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Thulium fiber laser in BPH surgery: Bench to bedside - a systematic review on behalf of YAU Urotechnology Working Group

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Introduction: The Thulium fiber laser (TFL) is a new device that in contrast to the other solid-state YAG-based lasers takes a different approach to pulse formation allowing for two different modes: in the QCW (quasi-continuous wave) function, TFL is convenient for soft tissue surgery and in the SP (Superpulsed) mode it is highly effective in lithotripsy. Thus, unlike the other thulium lasers (Tm : YAG), TFL can be used in a wide range of surgical procedures.

Materials and Methods: We conducted a systematic search in 3 databases: Medline, Scopus and Cochrane library. All original articles (both preclinical and clinical) on TFL application in soft tissue surgery were included in data analysis.

Results: In terms of its cutting properties, QCW TFL is not inferior to the other thulium lasers, and in fact allows for decreased carbonization (due to lower heat production) compared to continuous lasers (e.g. Tm : YAG). It has been used successfully in endoscopic enucleation of the prostate (EEP) and in en bloc resection of bladder tumors (ERBT). The efficacy and safety of this laser is comparable to TURP and simple prostatectomy, but the recovery period is shorter and the learning curve is slightly superior to other endoscopic procedures. There are no significant differences between TFL and Ho : YAG in terms of efficacy and safety during EEP. Unfortunately, there are no clinical studies that analyse the efficacy and safety of SP TFL in EEP or ERBT.

Conclusion: TFL is a safe and effective tool for BPH surgery. In terms of parameters, it is in no way inferior to Tm : YAG or Ho : YAG during EEP. However, TFL surpasses these lasers in terms of usability and serviceability. These advantages are likely to render it more popular over time.

KEYWORDS

thulium fiber laser (TFL), Ho : YAG (Holmium), lithotripsy, enucleation (EEP), vaporization, lasers, BPH, urolithiasis

Introduction

Lasers are now unquestionably an integral part of endoscopic surgery. Laser based techniques have become the standard modalities of choice in BPH surgery, NMIBC treatment and of course in lithotripsy procedures (1–5). This spectrum of capabilities is linked to the specific properties of the laser such as wavelength, pulse power and pulse duration (6). Whilst some types of lasers are better applied to soft tissue surgery others lend themselves more to lithotripsy. The most significant determining factor for a laser's efficiency is its wavelength. The laser affects only molecules whose absorption spectrum is as close as possible to the wavelength of the laser. They are called chromophores. Water and hemoglobin molecules are the most prevalent chromophores in the human body; their peak of absorption happens at 1910 nm and 532 nm respectively (7). Chromophores absorb the laser energy which leads to the heating of tissues containing those chromophores (8). If the laser wavelength is close to the chromophore absorption peak (high absorption coefficient), the majority of energy affects directly the chromophore without resulting in energy dispersion in the surrounding tissues. This means that collateral damage can be minimized by using lasers with a high absorption coefficient (9).

Since the late 1990s, the Holmium : YAG laser (Ho : YAG) has become the most frequently used device in endoscopy. Thanks to its wavelength, Ho : YAG is highly absorbed by water which leads to vaporization without deep coagulative necrosis with the depth of tissue penetration being 0.4-0.7 mm (10). The main feature of this laser is its high peak power (2-10 kW) and its ability to rapidly increase its power. This titanic outburst of power creates a large stream of vapor bubbles which can be a factor in soft tissue surgery, when it is not only the laser radiation which cuts the tissue, but the stream of vapor.

Thulium based lasers stepped into the limelight with the introduction of the solid-state Tm : YAG laser. This laser is a continuous, water-targeted laser with a wavelength of 2010 nm. Its theoretical penetration depth is approximately 0.2 mm, and its firing regimen is different to that of the Ho : YAG. Tm : YAG is a continuous wave device and is therefore characterized by effective hemostasis, and so we would expect it to become a suitable tool for soft tissue cutting (10). It can be used for prostate vaporization, vaporesection, vapoenucleation and for mostly mechanical enucleation (11–13). Also, it has turned out to be a highly effective, safe and convenient tool for en bloc resection of NMIBC (14, 15). In summary, one could say that this laser is a good option for the cutting of soft tissues but you could say that its advantage is also its limitation – being a continuous wave device it is not effective for lithotripsy.

TFL construction substantially differs from Tm : YAG. Firstly, the YAG laser medium was replaced with thulium doped silica fiber (16, 17). Thulium was chosen because the wavelength it creates is the closest to the water absorption peak (TFL – 1940 nm, water – 1910). For this reason, its theoretical penetration depth is only 0.15 mm (in comparison, for the Tm : YAG it is 0.2 mm, Ho : YAG – 0.4-0.7 mm) (10). This feature may decrease the risk of complications and minimize collateral damage (18). Secondly, the silica fiber instead of YAG-crystal decreases the energy consumption and heat production. It allows instead to create an air-cooling system (instead of water-cooling in Ho : YAG), so the device is smaller and lighter compared with other lasers (19). Also, the decreased energy consumption comes about from using the standard 220V wall plugs without any proprietary connectors or any custom voltage. Thirdly, in TFL a Q-switcher system was applied to convert the super pulsed (SP) mode to quasi-continuous (QCW) for better soft tissue cutting.

Due to those properties, the modifications of TFL combining in itself both (QCW) and (SP) modes exist today (20).

The thulium fiber laser (TFL) was created to combine the advantages of thulium-based effective cutting with holmium-like lithotripsy. The development of this device was followed by a series of preclinical tests, carefully studying each feature of the laser. This meant that the efficiency of the laser could be tested on a preclinical basis, and that the findings could be translated into surgical practice. In this paper, we will show how the preclinical results of TFL were tested in the clinic, and how our understanding of the device's physics and build will affect the outcomes.

Materials and methods

We performed a systematic literature search using two databases (Medline (PubMed), Scopus and Cochrane library) where the majority of the TFLs preclinical and clinical trials results are comprehensively described. We used the following search query: "(TFL OR "Thulium fiber laser" NOT tensor) AND ((Soft tissu*) OR Cutting OR ThuFLEP OR EEP OR enucleation OR BPH OR "en bloc" OR resection)". Such an approach was chosen because a precise search would definitely ensure that we do not miss any data related to the use of the Thulium fiber laser in BPH treatment.

The inclusion criteria were as follows: all types of studies (both prospective and retrospective) containing their own data on TFLs preclinical and clinical trial results. We included only articles in English. Any other literature without original data or sufficient information were excluded. These might include different types of reviews, comments, single cases, editorial material, books as well as conference abstracts.

Firstly, AA and CA performed a title review. No additional filters or limitations to the search were used. Only articles in English were included. Secondly, MT and AO independently performed abstract reviews according to the same criteria. Once the title and abstract were reviewed, AA and CA manually removed any duplicates. Different types of reviews, editorial material, books, comments and clinical case reports were excluded. In addition, all articles that deal with the use of TFL for lithotripsy were excluded. Also, MT, CA and AA excluded all studies which went beyond the scope of urologic surgery. As a last step, MT, AO and AA independently performed a full-text review. In the event of any disagreement, each party made their case and tried to resolve it. If they could not come to an agreement, DE made the final decision. All in all, 21 articles were included in our review – 9 preclinical and 12 clinical (Figure 1).

Thulium fiber laser for soft tissues

Thulium fiber laser for soft tissues: preclinical trials

The first *in-vitro* trial on TFL was conducted by Fried et al. (21, 22) showing the TFL potential in tissue cutting with a prostate (canine model) vaporization rate of 0.83+/-0.11 g/minute and with the hope that it would lead to an effective hemostasis. To assess the impact of the different TFL modes on soft tissue and to compare it with the other lasers, Taratkin et al. conducted a preclinical study using a non-frozen porcine kidney (23). The Ho : YAG incision had a conical ablation zone with a deep tissue rupture at the apex of the cone. The margins also were ruptured and shallow with a thin coagulation area without any carbonization. The QCW TFL mode made a coniform ablation zone approximately 1.5 times larger than Ho : YAG, with a rounded apex with a moderate carbonization. The Superpulsed (SP) mode of TFL produced an incision shape that was similar to Ho : YAG with minimal carbonization (23).

This finding was supported in another trial, assessing the impact of the fiber diameter (200 vs 600 µm) in different laser modes. No significant differences were observed irrespective of the fiber diameter except for the width of the coagulation zone for QCW TFL (smaller for 600 µm). QCW TFL made a coagulation zone 3 – 5 times larger than the SP TFL. The QCW laser mode cuts the tissues faster, its incision was 1.5-2 times deeper, and the vaporization volume was 2-5 times higher, and yet it leads to increased tissue carbonization. The SP TFL incision showed no carbonization, but its hemostasis may be considered insufficient due to lower coagulation depth. These results suggest that QCW TFL may be a good option for soft tissue cutting with adequate hemostasis (24).

Another preclinical study aimed to compare the distance-dependent impact of different lasers on soft tissue. Only Ho : YAG made an incision of a distance ≥ 2 mm (25). The deepest incision performed in the contact mode (fiber-tissue distance = 0 mm) was made by QCW TFL (70-90% higher than other lasers); at the fiber-tissue distance at 1 mm all of those lasers showed the similar results. The coagulation depth demonstrated similar patterns – QCW TFL coagulation was 70-90% deeper than that for other lasers at the distance <2 mm; no coagulation was noticed at the distance >3 mm. So, the authors recognized QCW TFL as the most effective for tissue cutting and cauterizing in contact mode. SP TFL has a similar pattern to Ho : YAG. However, the authors consider SP TFL to be the safer device as it showed no tissue damage at 2 mm (Ho : YAG show tissue rupture at >3 mm) (25). Doizi et al. (26) also compared the incision and coagulation depth of Ho : YAG and TFL. The results were in line with those of Taratkin et al.

Yilmaz et al. (27) in their study tried to simulate the prostate enucleation process using a model of porcine belly. The researchers compared the speed of anterior abdominal wall fascial layers with separation, coagulation performance of lasers and the ease with which the surgeon could operate. The high-power Ho : YAG (4.5 J, 22.3 Hz, 100 W, 0.15 ms) performed the fastest layer separation (31.5 cm^2 per minute). The other lasers produced more modest results: pulsed-Tm : YAG - 15 cm^2 at 3 J, 25 Hz, 75 W, and 0.86 ms pulse duration; TFL – 12 cm^2 at setting 4 J, 10 Hz, 40 W, and 8 ms; low-power

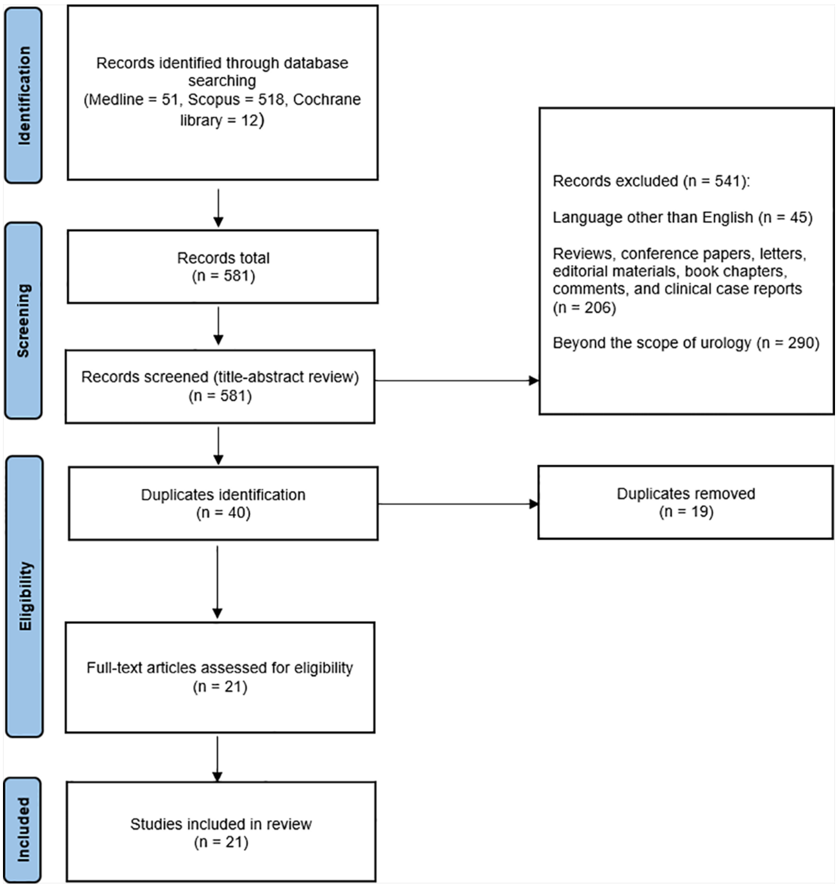

FIGURE 1
PRISMA flow diagram.

Ho : YAG – 6 cm^2 at 3.5 J, 10 Hz, 35 W and a pulse duration of 0.45 ms. At the same laser settings (3 J, 10 Hz), TFL demonstrated its higher efficacy - 5.25 cm^2 of layer separation compared to the other lasers: HP-Ho : YAG - 4.5 cm^2, p-Tm : YAG - 3 cm^2, LP-Ho : YAG 2 cm^2. P-Tm : YAG demonstrated the highest coagulation performance – a total score of 4.3 followed by TFL (3.5), LP-Ho : YAG (3.0) and HP-Ho : YAG (2.5), which was the least satisfactory in terms of coagulation properties. HP-Ho : YAG was rated subjectively as the most satisfactory laser in terms of surgeons' usability (Likert scale 4.06, NASA-TLX 4.38) due to its high enucleation speed and efficacy. TFL took the penultimate place with its Likert scale reading of 3.38 and NASA-TLX 3.92. LP-Ho : YAG was considered the least effective (Likert scale 3.25, NASA-TLX 4.09).

Comparing the impact on the soft tissues of TFL and Hybrid laser (combination of a Thulium fiber and Blue diode laser), Becker et al. obtained the following results (28): the Hybrid laser demonstrated the best vaporization and coagulation properties (50% more than TFL and 2-3 times more than Ho : YAG) with a coagulation zone smaller (by 10%) compared to the QCW TFL. The Hybrid laser's carbonisation was significantly lower than those for TFL (28). Those properties for both TFL and Hybrid laser were observed by Arkhipova et al. in their study (29).

All data on the preclinical studies is collected in Table 1.

Thulium fiber laser for soft tissues: clinical trials

The above-mentioned preclinical studies demonstrated that TFL lends itself to soft tissue surgery for it is efficient at both cutting and coagulation. As a next step, these findings should be backed up with evidence from clinical trials.

A pioneered clinical study for thulium fiber laser enucleation of the prostate (ThuFLEP) was presented by Enikeev et al. on 2018 (30). ThuFLEP's efficacy (in voiding parameters improvement) and safety (in complication rate) turned out to be in no way inferior to TURP which remains the standard benchmark when it comes to these kind of comparisons. Also,

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TABLE 1 Preclinical studies on TFL in soft tissue cutting.

Preclinical study	Laser	Laser mode	Settings					Fiber diameter, mcm	Experimental substrate	Results			
			Time, min	Energy, J	Frequency, Hz	Power, W	Pulse duration, ms						
Fried et al., 2005 (21)										Total energy, kJ	Mass loss, g	Ablation rate, g/min	Efficiency, kJ/g
	TFL	QCW	10			90		600	Canine prostate	54.0	6.9	0.69	7.8
	TFL	QCW	10			91.5		600	Canine prostate	54.9	7.2	0.72	7.6
	TFL	QCW	10			87.5		600	Canine prostate	52.5	8.2	0.82	6.4
	TFL	QCW	10			87		600	Canine prostate	52.2	8.0	0.80	6.5
	TFL	QCW	10			88		600	Canine prostate	52.8	9.6	0.96	5.5
	TFL	QCW	10			87		600	Canine prostate	52.2	9.8	0.98	5.3
	TFL	QCW	10			88.5		600	Canine prostate	53.1	8.3	0.83	6.5
Fried et al., 2005 (22)										Total energy, kJ	Mass loss, g	Ablation rate, g/min	Efficiency, kJ/g
	TFL	QCW	19			25		600	Canine prostate	28.5	4.3	0.23	6.6
	TFL	QCW	17			27.5		600	Canine prostate	28.1	3.6	0.21	7.8
	TFL	QCW	25			25		600	Canine prostate	37.5	5.4	0.22	6.9
	TFL	QCW	20			26.5		600	Canine prostate	31.8	4.3	0.22	7.4
	TFL	QCW	18			27		600	Canine prostate	29.2	3.0	0.17	9.7
	TFL	QCW	23			26		600	Canine prostate	35.9	5.2	0.23	6.9
	TFL	QCW	20			26.5		600	Canine prostate	31.8	4.0	0.20	8.0
	TFL	QCW	20.5			26.5		600	Canine prostate	32.6	4.3	0.21	7.6
	TFL	QCW	20.3			26.3		600	Canine prostate	32.0	4.3	0.21	7.6
Becker et al., 2020 (24)										Incision depth, mm	Vaporization volume, mm^3/s	Coagulation zone, mm	Thermo-mechanical damage zone, mm^3
	TFL	QCW				60		200	Porcine kidney	4.2	13.4	10.6	0
	TFL	QCW				60		600	Porcine kidney	2.9	8	7.7	0
	TFL	QCW				120		200	Porcine kidney	5.6	24.6	18.1	0
	TFL	QCW				120		600	Porcine kidney	5.7	28.2	12.3	0
	TFL	SP				60	10	200	Porcine kidney	3.4	8.6	3.2	1.4
	TFL	SP				60	10	600	Porcine kidney	3.7	11	5.1	1.2
	TFL	SP				120	10	200	Porcine kidney	2.7	4	3.1	1
	TFL	SP				120	10	600	Porcine kidney	3.4	6.2	2.2	2.6
Becker et al., 2020 (28)										Incision depth, mm	Vaporization speed, mm^3/s	Coagulation zone, mm	Carbonization grade (0 min; 3 max)
											2 mm/s	2 mm/s	5 mm/s 2 mm/s 5 mm/s

(Continued)

TABLE 1 Continued

Preclinical study	Laser	Laser mode	Settings					Fiber diameter, mcm	Experimental substrate	Results								
			Time, min	Energy, J	Frequency, Hz	Power, W	Pulse duration, ms											
										mm/s	mm/s			mm/s				
	Ho : YAG	Pulsed		2	50			550	Porcine kidney	2.5 ± 0.1	1.1 ± 0.1	6.0 ± 0.1		5.0 ± 0.1	4.0 ± 0.1	2.1 ± 0.1	0	0
	TFL	QCW				120		600	Porcine kidney	5.5 ± 0.1	4.5 ± 0.1	28.0 ± 0.1		17.5 ± 0.1	12.5 ± 0.1	6.5 ± 0.1	2	2
	TFL +BDL	QCW				120 + 60		600	Porcine kidney	7.3 ± 0.1	4.1 ± 0.1	36.0 ± 0.1		34.4 ± 0.1	10.0 ± 0.1	7.1 ± 0.1	0-1	0-1
Arkhipova et al., 2020 (29)										Ablation depth, mm		Coagulation depth, mm			Width of superficial coagulation, mm	Carbonization		
										2 mm/s	5 mm/s	2 mm/s		5 mm/s	2 mm/s	5 mm/s	2 mm/s	5 mm/s
	BDL	CW				20		600	Porcine kidney	3.3 ± 0.1	1.7 ± 0.1	0.3 ± 0.1		0.3 ± 0.1	0.5 ± 0.1	0.4 ± 0.1	no	no
	BDL	QCW			30	20	10	600	Porcine kidney	3.3 ± 0.2	1.6 ± 0.1	0.4 ± 0.1		0.5 ± 0.1	0.6 ± 0.1	0.4 ± 0.1	no	no
	BDL + TFL	QCW				20		600	Porcine kidney	4.1 ± 0.2	2.0 ± 0.1	0.5 ± 0.1		0.4 ± 0.1	0.7 ± 0.1	0.4 ± 0.1	no	no
	TFL	QCW				20		600	Porcine kidney	1.5 ± 0.2	0.7 ± 0.1	1.0 ± 0.1	0.8 ± 0.1	0.7 ± 0.1	0.6 ± 0.0	yes	no	
Taratkin et al., 2021 (25)										Fiber-tissue distance, mm			Incision depth, mm			Coagulation depth, mm		

(Continued)

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TABLE 1 Continued

Preclinical study	Laser	Laser mode	Settings					Fiber diameter, mcm	Experimental substrate	Results			
			Time, min	Energy, J	Frequency, Hz	Power, W	Pulse duration, ms						
	Ho : YAG	Pulsed		1.2	50			600	Porcine kidney	0 1 2	1.1 ± 0.1 0.9 ± 0.1 0.2 ± 0.1	0.6 ± 0.1 0.8 ± 0.1 0.7 ± 0.1	
	TFL	SP		1.2	50			600	Porcine kidney	0 1 2	1.0 ± 0.1 0.3 ± 0.1 -	0.7 ± 0.1 0.5 ± 0.1 0.4 ± 0.1	
	TFL	QCW				60		600	Porcine kidney	0 1 2	1.7 ± 0.1 1.0 ± 0.1 -	1.1 ± 0.1 0.8 ± 0.1 0.7 ± 0.1	
	BDL	QCW				60		600	Porcine kidney	0 1 2 3 4 5	0.9 ± 0.1 0.7 ± 0.1 - - - -	0.2 ± 0.1 0.3 ± 0.1 0.5 ± 0.1 0.5 ± 0.1 0.4 ± 0.1 0.4 ± 0.1	
Taratkin et al., 2022 (23)										Fiber speed, mm/s	Ablation depth, mm	Coagulation depth, mm	Carbonization, mode (range)
	Ho : YAG	Pulsed		1.5		40		550	Porcine kidney	2 5	1.1 ± 0.2 0.5 ± 0.2	0 0	0 (0–1) 0 (0–1)
	TFL	QCW		1.5		30		600	Porcine kidney	2 5	2.1 ± 0.2 0.7 ± 0.2	0.4 ± 0.1 0.3 ± 0.1	1 (1–2) 1 (0–2)
	TFL	SP		1.5		30		600	Porcine kidney	2 5	1.3 ± 0.2 0.5 ± 0.2	0.1 ± 0.1 0	0 (0–1) 0 (0–1)
	Ho : YAG	Pulsed		1.5		70		550	Porcine kidney	2 5	1.6 ± 0.2 1.1 ± 0.2	0.1 ± 0.1 0.2 ± 0.1	0 (0–2) 2 (1–3)
	TFL	QCW		1.5		60		600	Porcine kidney	2 5	2.7 ± 0.3 1.7 ± 0.1	0.6 ± 0.1 0.4 ± 0.1	2 (1–3) 2 (1–3)
	TFL	SP		1.5		50		600	Porcine kidney	2 5	2.2 ± 0.3 1.5 ± 0.2	0.4 ± 0.1 0.5 ± 0.1	1 (1–2) 1 (1–2)
Doizi et al., 2022 (26)										Results			
	TFL Ho : YAG	QCW Pulsed		Identical Identical	Identical Identical			550 550	Porcine kidney	Incision depths and areas of coagulation were greater with the Ho : YAG laser. No carbonization zone was found with the Ho : YAG laser, this was constant with the TFL. A fiber tip degradation was constantly observed with Ho : YAG laser, except in the case of a long pulse duration and low pulse energy (0.2 J), this was not the case with TFL.			

(Continued)

TABLE 1 Continued

Preclinical study	Laser	Laser mode	Settings					Fiber diameter, mcm	Experimental substrate	Results		
			Time, min	Energy, J	Frequency, Hz	Power, W	Pulse duration, ms					
Yilmaz et al., 2022 (27)										Pocket size, cm^2	Likert scale	NASA TLX
	Ho : YAG	Pulsed (high-power)	1	4.5 3	22.3 10	100	0.15		Porcine belly	31.5 4.5	4.06	4.38
	Ho : YAG	Pulsed (low-power)	1	3.5 3	10 10	35	0.45		Porcine belly	6 2	3.25	4.09
	Tm : YAG	Pulsed	1	3 3	25 10	75	0.86		Porcine belly	15 3	3.94	3.92
	TFL	SP	1	4 3	10 10	40	8		Porcine belly	12 5.25	3.38	3.90

TFL, Thulium fiber laser; Ho : YAG, Holmium solid-state laser; Tm : YAG, Thulium solid-state laser; BDL, blue diode laser; CW, continuous wave; QCW, quasi-continuous wave; SP, super pulsed; NASA TLI, NASA Task Load Index.

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ThuFLEP led to a pronounced prostate-specific antigen (PSA) decrease which implies that there was a more complete removal of the prostate tissue (30).

Compared to a simple prostatectomy in large volume BPH (> 80 cc), ThuFLEP proved to be as equally effective: the mean operative time, resection speed and resected tissue weight were comparable in both procedures (31). After simple prostatectomy, the patients stayed in hospital longer (9.0 days vs 3.3 days, p<0.001). At the 6-month follow-up, the stress urinary incontinence rate was 1,1% after ThuFLEP and 2.5% after simple prostatectomy (31). QCW TFL was successfully applied to different enucleation techniques like en bloc and two-lobe (32). Another study using this laser showed that routine stenting after ureteral orifice damage should not be considered mandatory, largely thanks to its short laser penetration depth (33).

A large retrospective study comparing ThuFLEP, HoLEP and MEP (monopolar enucleation of the prostate) reported no significant differences between those procedures regarding the complications rate at intraoperative, early postoperative period, as well as 6 months after surgery (34). As for the learning curve for these 3 endoscopic enucleation techniques, ThuFLEP was slightly superior (without significant difference [p>0.05]) to HoLEP and MEP in terms of the overall enucleation rate – 1.0 g/min vs. 0.8 g/min and 0.7 g/min, respectively. Also, similar enucleation rates at the initial stages of training (first 20 surgeries) were observed, but after that period laser endoscopic enucleation techniques favored MEP (p<0.001) (35).

Erectile function 6 months post-op after ThuFLEP compared to TURP differed significantly (p < 0.001) (36) favored ThuFLEP: a mean increase of IIEF-5 score in ThuFLEP 0.72 ± 1.6 vs mean decrease in TURP 0.24 ± 2.2. EF after TURP impaired in 34% of patients (18% in patients after ThuFLEP) and it improved in 21% of them (26% after ThuFLEP) (36).. The safety profile for ThuFLEP also was also acceptable with an overall complication rate of 9.7%, Clavien-Dindo grade III complications only in 1.9% of cases (37).

Also, Enikeev et al. compared the severity of irritative symptoms after HoLEP and ThuFLEP (38). No differences in functional outcomes (IPSS, Qmax), rate of SUI or irritative symptoms were found. Both surgeries were comparable in terms of duration and postoperative complication rates (38).

Elmansy et al. (39) compared TFL with Ho : YAG modified with Moses technology in patients with BPH undergoing transurethral enucleation of the prostate. The key differences were in median enucleation, hemostasis, and morcellation times which were longer in TFL group (p < 0.001). Otherwise, there were no significant differences – so, safety and efficacy profile with comparable postoperative outcomes were similar for those lasers (39).

The study of Maltagliati et al. (40) is of great interest because it compared ThuFLEP with Thulium solid-state laser enucleation of the prostate (ThuLEP). The authors reported only one difference between these procedures – the duration of ThuLEP was shorter than the duration of ThuFLEP (63.69 ± 41.44 vs 79.66 ± 48.70 minutes, respectively, p=0.045). Hemoglobin drop (0.47 g/dL after ThuFLEP and 0.45 g/dL after ThuLEP, p=0.32), catheterization time (1.9 vs 2.1 days, p=0.37), hospital stay (2.2 vs 2.6 days, p=0.22), irrigation volume (29.4 vs 32.8 L, p=0.43) and functional parameters (Qmax, IPSS, PVR, and QoL) at 3 months after surgery were comparable between both groups.

BPH surgery aside, TFL proved itself to be a suitable device for en bloc resection of bladder tumor (ERBT), predominantly NMIBC, within a prospective clinical trial (41). It was shown that patients after TFL ERBT had a better relapse-free rate than TURBT at both 3 (97.2% and 84.5%, p = 0.011) and 6 months (91.5% and 67.2%, p < 0.001). Also, TFL ERBT demonstrated a lower complication rate (like obturator nerve reflex, perforation) and better specimen quality compared to conventional TURBT (showing better detrusor rate on pathology). The only reported disadvantage for TFL ERBT was the prolonged surgery duration time (39.0 (± 16.5) vs 34.0 (± 8.8) min for TURBT) (41).

All data on the clinical studies is collected in Table 2.

Discussion

The thulium fiber laser is a novel device which can be applied for both soft tissue cutting and lithotripsy. This laser has 2 modes to complete these tasks – quasi-continuous (QCW) and super pulsed (SP), respectively. QCW is close in properties to Tm : YAG laser, so it can be applied only in soft tissue surgery – for surgical treatment of BPH or NMIBC. It also may be used for UTUC resection/vaporization but there are currently no studies regarding TFL application. SP TFL mode is close in its properties to Ho : YAG laser, so it may be used in both soft tissue and stone surgery.

There are 3 major differences between SP TFL and Ho : YAG. Firstly, SP TFL has a potentially higher frequency (up to 25 – 40 times – 2000 Hz for SP TFL and 50-80 Hz for Ho : YAG) (42). Secondly, its peak power is lower (SP TFL – 500 W, Ho : YAG – 2-10 kW). Thirdly, its pulse duration is longer (TFL: 500 ms; Ho : YAG: 350 at same Energy-Frequency settings) (43). The last difference is determined by different pulse profile – SP TFL has a Gaussian profile while Ho : YAG has a rapidly approaching power peak. In stone surgery those features are associated with lower stone retropulsion and faster soft stone dusting in favor of SP TFL. At the same laser setting, SP TFL and Ho : YAG do not differ in their soft tissue cutting properties – in *in vitro* studies they were almost the same in terms of ablation depth, coagulation depth and carbonization mode (23, 25). As for clinical practice in BPH surgery, SP TFL may be associated with longer operation time, decreased hemoglobin drop and reduced urinary incontinence rate due to sphincter damage compared to Ho : YAG. Those features may be associated with reduced peak power and increased laser frequency. Unfortunately, we have no data of SP TFL and Ho : YAG clinical comparison in different laser settings.

TABLE 2 Clinical studies on TFL in soft tissue cutting.

Clinical study	Procedure	Ablating/ enucleating agent	Laser mode	Fiber diameter, mcm	Number of patients, n	Results							
Enikeev et al., 2018 (36)						IPSS score (preop. – postop.)	QoL score (preop. – postop.)	Qmax score (preop. – postop.)		PVR score (preop. – postop.)		IIEF-5 score (preop. – postop.)	IIEF-5 change score
	EEP TURP	TFL Monopolar	QCW	600	211 258	21.8 ± 1.6 – 10.9 ± 3.0 21.6 ± 1.7 – 10.6 ± 3.2	4.0 ± 0.8 - 1.8 ± 0.6 3.9 ± 0.8 - 1.7 ± 0.6	7.5 ± 1.7 - 16.2 ± 3.3 7.8 ± 1.9 - 16.6 ± 1.5		70.1 ± 28.7- 17.3± 11.7 68.7 ± 21.5 -15.3 ± 13.6		11.1 ± 5.0- 11.7 ± 4.7 11.7 ± 4.5- 11.5 ± 4.7	+0.72 ± 1.6 -0.24 ± 2.2
Enikeev et al., 2018 (35)						Duration of enucleation, min	Mass of removed tissue, g	Enucleation rate, g/min		Catheterization – Hospitalization time, days		Hemoglobin decrease, g/dL	Complication rate (overall – severe), %
	EEP EEP EEP	TFL Ho : YAG Monopolar	QCW Pulsed	600 550	30 30 30	38.6 ± 15.7 32.8 ± 13.4 32.3 ± 12.2	51.7 ± 9.2 48.0 ± 12.9 46.4 ± 10.7	1.0 ± 0.4 0.8 ± 0.2 0.7 ± 0.2		1.3 ± 0.4 – 3.6 ± 1.0 1.3 ± 0.5 - 3.5 ± 1.1 2.3 ± 0.8 - 4.8 ± 1.0		1.4 ± 0.6 1.9 ± 0.5 3.3 ± 1.5	56 – 3 75 – 9 107 - 6
Enikeev et al., 2018 (33)						Age, years	Prostate volume, cc	Qmax, ml/s		IPSS, score		Stenting (n of stented patients/ overall)	Pain-scale degree
	EEP EEP	TFL Ho : YAG	QCW Pulsed	600 550	4 3	68 ± 7.3 67 ± 4.6	78.8 ± 6.8 82.3 ± 7.8	8.75 ± 2.6 9.2 ± 1.0		22.8 ± 1.5 21.7 ± 1.2		2/4 1/3	1.7 ± 2.1 2.25 ± 2.6
Enikeev et al., 2019 (31)						Operation time, min	Mass of removed tissue, g	Enucleation rate, g/min		Catheterization – Hospitalization time, days		Hemoglobin after surgery, g/ dL	Complication rate (overall – severe), %
	EEP SPE	TFL	QCW	600	90 40	103.2 ± 36.6 109.5 ± 11.0	104.5 ± 33.4 99.2 ± 35.3	1.01 0.9		1.4 ± 0.6 - 3.3 ± 0.6 6.4 ± 1.5 - 9.0 ± 2.4		12.7 ± 1.1 10.6 ± 1.6	25.4 – 3.3 47.5 – 0
Enikeev et al., 2019 (32)						Operation time, min	Mass of removed tissue, g	Enucleation rate, g/min		Morcellation rate, g/min Prostate volume			Overall complication rate, %
										< 80 cc	80-150cc	>150 cc	
	EEP (en bloc) EEP (two-lobe)	TFL Ho : YAG	QCW Pulsed	600 550	406 709	68.8 ± 30.6 67.4 ± 30.1	69.5 ± 32.3 71.1 ± 33.6	1.9 ± 0.7 1.9 ± 0.7		2.1 ± 0.8 2.0 ± 1.0	3.4 ± 2.0 2.9 ± 2.4	2.6 ± 1.1 3.5 ± 1.0	33.48 32.42
Enikeev et al., 2019 (30)						Operation time, min	Mass of removed tissue, g	Prostate volume decrease, %	Catheterization time, days	Hospital stay, days	Hemoglobin level decrease, g/dL	PSA level decrease, %	Complication rate (early - late), %

(Continued)

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TABLE 2 Continued

Clinical study	Procedure	Ablating/ enucleating agent	Laser mode	Fiber diameter, mcm	Number of patients, n	Results								
	EEP	TFL	QCW	600	51	46.6 ± 10.2		50.9 ± 9.8	81.0 ± 6.3	1.4 ± 0.6	3.4 ± 0.6	1.01 ± 0.4	80 ± 11.0	25.2–5.7
	TURP	Monopolar			52	39.9 ± 8.6		47.4 ± 13.8	71.5 ± 6.8	2.4 ± 1.1	4.7 ± 1.3	1.8 ± 0.8	72 ± 11.3	34.4–19
Enikeev et al., 2020 (41)								Operation time, min						Recurrence at 6 months, %
			Muscle fibers in	specimens, %				Complication rate, %						
	Obturator nerve reflex				Perforation		Acute bleeding		UTI					
ERBT	TFL	QCW	600	71		39.0 ± 16.5	8.5	32.8	91.5	0.00	0.00	0.00		8.4
TURBT	Monopolar			58		34.0 ± 8.8			58.6	17.2	10.3	5.2		8.6
Morozov et al., 2020 (34)						Operation time, min	Mass of removed tissue, g	Catheterization time, days	Hospital stay, days	PVR after surgery, ml	Qmax after surgery, ml/s	IPSS after surgery score	QOL after surgery score	Complication rate (early - late), %
	EEP	TFL	QCW	600	812	67 ± 29	69 ± 33	1.8 ± 0.8	3.8 ± 1.0	11.9 ± 9.3	22.2 ± 3.2	5 ± 2	1.6 ± 0.6	7.5-6.4
	EEP	Ho : YAG	Pulsed	550	509	76 ± 35	75 ± 36	1.4 ± 0.6	3.4 ± 0.6	17.2 ± 12.2	20.6 ± 4.5	5 ± 2	1.8 ± 0.7	10-8.4
	EEP	Monopolar			92	59 ± 27	55 ± 21	2.3 ± 1.4	4.2 ± 2.0	14.1 ± 9.5	18.9 ± 4.1	5.1 ± 1.9	1.7 ± 0.6	15.2-11.8

Clinical study	Procedure	Ablating/ enucleating agent	Laser mode	Fiber diameter, mcm	Number of patients, n	Total ICIQ-MLUTS score		Bother score		Voiding score		Incontinence score		Overall complication rate
Enikeev et al., 2022 (38)						1 month after surgery	3 months after surgery	1 month after surgery	3 months after surgery	1 month after surgery	3 months after surgery	1 month after surgery	3 months after surgery	
	EEP	TFL	QCW	600	86	6.3 ± 3.4	3.0 ± 2.2	20.4 ± 11.9	7.7 ± 6.8	0.3 ± 0.5	0.1 ± 0.4	3.9 ± 2.3	1.4 ± 1.6	4.7 11.7
	EEP	Ho : YAG	Pulsed	550	77	8.3 ± 6.3	4.1 ± 5.1	29.3 ± 22.4	11.8 ± 14.4	1.8 ± 3.4	0.9 ± 2.9	4.0 ± 2.5	1.6 ± 1.7	11.7

Clinical study	Procedure	Ablating/ enucleating agent	Laser mode	Fiber diameter, mcm	Number of patients, n	Operation time, min	Hemoglobin decrease, g/dL	Catheteriztion time, days	Hospital stay, days	Irrigation volume, L
Maltagliati et al., 2022 (40)	EEP	TFL	QCW		123	79.66 ± 48.7	0.45	1.9	2.2	29.4
	EEP	Tm : YAG	CW		117	63.69 ± 41.44	0.47	2.1	2.6	32.8

Clinical study	Procedure	Ablating/ enucleating agent	Laser mode	Fiber diameter, mcm	Number of patients, n	Operation time, min	Mass of removed tissue, g	Catheterization time, days	Hospital stay, days	PVR, ml	Qmax surgery, ml/s	IPSS score	QOL score	Complication rate (early - late), %
Petov et al., 2022 (37)	EEP	TFL	QCW	600	1328	70.5 ± 31.3	69.6 ± 33.6	1.7 ± 0.8	3.7 ± 1.0			3 years after surgery	3 years after surgery	

(Continued)

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TABLE 2 Continued

Clinical study	Procedure	Ablating/ enucleating agent	Laser mode	Fiber diameter, mcm	Number of patients, n	Results				
						3 years after surgery	3 years after surgery			
					Prostatic volume < 80 cc	17.0 ± 20.3	21.9 ± 5.4	4.1 ± 2.0	1.3 ± 1.1	24.5 – 2.4
					Prostatic volume ≥ 80 cc	18.2 ± 20.1	21.6 ± 5.7	4.1 ± 2.0	1.3 ± 1.1	27.9 – 4.3
Elmansy et al., 2022 (39)	EEP EEP	TFL MOSES Ho : YAG			12 62	Longer median enucleation, hemostasis, and morcellation times ($p < 0.001$) in TFL group. IPSS, QoL, Qmax, and PVR were comparable between the groups at 1, 3 and 6 months. The incidence of urge urinary incontinence ($p = 0.79$), stress urinary incontinence ($p = 0.97$), and hospital readmission rates ($p = 0.1$) were comparable between the two groups.				

EEP, endoscopic enucleation of the prostate; TURP, transurethral resection of the prostate; SPE, simple prostatectomy; ERBT, en bloc resection of bladder tumor; TURBT, transurethral resection of bladder tumor; TFL, thulium fiber laser; Ho : YAG, holmium solid-state laser; QCW, quasi-continuous wave mode; IPSS - International Prostate Symptom Score; QoL, quality of life index; PVR, post-void residual urine; Qmax, maximum flow rate; IIEF-5, international index of erectile function; PSA - Prostate-specific antigen; UTI, urinary tract infections; ICIQ-MLUTS - International Consultation on Incontinence Questionnaire Male Lower Urinary Tract Symptoms Module.

As for QCW TFL, it has established itself as a effective and safe device for EEP which is not inferior in these terms to Tm : YAG and Ho : YAG. QCW TFL may be safer than Tm : YAG in terms of carbonization – the quasi-continuous mode decreases the thermal damage to tissue reducing carbonization and simplifying the intraoperative navigation (16, 17). Unfortunately, there is no one preclinical comparison of those lasers yet. In a clinical comparison, TFL and Tm : YAG showed themselves to be similar in terms of safety and functional outcomes (40). TFL was associated with longer operation time, which may be caused with decreased vaporization speed. Thus, TFL may have a reduced tissue heating profile compared to Tm : YAG, so insignificant differences in hemoglobin drop and in catheterization or hospitalization time may be signs of its better safety profile. If our assumption is correct, carbonization may also be lower when using TFL. In comparing TFL and pulsed Tm : YAG (27), no significant differences were found. That can be explained by the change of laser pulse generation. Classic Tm : YAG is a continuous wave laser, so it influences the tissue continuously and the tissue heating occurs constantly over time. TFL is a quasi-continuous wave laser – prolonged periods of tissue heating alternate with transient periods of tissue relaxation. So, when Tm : YAG functions as a pulsed laser, the effect on the tissue is directly comparable to those for TFL. This explains the lack of significant differences between these lasers.

In comparison with Ho : YAG, TFL proved to be comparable in terms of efficacy and safety. At the same time, using TFL for EEP was associated with longer operation time, insignificant decrease of complication rate and hemoglobin drop and better functional outcomes. The prolonged operation time may be associated with lower laser tissue penetration depth, absence of explosive vaporization effect and complicated intraoperative navigation due to carbonization. A hemoglobin drop may be associated with better QCW TFL hemostatic properties due to deeper coagulation and the lack of an explosive vaporization effect. The reduced complication rate and the better functional outcomes may be associated with minimized sphincter traumatization due to lower tissue penetration depth and the lack of an explosive vaporization effect. So, TFL may be considered as an effective and safe tool for EEP on a par with Ho : YAG.

As for the difference in learning curves, residents may reach the plateau faster using TFL because of its physical properties. At first, the fact that there was no explosive vaporization makes it easier to dissect along the capsule – that effect would accelerate the operation time but slow down the learning curve. The resident is led to believe that he can do EEP easily, and so he slows down to perfect oneself. This assumption is also supported by the fact that surgeons leave more adenomatous tissue when using Ho : YAG then TFL (35). We assume that gradual and more slow cutting during ThuFLEP may lead to a more predictable dissection. So the resident studying ThuFLEP, begins to identify the prostate capsule and to get into subcapsular layer earlier then resident using other EEP procedures. However, there is no evidence to support these assumptions.

So far we have only discussed the properties of TFL and did not comment on its usability and serviceability. The thulium fiber laser setups are smaller than those for Ho : YAG, so they require less space in the operating theatre. Also TFL laser setups are lighter than those for Ho : YAG which makes it easier to use in theatre. Besides, the TFL setup requires a standard 220V or 110V electrical socket without any conversion. All these features are very useful and convenient for hospital administration because they make less demands on placement in small operation rooms. As for the surgeon's comfort, Moore et al. determined that TFL produces less noise than Ho : YAG (44). This makes it more pleasant to use TFL and means that surgeons and nurses can easily talk to one another during the procedure (44).

As it stands, TFL is something that urological residents who are just setting out to learn EEP should familiarize themselves with – they are likely to quickly reach an EEP learning curve plateau using TFL compared to other cutting agents. TFL may also be interesting for experienced surgeons who are accustomed to performing EEP or ERBT using thulium solid-state laser (Tm : YAG). TFL could also be used within hospital administration because this laser makes fewer demands on placement in small operation theatres and incorporates two tools – an effective laser for soft tissue cutting and a useful device for stone ablation.

Limitations

Our study has a few limitations. At first, we have not added any data regarding clinical studies laser settings because no relevant data in the original studies were to be found. So, the only data that we had was information about which laser mode was used – SP or QCW. Secondly, we have not found any preclinical studies that compare the effects of TFL with continuous-wave Tm : YAG. Therefore, we cannot compare the vaporization speed and the carbonization mode for those lasers. Yet, we have described in detail the physics of the lasers so that the reader may form easily his or her impression based on the theoretical background. We hope that this makes up for the lack of experimental data.

Conclusions

TFL is a safe and effective tool for BPH surgery. In terms of parameters, it is in no way inferior to Tm : YAG or Ho : YAG during EEP. However, TFL surpasses these lasers in terms of usability and serviceability. These advantages are likely to render it more popular over time.

Author contributions

MT Project development, Systematic search, Data analysis, Manuscript writing EC Project development, Data analysis, Manuscript editing AA Data analysis, Systematic search, Manuscript writing, Tabulation CA Data analysis, Systematic search, Manuscript editing BB Project development, Data analysis, Manuscript editing AM Data analysis, Systematic search, Manuscript writing SP Data analysis, Manuscript editing IB Data analysis, Manuscript editing K-FK Data analysis, Manuscript editing SR Data analysis, Manuscript editing JR Data analysis, Manuscript editing GC Data analysis, Manuscript editing DE Project development, Systematic search, Manuscript editing All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fruro.2022.1017069/full#supplementary-material

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