of the

1940-nm light of the TmFL might be considered disadvantageous for the treatment of bulky lesions. But the experience of this case series shows that the activated laser fiber can be introduced into exophytic intraluminal tissue to achieve deep tissue destruction followed by mechanical removal of the coagulated and carbonized tissue ($n = 82$). As a result of the well-circumscribed action of the laser energy, the depth of tissue destruction virtually corresponds to the depth of the fiber tip and thus can be well controlled by the operator. Using this beneficial technique, however, 2 potential risk factors should be kept in mind. The introduction of the fiber into tissue can induce bleeding by direct mechanical injury of vessels and there is a risk of perforating the airway wall if airway anatomy is not respected.

3. Cutting/incision: in 21 cases with a stricture, exact radial incisions were made by moving the activated laser fiber repeatedly across the tissue either in contact or at 2 mm distance, followed by mechanical dilation. The cutting effect of the TmFL in strictures is comparable with the effect of electrocautery using a monopolar electro-surgical knife.
4. Hemostasis: the light energy of the TmFL was highly effective for hemostasis. As a result of high absorption in water, blood and other fluids on the tissue surface were rapidly vaporized followed by superficial coagulation of the bleeding tissue in noncontact mode ($n = 28$).
5. Removal of stent-associated tissue: the TmFL was safely used for ablation of granulation tissue in airway stents when restricted to a power setting of 5 W ($n = 57$).

Using these handling principles, there was no evidence of a difference in the efficiency of tissue destruction in relation to the histology of the treated endobronchial lesions.

Endobronchial therapy by means of the TmFL was safe when adhering to restrictions in power setting (<20 W, ≤ 5 W with preexisting airway stents) and the fraction of inspired oxygen ($<40\%$), which is further supported by the relatively low-energy application of less than 20 W using 1940 nm compared with less than 45 W using the Nd:YAG laser.³ Furthermore, the TmFL enabled fast tissue ablation with few bleeding events and without any observation of the so-called popcorn-effect. The experience of this study shows that sparks can arise when high energy levels (>20 W) are applied to desiccated and charred tissue. The emission of sparks from the tissue should be regarded as a sign of imminent laser-induced fire, which should lead to immediate deactivation of the laser by the treating physician.

All interventions in this study were performed under general anesthesia using combined rigid and flexible bronchoscopy. This contributes to the safety of the procedure. General anesthesia guarantees the best

conditions for complex interventions. The rigid bronchoscope enables ventilation and access to the airways and allows the use of rigid instruments for rapid debridement of tissue destroyed by the laser. It is indispensable for the removal of airway stents. The flexible bronchoscope ensures accurate targeting of the laser fiber and increases the peripheral range of laser therapy. The results of this study cannot be generalized to a pure flexible bronchoscopy technique. Many of the complex procedures described in this study with a procedure time of up to 200 minutes could not have been performed with the same safety, accuracy, and efficacy using a flexible system alone.

The most remarkable aspect of this case series is the use of the TmFL for tissue removal within preexisting airway stents. Resection in close proximity to airway stents using the Nd:YAG laser carries the risk of damaging the stent, including ignition.^{30,31} Using the TmFL with the power restricted to 5 W and applying the laser energy tangential to the stent wall, tissue overgrowing stents can be safely resected without obvious damage to the stents and the adjacent airway wall.

In benign airway stenosis, the use of metallic stents has been discouraged because of the long-term risks including incorporation in severe granulation tissue. Removal of these stents can be hazardous.^{32,33} As a result of its superficial effects, the TmFL seems to be an excellent tool for the removal of metallic airway stents. In this study, the TmFL was successfully used for severe stent overgrowth. However, this observation needs to be supported by ex vivo investigations²⁹ and comparison trials with the Nd:YAG laser.

In this study, TmFL laser resection was frequently combined with other endobronchial treatments, indicating that laser bronchoscopy is most effective as part of a multimodality endobronchial approach. The high number of stents placed in this study is explained by the high percentage of combined stenosis of exophytic tissue and extrinsic compression, for which laser-assisted resection was followed by stenting to achieve full patency of the airway.³⁴ Otherwise, laser light application was frequently used for hemostasis of bleeding after cryoextraction of exophytic tumor tissue.

Several limitations of this study should be addressed. First, there are no long-term follow-up or mortality data for this patient cohort. Second, a heterogeneous patient group with a large variety of benign and malignant lesions was included in this trial. Third, the results of the procedures were assessed visually and subjectively by the investigators. Objective means, such as radiographic assessment of bronchial diameter, were not used. Fourth, the study does include comparison with the Nd:YAG laser. Definitive conclusions regarding the superiority of the TmFL cannot be drawn.

However, because the authors have historical experience with endobronchial Nd:YAG laser therapy, a perspective on this issue can be given. The TmFL seems to have several promising advantages: higher absorption in tissue renders higher efficiency, accelerating tissue destruction and improving safety using lower power settings. The precise effect allows for better targeting of pathologic tissue conserving healthy deeper layers of the airway wall, which is especially important in delicate situations like the removal of ingrown stents. The results of this study show that, particularly with laser treatment of in-stent tissue, the TmFL enables interventions that would not be possible with an Nd:YAG laser.

Further trials covering these limitations, especially addressing the long-term effects in distinct patient populations and comparing TmFL with Nd:YAG laser treatment, should be undertaken to evaluate the potential of TmFL to improve endobronchial laser therapy.

CONCLUSIONS

Endobronchial therapy with the TmFL emitting at 1940 nm looks promising as a safe and versatile treatment modality for airway stenoses and stent obstructions caused by tissue ingrowth, with potential advantages compared with the Nd:YAG laser. Comparison studies are warranted.

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