REVIEW

OPEN

Outcomes of thulium fibre laser for treatment of urinary tract stones: results of a systematic review

Peter Kronenberg[a], BM Zeeshan Hameed[b] and Bhaskar K. Somani[c]

Purpose of review

Lasers have become a fundamental aspect of stone treatment. Although Holmium:Yttrium-Aluminum-garnet (Ho:YAG) laser is the current gold-standard in endoscopic laser lithotripsy, there is a lot of buzz around the new thulium fibre laser (TFL). We decided to evaluate the latest data to help create an objective and evidence-based opinion about this new technology and associated clinical outcomes.

Recent findings

Sixty full-text articles and peer-reviewed abstract presentations were included in the qualitative synthesis of this systematic review performed over the last 2 years. Current super pulsed TFL machines are capable of achieving peak powers of 500W and emit very small pulse energies of 0.025 Joules going up to 6 Joules, and capable of frequency over 2000 Hz. This makes the TFL ablate twice as fast for fragmentation, 4 times as fast for dusting, more stone dust of finer size and less retropulsion compared to the Ho:YAG laser. Because of the smaller laser fibres with the TFL, future miniaturization of instruments is also possible.

Summary

Based on the review, the TFL is a potential game-changer for kidney stone disease and has a promising role in the future. However larger multicentric prospective clinical studies with long-term follow-up are needed to establish the safety and efficacy of the TFL in endourology.

Keywords

holmium laser, kidney calculi, laser, thulium fibre laser, thulium fibre laser, ureteroscopy

INTRODUCTION

In the last few years, many rumours and hype has surrounded a new laser technology, the thulium fibre laser (TFL). Many claims of better performance in comparison to the Holmium:Yttrium-Aluminum-garnet (Ho:YAG) laser, the current gold-standard in endoscopic laser lithotripsy have been made in several papers, congress presentations or scientific news outlets [1–6]. Additionally, some reviews of the technology have been made [2,7▪,8▪,9], however, the technology has not been readily available till recently. Despite being a promising technology, until recently only one single Russian manufacturer had this kind of lasers available and approved for clinical use in Russia [10], and consequently, the first studies were also done mostly by Russian colleagues [11,12]. With the recent FDA approval in 2019 and the European CE mark approval in 2020, Thulium fibre laser technology has become more widely available, but is still a rarity in most urological departments in the US, Europe and worldwide. Despite its rarity, new studies, including basic science and clinical studies are being reported more frequently. Thus, we decided to evaluate the latest data available to date, helping the readers to create an objective and evidence-based opinion about this new technology and associated clinical outcomes.

METHODS

A PubMed search was performed (October 2020) for papers including the terms ‘thulium’ in association

[a]Hospital CUF Descobertas, Lisbon, Portugal, [b]Kasturba Medical College Manipal, Manipal Academy of Higher Education, Manipal, Karnataka, India and [c]University Hospital Southampton NHS Foundation Trust, Southampton, UK

Correspondence to Peter Kronenberg, MD, Hospital CUF Descobertas, Rua Mário Botas, 1998-018 Lisbon, Portugal. Tel: +351 210025200; e-mail: peterkronenberg@gmail.com

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KEY POINTS

- TFL technology has a promising role in the future of laser lithotripsy.
- The advantages of the TFL over the Ho:YAG laser are numerous and ubiquitous, including significant improvements in ablation efficiency, retropulsion, lithotripsy settings, laser fibres, safety and machine form-factor.
- TFL technology is capable of reducing operating room time, expanding the role of RIRS in the treatment of larger kidney stones and changing the current guidelines on stone management.
- The TFL has potential to compete or even replace the Ho:YAG laser, but more clinical studies are needed to determine if it will become the new gold standard.

with any of the following terms 'lithotripsy', 'lithiasis', 'stone(s)', 'calculus', 'calculi', 'lithotripter(s)', 'lithotrite(s)', 'kidney', 'ureter', 'fiber(s)', 'fibre(s)', '(endo)urology', '(endo)urologic(al)', or 'intrarenal'. The search covered articles published between the years 2019 and 2020, as well as articles already accepted in 2020 but not yet published. Grey literature including the medical sections of ScienceDirect, Wiley, SpringerLink, and Mary Ann Liebert publishers as well as Google Scholar were also searched for peer-reviewed abstract presentations published within the previously stated time frame that were not indexed on PubMed. The authors adhered to PRISMA guidelines for this review [13]. All relevant data was identified and selected, and is summarized below.

BIBLIOGRAPHIC SEARCH RESULTS

The PubMed search returned 260 articles and the medical sections of ScienceDirect, Wiley, SpringerLink, Mary Ann Liebert, and Google Scholar returned 39 additional papers, some of them in duplicate. After duplicate removal, the abstracts of the remaining 220 records were read. 144 (65%) of these records related to basic technical laser research, to the use of lasers in nonurological medical specialities or the use of lasers in a nonlithotripsy-related urological setting, such as Ho:YAG or

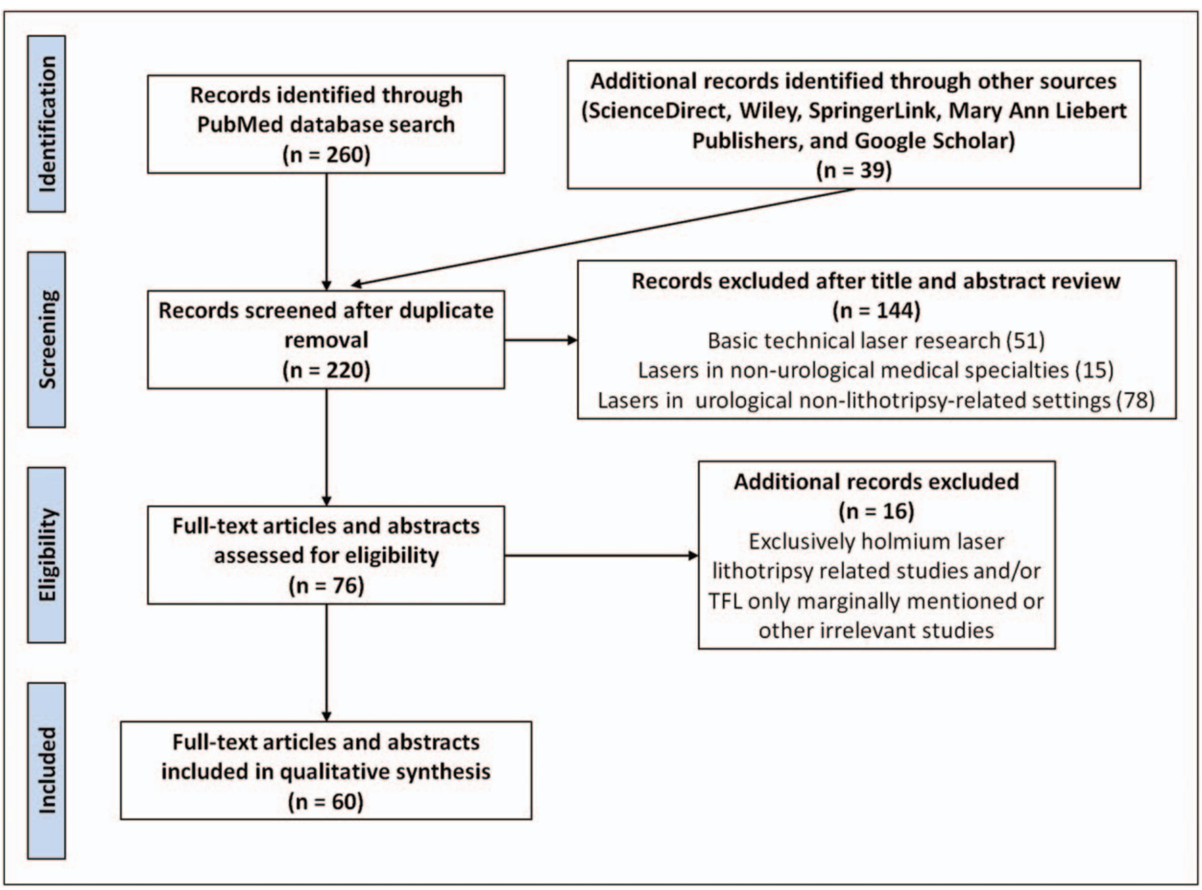

FIGURE 1. Flow chart documenting the source of information selection process through the different phases, according to PRISMA guidelines [13].

Table 1. Main features and advantages of the TFL according to different topics (in comparison to Ho:YAG laser technology) based on the bibliography of the current review, including in-vivo and in-vitro studies

Analyzed TFL Features	Features in Detail
TFL Machine Specifications	- Electronically controlled laser diodes providing constant peak power up to 500W - Same pulse energy range as any high-power Ho:YAG laser (0.2–6.0 Joules) plus additional very low pulse energies of 0.025–0.1 Joules. - Pulse frequencies up to 2400 Hz - Very long pulse durations available (up to 50 milliseconds) - Several times smaller and lighter than Ho:YAG lasers - Quiet air-cooling mechanism - Reduced energy consumption - Connects to any standard electrical power outlet
Ablation Efficiency	- Fragments 2x faster than Ho:YAG - Dusts 4–5x faster than Ho:YAG - higher ablation efficiency should translate to less operating room time
Dust and Residual Particles	- Produces more dust quantity - Dust and residual fragments significantly smaller than with Ho:YAG
Retropulsion	- Reduced retropulsion, sometimes even absent - Clinical significant retropulsion at 1J (vs 0.2J with Ho:YAG)
Visibility	- Optimal visibility in 95% of cases - Visibility decrease at higher frequencies (>200Hz)
Laser Fibres	- Smaller, more flexible and energy resistant laser fibres - Smaller size offers future miniaturization possibilities
Safety	- Can be used in any anatomical location - Can be used in any endoscopic approach - Smaller residual fragments = less basketing passes - Better visibility = less unintended laser damages to structures
Temperature Safety	- No temperature differences between TFL and Ho:YAG - There is no amplified temperature rise with the TFL - The thermal safety precautions used with the Ho:YAG are exactly the same for the TFL

TFL enucleation of the prostate. After the exclusion of additional 16 records, 60 full-text articles and peer-reviewed abstract presentations were included in the qualitative synthesis of this systematic review (Fig. 1). Yet, as with any new technology, most of the references pertain to clinical abstracts, with very little fully published studies, being a limitation of the current review.

Despite the majority of the initial laboratory and clinical studies were from Russian researchers, many more recent studies were done by researchers all around the world, showing promising results [14▪▪,15–18]. Still, after evaluating our bibliographic search results, more than 40% of the recent published research on TFL is from Russian origin or has Russian researchers participating in it. And considering exclusively recent clinical studies, over 75% come from Russian investigators. This only highlights the leading position that Russian urologists and researchers have as one of the primary users concerning this ground-breaking and innovative technology.

The relevant data retrieved from the bibliographic search has been categorized and summarized into the following sections: TFL machine specifications, Ablation efficiency, Dust issues, Retropulsion, Optimal settings, Laser fibres, Safety, and Ongoing and future research. Table 1 summarizes the main results of this review.

THULIUM FIBRE LASER MACHINE SPECIFICATIONS

Previous reports about TFL have been lab-based studies, but they were skewed because the TFL prototypes had low peak powers. However now there are new Super pulsed TFL machines that use electronically modulated laser diodes (instead of using flash lamps as in Ho:YAG lasers) and are capable of higher and constant peak power, thereby offering wider range of laser parameters, thus turning the TFL into one of the most awaited innovations in endourology [14▪▪,19,20].

The TFL is called a fibre laser because the laser beam is generated inside a very small core laser fibre (the gain medium) within the laser generator, whereas Ho:YAG lasers use laser rods inside resonance chambers with complex optical systems and precision alignment [7▪,8▪]. Although Ho:YAG Lasers use laser radiation at 2100 nm wavelength, the TFL uses 1940 nm wavelength and its radiation absorption is four times higher in water, which is probably the reason for its higher ablation efficiency of any type of urinary calculi (see below) [21,22▪▪]. Although Ho:YAG lasers are big, heavy, power-hungry machines that need dedicated high-power outlets and use noisy water cooling, TFL machines are several times lighter, smaller, use quiet air-cooling mechanisms, that consume less energy and can be run from a standard power outlet [8▪,10,23–26].

Current super pulsed TFL machines are capable of achieving peak powers of 500W and emit very small pulse energies of 0.025 Joules going up to 6 Joules [14▪▪]. But what makes the TFL stand out in comparison to the Ho:YAG laser are its frequency capabilities. Although the current top of the line Ho:YAG laser machines are capable of achieving 120 Hz of pulse frequency, the TFL is capable to have frequency over 2000 Hz [7▪,8▪], and the latest commercially available TFL goes even up to 2400 Hz [23]. Another innovation concerns pulse duration, since the TFL can be operated in both using very low pulse energies and very long pulse durations (up to 50 milliseconds) [14▪▪]. The very low pulse energies, the higher frequencies and the longer pulse durations, are features that Ho:YAG lasers do not have, thus giving the TFL a significant advantage.

ABLATION EFFICIENCY

Several papers conclude that the TFL is more efficient for urinary calculus lithotripsy than the Ho:YAG laser [27], even at equivalent lithotripsy settings using the same pulse energy and the same pulse frequency [28–30]. With fragmentation settings, the TFL ablates twice as fast, and with dusting settings it ablates 4 to 5 times faster than the best Ho:YAG lasers [28,31,32]. Even comparisons with high-power Ho:YAG lasers equipped with pulse modulating Moses technology from Lumenis [26] showed the superior lithotripsy performance of the TFL technology, sometimes by a factor of 3 [20,33–36]. One of the reasons for this improved performance is the steady and prolonged peak power levels that the TFL is capable of delivering associated with its four times higher wavelength absorption in water, thereby causing explosive thermomechanical interactions in addition to the already known photothermal effects [14▪▪,20,21,22▪▪]. Still, there are some debatable results such as accrediting solely the higher frequencies of the TFLs for its increased ablation speeds, less retropulsion or operating room time reduction [37], in spite of the use of lower pulse energies together with higher frequencies or the higher ablation performance per Joule of TFL energy. However, most authors are unanimous in accrediting the TFL with time-saving properties and reducing operating room time [27,32,35–37].

DUST ISSUES

Interestingly, it is not only the four to fivefold higher dusting rate of the primary stones that makes the TFL so attractive [28,30,31]. The resulting stone particles and fragments are also significantly different from those resulting with Ho:YAG lasers. Not only is the TFL able to produce stone dust from all prevailing stone types [22▪▪], but it also produces at least twice as much dust even when compared to Moses technology [35]. The resulting mean stone particle sizes are also significantly smaller in all size categories of less than 1 mm or 0.5 mm [14▪▪,36,37]. One study even analyzed the mean maximal remaining stone fragments with the TFL, and depending on stone composition, the largest residual fragments had 116 to 254 μm sizes [22▪▪]. Another advantage of small particles means less basketing passes [36], which further reduces complications and operating room times. Regardless of the current controversial definition of dust one thing is clear that the TFL produces not only a larger quantity of dust, but also a finer quality of dust.

RETROPULSION

Another issue that many studies refer to is the reduced or even absent retropulsion with the TFL. This was not only objectively evaluated in in vitro studies, but also subjectively perceived in several clinical studies including (flexible) ureteroscopy and percutaneous nephrolithotomy (PCNL) procedures [27,31,37–40]. At equal pulse energies, stone retropulsion threshold is up to four times higher with the TFL [20,29]. With Ho:YAG lasers, retropulsion becomes already evident at 0.2J pulse energies, while with the TFL retropulsion begins at around 1 J pulse energy, being clinically insignificant in many cases [29,41]. The reason for this reduced retropulsion in comparison to the Ho:YAG lays not only in the lower peak power of the TFL, but also in the more constant and prolonged peak power with longer pulse duration, thus delivering more energy to the stone without sacrificing ablation efficiency [20,42]. Yet, there is still some controversy with some authors claiming that the TFL has significantly less retropulsion than Moses technology [34], whereas other authors do not [43]. Another aspect mentioned by authors was the better visibility using the TFL which was optimal in up to 95% of clinical cases [38,40,41,44,45]. At very high frequencies, however (200 Hz) some deterioration in visibility was noticed due to the snowstorm effect [37].

OPTIMAL SETTINGS

With the TFL's improved performance on several levels and the wide range of adjustable parameters, some authors have attempted to clinically determine the best lithotripsy settings for (flexible) ureteroscopy, PCNL or cystolithotripsy. Settings such as, 1–1.5 J and 15–30 Hz for fragmentation and 0.1–0.3 J and 50–100 Hz for dusting in (micro-) PCNL, 0.1–0.2J with 15–30W for dusting in the kidney, 0.2–0.5J with 10–15W for dusting and fragmentation in the ureter, and 2–5J and 5–10 Hz for bladder stones treatment [38,41,46]. However, there are even reports of some authors using up to 500 Hz in the upper tract [15]. Yet, this is very preliminary data and the optimal laser settings are far from being established, needing future studies on it [8▪,47].

LASER FIBRES

TFL laser fibres are smaller (150 μm), more flexible, resistant to bending and suffering less burnback in comparison to Ho:YAG laser fibres or even special Moses fibres [43,48,49]. One study using exclusively Ho:YAG laser fibres with a Ho:YAG laser and comparing it with a TFL using exactly the same fragmentation and dusting parameters at 7.5 W total power levels, showed up to 90% fibre breakages at extreme 9 mm bending diameters with the Ho:YAG laser but none with the TFL. Furthermore, the same authors even tested 50W settings with the TFL at 9 mm bending diameter with the same 200 μm Ho:YAG laser fibres, and still none of the fibres broke [50▪▪]. This irrefutably shows that it is the quality of the laser beam generation within the TFL that protects the laser fibres, even protecting native Ho:YAG laser fibres.

The smaller diameter of the TFL laser fibres has also been shown to contribute to produce smaller stone fragments [49], and despite their diameter, they still produce higher ablation volumes than their larger Ho:YAG counterparts [28,30]. By using smaller core diameters the energy density delivered by these fibres is also significantly higher [7▪], as well as allowing better instrument deflection and offering future miniaturization possibilities [8▪,51,52]. The better and speedier performance of the TFL enabled the tackling of larger stone through retrograde intrarenal surgery (RIRS), like demonstrated by several clinical studies [53–55]. Thus, TFL technology is capable of expanding the role of RIRS in the treatment of larger kidney stones with shorter operating times and in changing the current guidelines on stone management [53,56].

SAFETY

Concerning the safety of this new technology, the clinical and prospective data from several patient cohorts is coherent in deeming the TFL safe to use, in any anatomical location, and regardless of its endoscopic surgical approach [15–17,27,38–40,45,46,51,55,57,58]. One of the safety features of the TFL is its laser fibres higher resistance to extreme bending diameters, even using high power, thereby avoiding their breakage with consequent laser emission inside the fragile flexible scopes [50▪▪,59]. The ability of the TFL to ablate urinary stones into finer particles and smaller residual fragments implies less basketing passes and complicated endoscope manoeuvres that can cause additional wear and tear to our instruments [36]. Moreover, the optimal and clear visibility reported with the TFL use [27,37,38,40,41,44,45] represents an additional safety feature, allowing the surgeon to better judge its fibre tip position in relation to other structures, reducing unintentional firing against soft tissues or instruments.

However, there is a controversial safety issue that comes up again and again in the social media and literature with the alleged high-temperature rise with the TFL. Urologists are afraid of heating the fluid medium too much, potentially causing damage or ureteral stenosis [59]. Claims have been made that the TFL's higher absorption coefficient in water equals higher water temperature [60] or that the heat production of 1 Joule of TFL energy is four times that of the Ho:YAG laser [29]. Perceptions like these with TFL continue being repeated and some authors even name it the 'thermal effect of the TFL' [61]. Yet there are plenty of papers showing that with similar energy and frequency settings, both the Ho:YAG and the TFL cause precisely the same temperature changes [29,62▪▪,63▪▪]. Only using high power settings and reduced or absent irrigation, there is dangerous temperature rises with the Ho:YAG as with the TFL (with exactly similar temperature variations) [64,65]. Thus urologists should be aware of this problem and implement variety of techniques, if needed, such as higher irrigation flow rates, intermittent laser activation, cooled irrigation fluid or avoidance of high power settings to limit thermal lesions during laser lithotripsy, regardless of the laser technology employed [60,64,66▪]. One paper even evaluated strictures or stenosis at 3-month follow-up of a TFL procedure and found none [40]. The authors of the present systematic review can't state enough that 1 Joule of energy originating from whatever energy source, will always heat a certain medium to the same degree, regardless of the energy source (1 Joule of TFL energy = 1 Joule of Ho:YAG energy = 1 Joule of candle energy), a statement which is by itself similar to the definition of the thermodynamical calorie [67]. Recently, other researchers are also trying to eradicate this misbelief regarding the TFL [63■■].

ONGOING AND FUTURE RESEARCH

Other technological developments and lines of research are underway for the TFL. These include vibrating laser fibre tips [52], or detailed research on vapour bubble formation and surfactant supplementation of irrigation fluids or tweaking of the energy pulse shape to increase working distance if desired [42,68,69], as well as to associate TFL lithotripsy with suction [70]. All of these features are to further enhance TFL efficiency. Because of the smaller laser fibres that one can use with this technology, there are also future miniaturization possibilities of instruments, making an already minimally invasive technique even less invasive [8■].

CONCLUSION

Based on the review, we consider that the TFL is a game changer and has a promising role in the future. Considering its additional versatility for soft tissue applications, the TFL has the potential to compete or even replace the Ho:YAG laser and becoming the new gold standard [4,59,71,72]. The evidence supporting the TFL seems very promising, but we have to be careful before fully embracing the TFL as an alternative to the Ho:YAG laser [8■,19,73]. Considering the current rarity and absence of TFL machines throughout the world, most studies regarding the TFL have relative small sample size and almost no clinical comparative studies exist in relation to the Ho:YAG laser. Thus, large multicentric prospective studies and randomized clinical trials with Ho:YAG comparison (control arm) are needed, with long-term follow-up to irrefutably confirm all the aforementioned observations and conclusions. Only then can we consider to replace our 30-year-old Ho:YAG technology with the apparently safer and more efficacious TFL technology.

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Conflicts of interest

Peter Kronenberg has participated in advisory board meetings for Olympus and in industry breakout session for Lumenis. Bhaskar Somani has participated in industry session for Lumenis.

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