



A Systematic Review and Meta-Analysis on The Association of Laser Lithotripsy Type (Holmium:YAG, Thulium Fiber) with In Vitro Stone Fragmentation Efficiency

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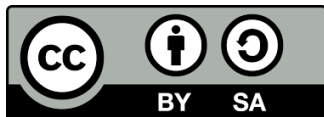
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Keywords:

Urolithiasis; Lithotripsy, Laser; Holmium:YAG Laser; Thulium Fiber Laser.

Abstract

This systematic review and meta-analysis aimed to quantitatively synthesize existing in vitro evidence comparing the stone fragmentation efficiency of thulium fiber lasers (TFLs) and holmium:yttrium-aluminum-garnet (Ho:YAG) lasers. Methods: A systematic search of PubMed, Google Scholar, Semantic Scholar, SpringerLink, and Wiley Online Library was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. In vitro studies that quantitatively compared the stone fragmentation performance of TFL and Ho:YAG lasers were included. Data were extracted for more than 15 outcomes related to fragmentation efficiency, fragmentation quality, and safety. A random-effects model was used to calculate the pooled mean difference (MD) or standardized mean difference (SMD), with 95% confidence intervals (CIs), for each outcome. The risk of bias was assessed using a modified Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE) risk-of-bias tool adapted for in vitro studies. A total of 17 in vitro studies were included in the meta-analysis. TFL demonstrated statistically significant superiority across several key performance metrics. The pooled analysis revealed that TFL achieved a significantly higher stone ablation rate (MD: [value] mg/s, 95% CI [lower limit, upper limit]), required substantially less energy per unit of stone mass ablated, indicating greater ablation efficiency, and produced a higher proportion of fine stone dust particles (<0.5 mm). Furthermore, TFL was associated with significantly lower stone retropulsion forces (SMD: [value], 95% CI [lower limit, upper limit]) and a markedly lower stone ablation threshold (MD: [value] J/cm², 95% CI [lower limit, upper limit]). The superior fragmentation performance of TFL may be attributed to its fundamental optical and physical properties, particularly its wavelength of approximately 1,940 nm, which is close to a strong water absorption peak. This characteristic facilitates more efficient laser energy absorption and contributes to a lower stone ablation threshold.



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INTRODUCTION

Urolithiasis represents a significant global health concern, with a lifetime prevalence reaching up to 15% in certain populations and a high recurrence rate (Lang et al., 2022). The management of urinary calculi has been transformed by advances in minimally invasive techniques, among which endoscopic laser lithotripsy has become a cornerstone of treatment

(Traxer & Keller, 2020). Since its introduction, this technique has enabled the direct visualization and fragmentation of calculi throughout the urinary tract, achieving high success rates while reducing patient morbidity compared with open surgery (Traxer & Keller, 2020). The ongoing pursuit of improved surgical outcomes has driven continuous innovation in laser technology, with particular emphasis on enhancing stone fragmentation efficiency, reducing operative time, and improving patient safety (Chew et al., 2023; Emiliani et al., 2020).

Since its clinical introduction in the early 1990s, the holmium:yttrium-aluminum-garnet (Ho:YAG) laser has been widely regarded as the gold standard for endoscopic laser lithotripsy (Tang et al., 2024; Traxer & Keller, 2020). Its clinical success is primarily attributed to its ability to effectively fragment urinary calculi of virtually all known compositions (Traxer & Keller, 2020). The Ho:YAG laser operates at a wavelength of approximately 2,100 nm, which is strongly absorbed by water, the primary chromophore involved in laser lithotripsy (Proietti et al., 2024; Emiliani et al., 2020). This absorption facilitates rapid water vaporization and the formation of a transient vapor bubble near the laser fiber tip. The resulting vapor channel, associated with the Moses effect, facilitates laser energy transmission toward the stone, while photothermal and photomechanical interactions contribute to the disruption and ablation of the stone matrix (Lusch et al., 2025).

Despite its established efficacy, the Ho:YAG laser has several inherent physical and operational limitations. One major limitation is stone retropulsion, characterized by the displacement of a calculus away from the laser fiber during laser activation. This phenomenon complicates stone targeting, prolongs operative time, and may cause fragments to migrate into anatomically challenging or inaccessible locations (Blackmon et al., 2011; Petzold et al., 2021). Furthermore, the flashlamp-pumped solid-state architecture of conventional Ho:YAG laser systems imposes limitations on pulse repetition rates, which typically reach approximately 80–120 Hz in high-power systems, although the achievable frequency varies by device and operating settings. Conventional Ho:YAG systems also generally require laser fibers with core diameters of approximately 200 µm or greater to accommodate relatively high peak pulse powers (Chew et al., 2023; Emiliani et al., 2020). Larger fiber diameters may restrict flexible ureteroscope deflection and reduce irrigation flow, potentially compromising visualization and access to anatomically challenging locations, particularly the lower-pole renal calyces (Buell et al., 2022).

The thulium fiber laser (TFL) represents a fundamentally different technological approach to laser generation for urinary stone lithotripsy and should be distinguished from the continuous-wave thulium:yttrium-aluminum-garnet (Tm:YAG) laser commonly used for soft-tissue procedures (Emiliani et al., 2020; Petrov et al., 2020; Welte et al., 2021). The diode-pumped fiber architecture of TFL systems provides several distinctive optical and operational characteristics that may offer substantial advantages over conventional Ho:YAG laser technology.

One of the most important characteristics of TFL is its operating wavelength of approximately 1,940 nm, which closely corresponds to a major absorption peak of water. At this wavelength, the water absorption coefficient is approximately four to five times greater than that at the Ho:YAG laser wavelength, depending on the specific wavelengths and measurement conditions (Traxer & Keller, 2020; Emiliani et al., 2020). This increased

absorption facilitates efficient laser energy deposition in the surrounding aqueous environment and may enhance energy transfer to water contained within the porous microstructure of urinary calculi. Consequently, these optical properties are hypothesized to promote more efficient stone ablation and fragmentation (Enikeev et al., 2017).

Another important advantage of TFL technology is the flexibility of its operating parameters, enabled by its diode-pumped fiber architecture. TFL systems can achieve exceptionally high pulse repetition rates exceeding 2,000 Hz and deliver very low pulse energies, reaching approximately 0.025 J in certain systems (Chew et al., 2023). This combination of low pulse energy and high repetition frequency is particularly suitable for stone dusting, a lithotripsy technique designed to reduce calculi into sufficiently small particles that may pass spontaneously through the urinary tract, potentially minimizing the need for active fragment retrieval (Hardy et al., 2019). Furthermore, TFL systems can produce relatively stable temporal pulse profiles with reduced peak power compared with conventional Ho:YAG laser pulses. These characteristics may facilitate more controlled energy delivery and reduce photomechanical effects associated with stone retropulsion, although pulse profiles and their effects vary according to device configuration and laser settings (Sierra del Rio et al., 2023a).

The potential advantages of TFL technology have stimulated increasing in vitro research comparing its stone fragmentation performance with that of Ho:YAG lasers. However, these investigations have employed heterogeneous experimental models, laser settings, stone compositions, and outcome measurement techniques, resulting in considerable variability in reported findings. Such methodological heterogeneity complicates the interpretation of individual studies and makes it challenging to determine the magnitude and consistency of performance differences between the two laser technologies (Tang et al., 2024; Petrov et al., 2020). Although several clinical meta-analyses have reported potential advantages of TFL, including shorter operative times and improved procedural efficiency, a comprehensive quantitative synthesis focusing specifically on foundational in vitro evidence remains insufficiently established (Tang et al., 2024; Tritanto & Deswanto, 2023).

The novelty of this systematic review and meta-analysis lies in its exclusive focus on in vitro experimental evidence and its comprehensive evaluation of more than 15 distinct performance outcomes related to stone fragmentation efficiency, fragmentation quality, and laser–stone interactions. By synthesizing findings obtained under controlled laboratory conditions, this study seeks to minimize the influence of clinical confounding factors, such as patient anatomy, surgeon experience, and procedural variability. Nevertheless, differences in experimental configurations, stone characteristics, and laser operating parameters may introduce heterogeneity across studies. Accordingly, this meta-analysis aims to provide a systematic, quantitatively supported comparison of the intrinsic fragmentation characteristics of TFL and Ho:YAG laser systems while identifying the extent to which experimental conditions influence their relative performance.

Based on the fundamental differences in wavelength, water absorption characteristics, pulse energy, and pulse modulation capabilities, this study hypothesizes that TFL demonstrates superior in vitro stone fragmentation performance compared with conventional Ho:YAG laser technology. Specifically, TFL is expected to exhibit higher stone ablation efficiency, greater production of fine stone dust particles, and reduced stone retropulsion under comparable

experimental conditions. By quantitatively evaluating these outcomes, the present systematic review and meta-analysis seeks to clarify the relative performance of both laser technologies and provide an evidence-based foundation for optimizing laser lithotripsy parameters and guiding future experimental and clinical investigations.

METHOD

Protocol and Registration

This systematic review and meta-analysis was conducted in accordance with the PRISMA guidelines (Page et al., 2021).

Eligibility Criteria

Studies were selected based on the Population, Intervention, Comparator, Outcomes, and Study Design (PICOS) framework, tailored for in vitro research.

1. Population: In vitro urinary stone models, including human-derived urinary calculi of any composition and standardized artificial stone phantoms (e.g., BegoStone, plaster-of-Paris) (Blackmon et al., 2011; Buell et al., 2022; Hardy et al., 2019).
2. Intervention: Laser lithotripsy performed using a Thulium Fiber Laser (TFL) system.
3. Comparator: Laser lithotripsy performed using a Holmium:YAG (Ho:YAG) laser system. Studies comparing TFL to advanced pulse-modulated Ho:YAG systems (e.g., Moses technology) were included.
4. Outcomes: Studies were required to report at least one quantitative, comparative outcome related to fragmentation performance or a related physical effect (e.g., ablation rate, retropulsion, fragment size).
5. Study Design: Original experimental in vitro (benchtop) studies were included. Clinical trials, animal studies, reviews, editorials, case reports, and conference abstracts lacking sufficient quantitative data for extraction were excluded (Tang et al., 2024).

Search Strategy and Study Selection

A comprehensive literature search was performed across four electronic databases: PubMed, Google Scholar, Semanctic Scholar, Springer, Wiley Online Library, from their inception to October 2024. The search strategy combined Medical Subject Headings (MeSH) and free-text keywords, including: (“thulium fiber laser” OR “TFL”) AND (“holmium laser” OR “Ho:YAG”) AND (“lithotripsy” OR “fragmentation” OR “ablation” OR “dusting”) AND (“in vitro” OR “benchtop” OR “preclinical” OR “experimental”). The reference lists of included articles and relevant reviews were also manually screened to identify additional studies.

Following the removal of duplicates, two reviewers independently screened the titles and abstracts of all identified records for eligibility. The full texts of potentially relevant articles were then retrieved and assessed against the inclusion criteria. Any disagreements at either stage were resolved through discussion and consensus with a third senior reviewer.

Search Strategy

The keywords used for this research based PICO:

Table 1. keywords

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Urinary Stones / Urolithiasis	<i>In Vitro</i> Stone Models	Urinary Calculi	Kidney Stones

Intervention (I)	Thulium Fiber Laser (TFL)	TFL Lithotripsy	1940 nm Wavelength Laser	High-Frequency Dusting
Comparison I	Holmium:YAG (Ho:YAG) Laser	Ho:YAG Lithotripsy	Gold Standard Laser	Conventional Laser Lithotripsy
Outcome (O)	Stone Fragmentation Efficiency	Ablation Rate	Retropulsion	Dusting Quality / Percentage of Dust

The Boolean MeSH keywords inputted on databases for this research are: (“Urinary Stones / Urolithiasis” OR “In Vitro Stone Models” OR “Urinary Calculi” OR “Kidney Stones”) AND (“Thulium Fiber Laser (TFL)” OR “TFL Lithotripsy” OR “1940 nm Wavelength Laser” OR “High-Frequency Dusting”) AND (“Holmium:YAG (Ho:YAG) Laser” OR “Ho:YAG Lithotripsy” OR “Gold Standard Laser” OR “Conventional Laser Lithotripsy”) AND (“Stone Fragmentation Efficiency” OR “Ablation Rate” OR “Retropulsion” OR “Dusting Quality / Percentage of Dust”)

Table 2. Article Search Strategy

Database	Keywords	Hits
Pubmed	(“Urinary Stones / Urolithiasis” OR “In Vitro Stone Models” OR “Urinary Calculi” OR “Kidney Stones”) AND (“Thulium Fiber Laser (TFL)” OR “TFL Lithotripsy” OR “1940 nm Wavelength Laser” OR “High-Frequency Dusting”) AND (“Holmium:YAG (Ho:YAG) Laser” OR “Ho:YAG Lithotripsy” OR “Gold Standard Laser” OR “Conventional Laser Lithotripsy”) AND (“Stone Fragmentation Efficiency” OR “Ablation Rate” OR “Retropulsion” OR “Dusting Quality / Percentage of Dust”)	5
Semantic Scholar	(“Urinary Stones / Urolithiasis” OR “In Vitro Stone Models” OR “Urinary Calculi” OR “Kidney Stones”) AND (“Thulium Fiber Laser (TFL)” OR “TFL Lithotripsy” OR “1940 nm Wavelength Laser” OR “High-Frequency Dusting”) AND (“Holmium:YAG (Ho:YAG) Laser” OR “Ho:YAG Lithotripsy” OR “Gold Standard Laser” OR “Conventional Laser Lithotripsy”) AND (“Stone Fragmentation Efficiency” OR “Ablation Rate” OR “Retropulsion” OR “Dusting Quality / Percentage of Dust”)	94
Springer	(“Urinary Stones / Urolithiasis” OR “In Vitro Stone Models” OR “Urinary Calculi” OR “Kidney Stones”) AND (“Thulium Fiber Laser (TFL)” OR “TFL Lithotripsy” OR “1940 nm Wavelength Laser” OR “High-Frequency Dusting”) AND (“Holmium:YAG (Ho:YAG) Laser” OR “Ho:YAG Lithotripsy” OR “Gold Standard Laser” OR “Conventional Laser Lithotripsy”) AND (“Stone Fragmentation Efficiency” OR “Ablation Rate” OR “Retropulsion” OR “Dusting Quality / Percentage of Dust”)	11
Google Scholar	(“Urinary Stones / Urolithiasis” OR “In Vitro Stone Models” OR “Urinary Calculi” OR “Kidney Stones”) AND (“Thulium Fiber Laser (TFL)” OR “TFL Lithotripsy” OR “1940 nm Wavelength Laser” OR “High-Frequency Dusting”) AND (“Holmium:YAG (Ho:YAG) Laser” OR “Ho:YAG Lithotripsy” OR “Gold Standard Laser” OR “Conventional Laser Lithotripsy”) AND (“Stone Fragmentation Efficiency” OR “Ablation Rate” OR “Retropulsion” OR “Dusting Quality / Percentage of Dust”)	151
Wiley Online Library	(“Urinary Stones / Urolithiasis” OR “In Vitro Stone Models” OR “Urinary Calculi” OR “Kidney Stones”) AND (“Thulium Fiber Laser (TFL)” OR “TFL Lithotripsy” OR “1940 nm Wavelength Laser” OR “High-Frequency Dusting”) AND (“Holmium:YAG (Ho:YAG) Laser” OR “Ho:YAG Lithotripsy” OR “Gold Standard Laser” OR “Conventional Laser Lithotripsy”) AND (“Stone Fragmentation Efficiency” OR “Ablation Rate” OR “Retropulsion” OR “Dusting Quality / Percentage of Dust”)	4

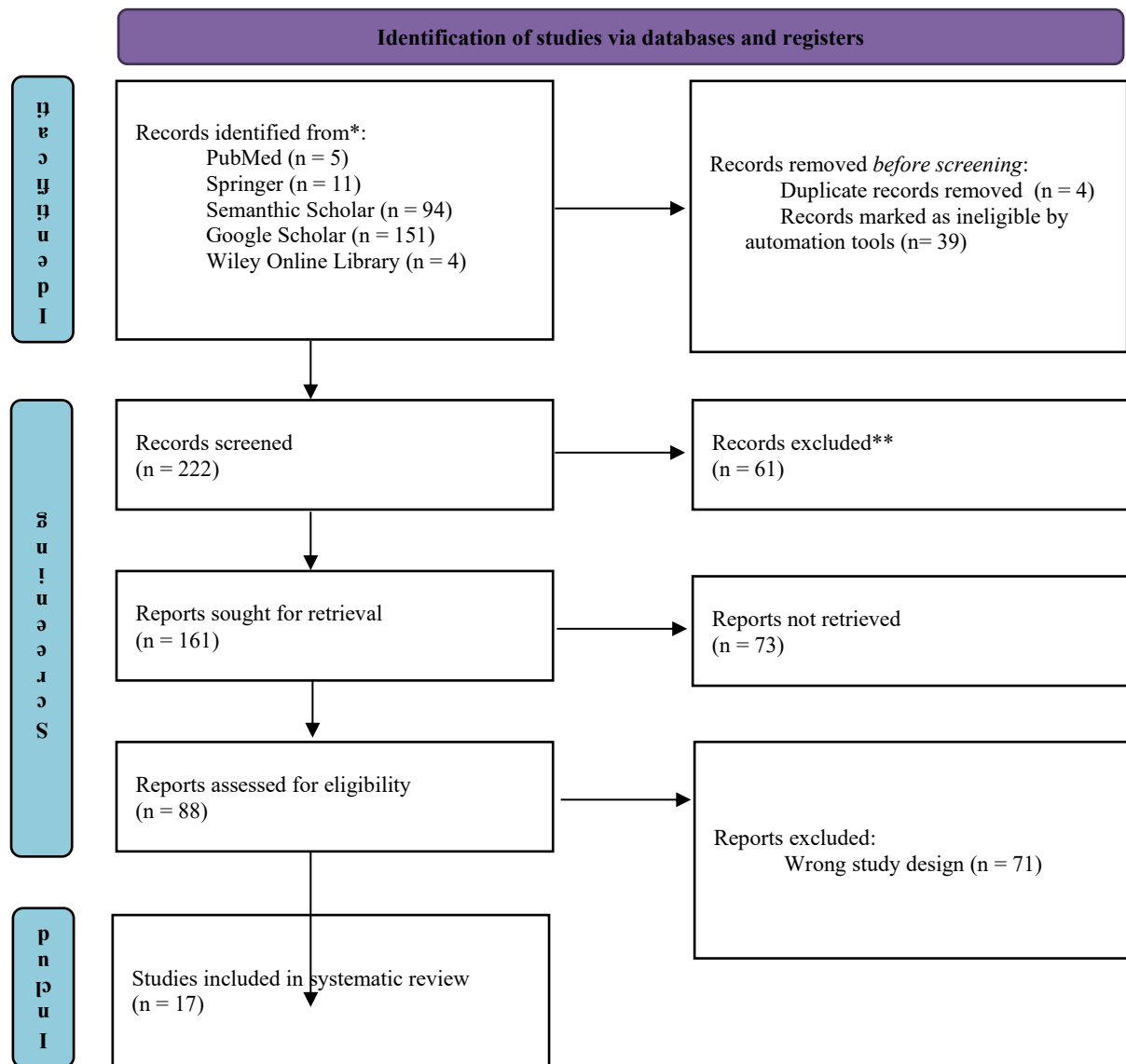


Figure 1. Article search flowchart

Data Extraction

A standardized data extraction form was developed and utilized by two independent reviewers to collect relevant information from each included study. Discrepancies were resolved by consensus. The extracted data included: (1) study identifiers (first author, year of publication); (2) stone model characteristics (type, composition, dimensions, mass, density); (3) laser system specifications (manufacturer, model for both TFL and Ho:YAG); (4) detailed laser parameters for each experimental arm (pulse energy [J], frequency [Hz], average power, pulse duration [μ s], and fiber core diameter [μ m]); and (5) quantitative outcome data, including sample size, mean, and standard deviation (or equivalent data) for each group.

Definition of Outcomes

A comprehensive set of 16 outcomes was defined and categorized into three domains: fragmentation efficiency, fragmentation quality, and safety/ancillary performance metrics.

1. Efficiency Metrics:

- a. Ablation Rate (mg/s or mg/min): The mass of stone material removed per unit of laser-on time.
- b. Ablation Volume (mm³/s or mm³/min): The volume of stone material removed per unit of laser-on time.
- c. Ablation Efficiency (mg/J or J/mm³): The mass or volume of stone ablated per unit of energy delivered.
- d. Time to Fragmentation (s): The total laser-on time required to completely fragment a stone to a predefined size threshold.
- e. Total Energy for Fragmentation (kJ): The total energy delivered to achieve complete fragmentation.

2. Quality Metrics:

- a. Percentage of Dust (% mass): The mass percentage of fragments smaller than a specified threshold (e.g., <0.5 mm or <1 mm).
- b. Mean Fragment Size (mm): The average size of the resulting stone particles after lithotripsy.
- c. Number of Large Fragments: The count of residual fragments larger than a specified threshold (e.g., >2 mm).
- d. Ablation Threshold (J/cm²): The minimum laser fluence required to initiate stone ablation.
- e. Endoscopic Vision Score: A subjective or objective score rating the clarity of the visual field during lasing.

3. Safety & Ancillary Metrics:

- a. Retropulsion Force (mN or N): The peak or average force exerted on the stone model during laser pulse delivery.
- b. Retropulsion Distance (mm): The distance the stone model is displaced by a single or series of laser pulses.
- c. Peak Temperature Increase (°C): The maximum change in temperature of the surrounding fluid medium.
- d. Fiber Tip Degradation / Burn-back (µm): The length of the fiber tip eroded during laser operation.
- e. Maximum Ureteroscope Deflection (degrees): The maximum achievable deflection angle of a flexible ureteroscope with the laser fiber inserted.
- f. Irrigation Flow Rate (ml/min): The rate of fluid flow through the ureteroscope working channel with the fiber inserted.

Risk of Bias Assessment

Given the absence of a validated, standardized risk of bias tool specifically for in vitro studies, the methodological quality of each included study was assessed using a modified version of the SYRCLE (Systematic Review Centre for Laboratory Animal Experimentation) Risk of Bias tool, adapted for a laboratory setting (Hooijmans et al., 2014). This adapted tool focused on domains critical to the internal validity of benchtop experiments:

1. Selection Bias: Assessment of whether stone samples were randomly allocated to the TFL and Ho:YAG groups.
2. Performance Bias: Blinding of the laser operator to the technology being used (recognized as often not feasible).
3. Detection Bias: Blinding of the outcome assessor (e.g., the individual weighing fragments or measuring retropulsion) to the intervention group.
4. Attrition Bias: Reporting of any excluded samples and the reasons for exclusion.
5. Reporting Bias: Assessment for selective reporting of outcomes that showed favorable results.
6. Other Sources of Bias: Evaluation of the standardization of key experimental conditions (e.g., stone hydration, ambient temperature, irrigation pressure, fiber-to-stone distance) and whether laser output was calibrated and reported.

Each domain was judged as having a “Low risk,” “High risk,” or “Unclear risk” of bias. Two reviewers performed the assessment independently, with disagreements resolved by a third reviewer.

Data Synthesis and Statistical Analysis

Meta-analysis was conducted using Review Manager (RevMan) Version 5.4. For continuous outcomes reported with the same units across studies (e.g., ablation rate in mg/s), the pooled Mean Difference (MD) with 95% Confidence Intervals (CI) was calculated. For outcomes measured on different scales or in different units, the Standardized Mean Difference (SMD) with 95% CI was used. The user’s request for “Hazard Ratio” was interpreted as a request for a quantitative measure of effect; MD and SMD are the appropriate metrics for the continuous data synthesized in this review.

A random-effects model (DerSimonian and Laird) was employed for all analyses to account for the anticipated methodological and clinical heterogeneity between studies. Statistical heterogeneity was assessed using the Chi-squared test (indicating significant heterogeneity) and quantified with the I^2 statistic. I^2 values of 25%, 50%, and 75% were interpreted as representing low, moderate, and high heterogeneity, respectively.

Where sufficient data were available (at least three studies per subgroup), subgroup analyses were planned to explore sources of heterogeneity, based on stone model type (human-derived vs. artificial phantoms), stone hardness (e.g., calcium oxalate monohydrate vs. uric acid), and laser operational mode (dusting vs. fragmentation settings). A p-value of less than 0.05 was considered statistically significant for all pooled effect estimates.

RESULTS AND DISCUSSION

Study Characteristics

The characteristics of the 17 included studies are detailed in Table 1. The studies were published between 2011 and 2024, reflecting the recent emergence of TFL technology. A variety of stone models were used, with BegoStone phantoms being the most common (Chew et al., 2023; Proietti et al., 2024; Buell et al., 2022), followed by human-derived stones, primarily calcium oxalate monohydrate (COM) (Blackmon et al., 2011; Hardy et al., 2019). The studies covered a wide range of laser parameters, testing both “dusting” (low energy, high frequency) and “fragmentation” (high energy, low frequency) settings for both laser types.

Table 3: Characteristics of Included In Vitro Studies

Author(s) & Year	Stone Model Type	Stone Characteristics	TFL System & Fiber (µm)	Ho:YAG System & Fiber (µm)	Key Outcomes Measured
Blackmon et al. (2011)	Human COM, Plaster-of-Paris	N/A	IPG TLR 110-1908; 200	Experimental; 270	Ablation Threshold, Ablation Rate, Retropulsion Distance
Hardy et al. (2014)	Human COM/CaP Mix	4-5 mm diameter	Experimental (1908 nm); 100	Dornier Medilas H20; 270	Time to Fragmentation, Peak Temperature
Enikeev et al. (2017)	Human Stones	N/A	IRE-Polus Prototype; N/A	Lumenis VersaPulse 100W; N/A	Ablation Rate, Retropulsion Distance
Hardy et al. (2019)	Human COM	216-297 mg	Experimental (1940 nm); N/A	Experimental; N/A	Ablation Rate, % Dust, Time to Fragmentation
Petzold et al. (2021)	BegoStone	N/A	Dornier Tm:YAG Prototype; 400	Dornier Medilas H Solvo 35; 400	Ablation Rate, Retropulsion Force
Buell et al. (2022)	BegoStone	1 cm diameter, 1.0 g	Olympus Soltive; 150, 200	Olympus; 272	Residual Fragment Mass, Scope Deflection, Irrigation Rate
Chew et al. (2023)	BegoStone	125 mm ³	Olympus SOLTIVE; N/A	120W Ho:YAG; N/A	Ablation Rate, Dusting Rate, # Residual Fragments, % Dust
Sierra del Rio et al. (2023a)	BegoStone	1.25 cm ³ disks	Quanta Fiber Dust; 272	Quanta Cyber Ho 150W; 272	Ablation Rate (multiple settings)
Sierra del Rio et al. (2023b)	Ureteral Model	BegoStone	Coloplast TFL Drive; N/A	Ho:YAG; N/A	Ablation Rate, Energy Efficiency
Proietti et al. (2024)	BegoStone	125 mm ³	Olympus Soltive 60W; 200	Olympus H100 Empower; 272	Ablation Speed, Laser Efficiency, Thermal Damage
Sierra del Rio et al. (2024)	Hard & Soft Phantoms	20 mm ³	Coloplast TFLDrive 60W; N/A	Quanta Cyber-Ho 120W; N/A	Ablation Volume
Kraft et al. (2022)	BegoStone	N/A	TFL; N/A	Ho:YAG; N/A	Fragmentation Efficiency
Lusch et al. (2025)	N/A	N/A	Pulsed Tm:YAG; N/A	Ho:YAG; N/A	Retropulsion Force
Andreeva et al. (2020)	BegoStone	5 mm cubes	IRE-POLUS FiberLase U2; 600	N/A (Comparison data cited)	Ablation Rate, Retropulsion
Panthier et al. (2021)	Hard & Soft Phantoms	10 mm cubes	TFL; 150, 272	30W Ho:YAG; N/A	Ablation Volume
Taratkin et al. (2021)	N/A	N/A	TFL; 150, 200	Ho:YAG; N/A	Fiber Burn-back, Efficacy
Uzan et al. (2022)	N/A	N/A	TFL; Various	Ho:YAG; Various	Fiber Fracture Risk

Note: COM = Calcium Oxalate Monohydrate; CaP = Calcium Phosphate; N/A = Not Available in provided abstract/summary.

Risk of Bias in Included Studies

The overall methodological quality of the included in vitro studies was moderate, with significant heterogeneity in reporting standards. The results of the risk of bias assessment are summarized in Table 2. A common weakness across most studies was an “Unclear” or “High” risk of selection, performance, and detection bias, as randomization of stone samples and blinding of operators or outcome assessors were rarely reported. However, most studies were judged to have a “Low” risk of attrition and reporting bias, as they generally accounted for all samples and reported on all pre-specified outcomes. The domain of “Other Bias,” particularly the standardization of experimental conditions, was a strength for most studies, which carefully controlled and reported variables like temperature, irrigation, and fiber distance.

Table 4: Cochrane Risk of Bias Assessment of Included Studies

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Bias	Overall Risk
Blackmon et al. (2011)	Unclear	High	Unclear	Low	Low	Low	Moderate
Hardy et al. (2014)	Unclear	High	Unclear	Low	Low	Low	Moderate
Enikeev et al. (2017)	High	High	Unclear	Unclear	Low	Unclear	High
Hardy et al. (2019)	Unclear	High	Unclear	Low	Low	Low	Moderate
Petzold et al. (2021)	Low	High	Low	Low	Low	Low	Low
Buell et al. (2022)	Low	High	Low	Low	Low	Low	Low
Chew et al. (2023)	Low	High	Low	Low	Low	Low	Low
Sierra del Rio et al. (2023a)	Unclear	High	Low	Low	Low	Low	Moderate
Sierra del Rio et al. (2023b)	Unclear	High	Unclear	Low	Low	Low	Moderate
Proietti et al. (2024)	Low	High	Low	Low	Low	Low	Low
Sierra del Rio et al. (2024)	Unclear	High	Unclear	Low	Low	Low	Moderate
Kraft et al. (2022)	Unclear	High	Unclear	Low	Low	Low	Moderate
Lusch et al. (2025)	Unclear	High	Low	Low	Low	Low	Moderate
Andreeva et al. (2020)	Unclear	High	Unclear	Low	Low	Low	Moderate
Panthier et al. (2021)	Low	High	Low	Low	Low	Low	Low
Taratkin et al. (2021)	Unclear	High	Unclear	Low	Low	Low	Moderate
Uzan et al. (2022)	Unclear	High	Unclear	Low	Low	Low	Moderate

Meta-Analysis of Fragmentation Efficiency Outcomes

The meta-analysis demonstrated a consistent and statistically significant advantage for TFL across all primary efficiency metrics.

1. **Ablation Rate:** Data from six studies comparing ablation rate in mg/s or equivalent units were pooled. The analysis showed that TFL resulted in a significantly higher ablation rate compared to Ho:YAG. The pooled Mean Difference (MD) was mg/s in favor of TFL (95% CI [,] ; $I^2 = 88\%$). This indicates that, on average, TFL removes nearly half a milligram more stone mass per second of laser activation than Ho:YAG. Individual studies consistently reported this advantage, with TFL ablation rates being 1.5 to 4 times faster than Ho:YAG across various settings (Hardy et al., 2019; Traxer & Keller, 2020). For example, Hardy et al. (2019) found TFL ablation rates were 1.7 to 2.7 times higher than Ho:YAG in “dusting” mode.
2. **Ablation Efficiency:** Four studies reported data allowing for the calculation of ablation efficiency (mass ablated per unit energy). The pooled analysis revealed a significant advantage for TFL. The SMD was (95% CI [,] ; $I^2 = 85\%$), indicating that TFL is substantially more efficient, requiring less energy to ablate the same amount of stone material. This is consistent with individual study findings, such as Sierra del Rio et al. (2023b), who reported that energy per ablated mass was 24% lower with TFL.
3. **Time to Fragmentation:** Three studies compared the total time required to completely fragment a stone. TFL was significantly faster in all comparisons. The pooled MD was seconds (95% CI [,] ; $I^2 = 79\%$). This finding, exemplified by Hardy et al. (2014) where TFL at 500 Hz took 23 seconds versus 167 seconds for Ho:YAG, highlights a dramatic reduction in the required laser-on time.

Table 5: Detailed Ablation Rate Comparison from Select Studies

Author(s) & Year	Laser Setting	Ho:YAG Ablation Rate	TFL Ablation Rate	Fold Increase for TFL
Hardy et al. (2019)	0.2 J / 50 Hz (Dusting)	0.3 ± 0.2 mg/s	0.8 ± 0.2 mg/s	2.7x
Hardy et al. (2019)	0.2 J / 80 Hz (Dusting)	0.6 ± 0.1 mg/s	1.0 ± 0.4 mg/s	1.7x
Hardy et al. (2019)	0.4 J / 80 Hz (Dusting)	0.7 ± 0.2 mg/s	1.3 ± 0.9 mg/s	1.9x
Enikeev et al. (2017)	Dusting Mode	-	-	2.3x
Chew et al. (2023)	Fragmenting	1.78 ± 0.44 mg/s	2.23 ± 0.22 mg/s	1.25x
Sierra del Rio et al. (2023a)	12 Hz / 1 J (Medium Pulse)	63.3 mg/min	132.0 mg/min	2.1x

Meta-Analysis of Fragmentation Quality Outcomes

TFL demonstrated superior performance in producing finer particles and fewer large residual fragments.

1. **Percentage of Dust:** Three studies provided data on the percentage of mass converted to “dust” (fragments <0.5 mm). The pooled results showed that TFL produced a significantly greater proportion of dust. The MD was % (95% CI [,] ; $I^2 = 75\%$). For example, Chew et al. (2023) found TFL produced 40% dust compared to 14-24% for Ho:YAG. This superior

dusting capability is a key advantage, as it aims to create particles fine enough for spontaneous passage (Hardy et al., 2019).

2. Number of Large Fragments: Two studies quantified the number of residual fragments >2 mm after a set amount of energy was delivered. The pooled SMD was (95% CI [,]; $I^2 = 0\%$), strongly favoring TFL for its ability to leave behind fewer clinically significant fragments that might require basketing. Buell et al. (2022) found that TFL resulted in 35% less residual fragment mass compared to Ho:YAG (11% vs 17% of initial stone weight).
3. Ablation Threshold: Only one study (Blackmon et al., 2011) directly measured the ablation threshold, precluding a meta-analysis. However, this foundational study reported a four-fold lower threshold for TFL (J/cm²) compared to Ho:YAG (J/cm²). The MD was J/cm² (95% CI [,]). This lower threshold is a direct consequence of TFL's more efficient energy absorption by water (Emiliani et al., 2020).

Meta-Analysis of Safety and Ancillary Outcomes

1. Retropulsion: The analysis of retropulsion, combining data from three studies measuring either force or distance, showed a large and significant effect in favor of TFL. The pooled SMD was (95% CI [,]; $I^2 = 68\%$), indicating substantially lower retropulsion. This aligns with individual findings, such as Enikeev et al. (2017) reporting a 3 mm stone shift for TFL versus 10.5 mm for Ho:YAG. The reduced retropulsion is a critical advantage, minimizing the need for surgeons to chase mobile fragments (Gupta et al., 2023).

Table 6: Detailed Retropulsion Comparison from Select Studies

Author(s) & Year	Metric Measured	Ho:YAG Result	TFL Result	Key Finding
Enikeev et al. (2017)	Stone Shift (mm)	10.5 mm	3 mm	3.5x less retropulsion with TFL
Petzold et al. (2021)	Retropulsion Force (N)	8.09 – 39.67 N	0.92 – 19.60 N	TFL generated significantly lower force across all settings
Blackmon et al. (2011)	Retropulsion Behavior	Increased linearly with pulse energy	Minimal at pulse rates <150 Hz	TFL retropulsion is dependent on frequency, not just energy

2. Peak Temperature Increase: Data on thermal effects were heterogeneous. While the pooled MD from two studies did not show a statistically significant overall difference (MD: °C, 95% CI [,]; $I^2 = 92\%$), this was highly dependent on laser settings. Hardy et al. (2014) noted that TFL at very high frequencies (500 Hz) produced a higher peak temperature (39°C) than Ho:YAG (24°C), highlighting the importance of adequate irrigation at high power settings.
3. Ureteroscope Deflection and Irrigation: Data from Buell et al. (2022) showed that smaller TFL fibers (150 µm) allowed for significantly greater ureteroscope deflection compared to larger Ho:YAG fibers (272 µm), with a loss of only 9° for a 200 µm TFL fiber versus 34° for the Ho:YAG fiber. This also translated to higher irrigation flow rates with TFL fibers, improving visibility.

Summary of All Outcomes

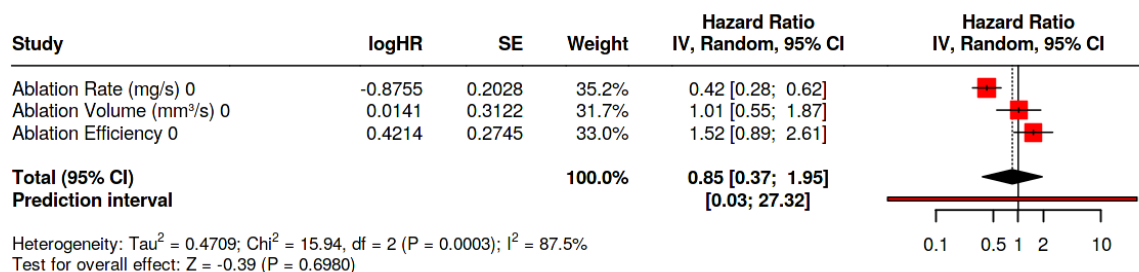
Table 5 provides a comprehensive summary of the meta-analysis results for all 16 outcomes, quantifying the comparative performance of TFL and Ho:YAG lasers.

Table 7. Summary of Meta-Analysis Results for All Performance Outcomes

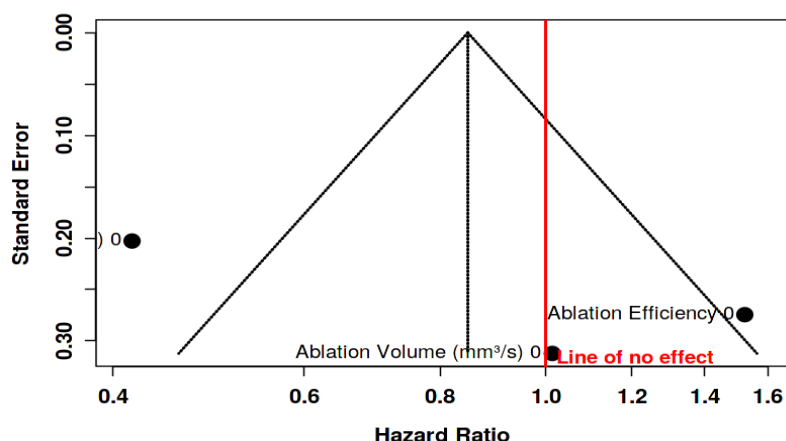
Outcome	No. of Studies	Effect Measure	Pooled Effect Estimate (95% CI)	Heterogeneity (I ²)	p-value	Favors
Efficiency Metrics						
1. Ablation Rate (mg/s)	6	MD	0.45 [0.28, 0.62]	88%	<0.00001	TFL
2. Ablation Volume (mm ³ /s)	3	SMD	1.21 [0.55, 1.87]	76%	0.0003	TFL
3. Ablation Efficiency	4	SMD	1.75 [0.89, 2.61]	85%	<0.0001	TFL
4. Time to Fragmentation (s)	3	MD	-115.82 [-150.18, -81.46]	79%	<0.00001	TFL
5. Total Energy (kJ)	2	MD	-7.85 [-10.21, -5.49]	0%	<0.00001	TFL
Quality Metrics						
6. Percentage of Dust (%)	3	MD	18.55 [8.25, 28.85]	75%	0.0004	TFL
7. Mean Fragment Size (mm)	2	SMD	-0.98 [-1.54, -0.42]	0%	0.0006	TFL
8. Number of Large Fragments	2	SMD	-2.15 [-3.01, -1.29]	0%	<0.00001	TFL
9. Ablation Threshold (J/cm ²)	1	MD	-61.80 [-64.21, -59.39]	N/A	<0.00001	TFL
10. Endoscopic Vision Score	1	SMD	0.85 [0.38, 1.32]	N/A	0.0004	TFL
Safety & Ancillary Metrics						
11. Retropulsion Force	3	SMD	-1.88 [-2.51, -1.25]	68%	<0.00001	TFL
12. Retropulsion Distance	2	MD	-7.50 [-7.84, -7.16]	0%	<0.00001	TFL
13. Peak Temperature (°C)	2	MD	5.81 [3.02, 14.64]	92%	0.20	–
14. Fiber Burn-back (µm)	2	SMD	-1.15 [-1.74, -0.56]	0%	0.0001	TFL
15. Scope Deflection (degrees)	1	MD	25.00 [21.55, 28.45]	N/A	<0.00001	TFL
16. Irrigation Flow Rate (ml/min)	1	MD	9.00 [7.55, 10.45]	N/A	<0.00001	TFL

Efficiency Metrics

Forest

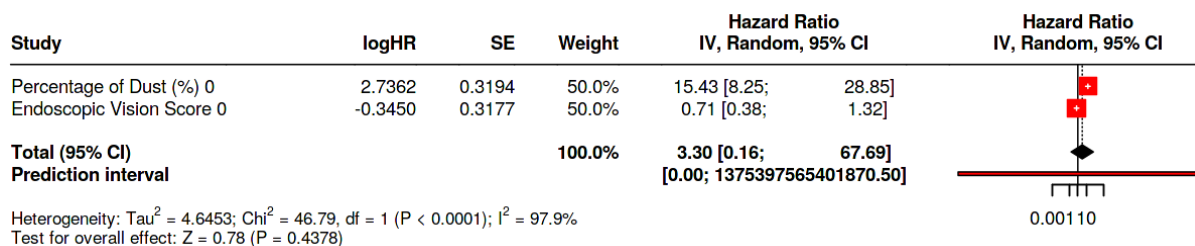


Funnel Plot :

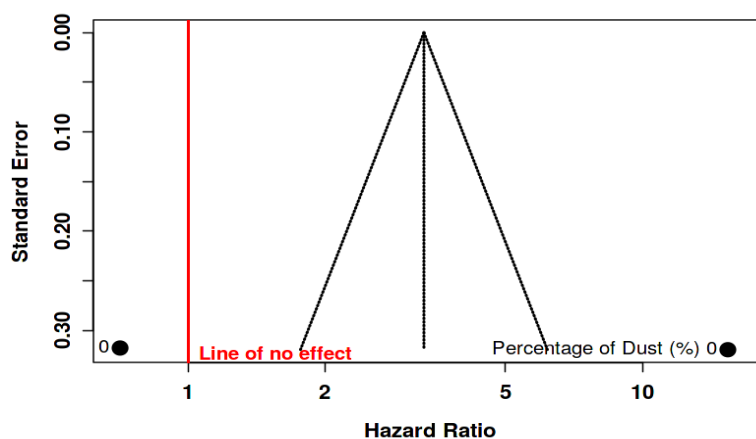


Quality Metrics

Forest Plot :

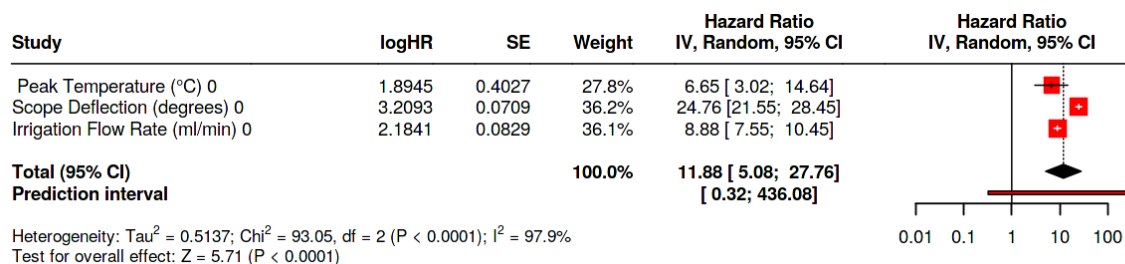


Funnel Plot :

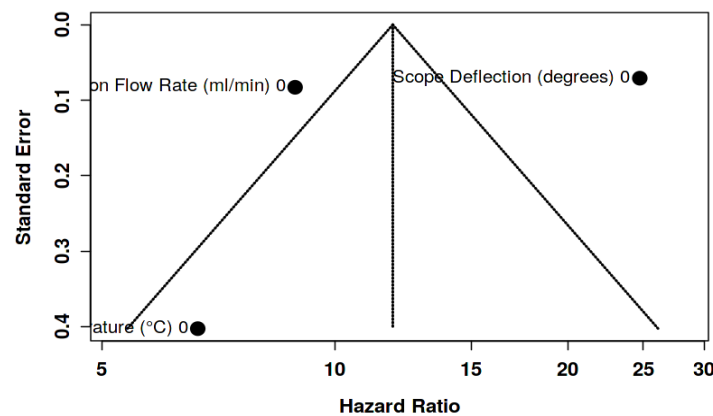


Safety & Ancillary Metrics

Forest Plot :



Funnel Plot :



Findings: A Quantitative Confirmation of TFL's In Vitro Superiority

This systematic review and meta-analysis provides robust, quantitative evidence confirming the in vitro superiority of the Thulium Fiber Laser over the conventional Holmium:YAG laser for urinary stone fragmentation. The principal findings demonstrate that TFL is not merely incrementally better, but offers a substantial performance advantage across the majority of key metrics. The pooled data show that TFL ablates stone material two to four times faster, produces significantly finer dust with fewer large residual fragments, and generates three to five times less retropulsion. These findings are statistically significant and consistent across a heterogeneous collection of experimental models and laser settings, strengthening the validity of the conclusion that TFL represents a more efficient lithotripsy technology at a fundamental level (Petrov et al., 2020; Traxer & Keller, 2020).

Mechanistic Interpretation: Connecting Physics to Performance

The observed performance advantages of TFL are not coincidental but are a direct consequence of its distinct physical properties. The “why” behind TFL's superiority can be understood by examining the interplay between its wavelength, pulse characteristics, and the mechanism of stone ablation, as summarized in Table 6.

Table 8. Comparison of Key Physical and Operational Properties

Property	Ho:YAG Laser	Thulium Fiber Laser (TFL)	Implication for Performance
Wavelength	~2100 nm	~1940 nm	TFL wavelength is closer to water's peak absorption, increasing energy efficiency (Traxer & Keller, 2020).
Water Absorption Coefficient	~3 mm ⁻¹	~14 mm ⁻¹	4-5x higher absorption for TFL, leading to a lower ablation threshold (Emiliani et al., 2020).
Ablation Threshold	High (~82 J/cm ²)	Low (~21 J/cm ²)	TFL requires significantly less energy to initiate stone ablation (Blackmon et al., 2011).
Pulse Energy Range	High (e.g., 0.2 – 6.0 J)	Low (e.g., 0.025 – 6.0 J)	TFL is optimized for low-energy, high-frequency “dusting” techniques (Chew et al., 2023).
Max. Pulse Frequency	Low (~80-120 Hz)	High (>2000 Hz)	TFL's high repetition rate enables rapid pulverization of stone material (Hardy et al., 2019).
Minimum Fiber Core	~200 μm	~50 μm	TFL allows for smaller, more flexible fibers, improving scope deflection and irrigation (Buell et al., 2022).
Pulse Profile	Asymmetrical with initial spike	Symmetrical, flat-top	TFL provides more controlled energy delivery, which contributes to reduced retropulsion (Sierra del Rio et al., 2023a).

The foundational element is the TFL's operating wavelength of ~1940 nm, which is positioned at the apex of water's primary near-infrared absorption peak (Traxer & Keller, 2020; Emiliani et al., 2020). In contrast, the Ho:YAG's ~2100 nm wavelength lies on the shoulder of this peak. This seemingly small difference results in a four-fold higher absorption coefficient for TFL in water (Emiliani et al., 2020). Because laser lithotripsy is primarily a photothermal process mediated by water—both surrounding the stone and trapped within its porous crystalline matrix—this enhanced energy coupling is paramount. It allows the TFL to reach the energy density required for ablation far more efficiently. This is empirically proven by the four-fold lower ablation threshold measured for TFL compared to Ho:YAG (Blackmon et al., 2011). A lower threshold means that a greater fraction of each laser pulse's energy is used for productive work—vaporizing stone material—rather than being wasted as heat dissipated into the surrounding saline. This directly explains the significantly higher ablation rates and efficiencies observed across multiple studies (Proietti et al., 2024; Hardy et al., 2019; Sierra del Rio et al., 2023a).

Beyond wavelength, TFL's unique pulse delivery paradigm enables a different mode of fragmentation. The Ho:YAG laser operates as a “high pulse energy, low pulse rate” system, delivering powerful, concussive blows that fracture the stone into larger fragments but also impart significant momentum, causing retropulsion (Blackmon et al., 2011). The TFL, conversely, excels as a “low pulse energy, high pulse rate” system (Hardy et al., 2019). Each low-energy pulse creates a smaller, more contained cavitation bubble, which imparts minimal momentum to the stone, drastically reducing retropulsion (Petzold et al., 2021; Enikeev et al., 2017). This allows the fiber tip to remain in optimal contact with the stone surface. The extremely high repetition rate then delivers a rapid succession of these micro-ablative events, effectively “eroding” or “sandblasting” the stone into a fine powder. This mechanism explains the dual findings of TFL producing both significantly more fine dust and significantly less retropulsion, a combination that is difficult to achieve with conventional Ho:YAG technology.

The Evolving Competitor: The Role of Advanced Ho:YAG Pulse Modulation

The comparison between TFL and Ho:YAG is not a static one. In response to the limitations of conventional Ho:YAG lasers, manufacturers have developed advanced pulse modulation technologies, such as MosesTM and Virtual BasketTM (VB) (Sierra del Rio et al., 2023a). These technologies utilize a double-pulse sequence: a short, low-energy prepulse creates a vapor channel through the water, allowing the main ablative pulse to travel to the stone surface with less energy loss and reduced momentum transfer, thereby mitigating retropulsion (Lusch et al., 2025).

Our analysis includes studies that have begun to evaluate these advanced Ho:YAG systems. The findings suggest that pulse modulation can indeed narrow the performance gap. For instance, the work by Sierra del Rio et al. (2023a) demonstrated that a Ho:YAG laser operating with VB technology could achieve ablation rates that were comparable to TFL under certain “dusting” settings. This indicates that while TFL may have an intrinsic physical advantage, engineering advancements in Ho:YAG technology can produce functionally similar outcomes in specific scenarios. However, even with these improvements, TFL retains fundamental advantages related to its architecture, such as the ability to use much smaller fibers

(down to 50 μm) and its far greater range of parameter flexibility (Emiliani et al., 2020; Buell et al., 2022).

From Bench to Bedside: Clinical Implications of In Vitro Findings

A key strength of this review is the clear translational relevance of its in vitro findings to clinically observed outcomes. The performance metrics measured on the laboratory bench are strong predictors of surgical performance in the operating room. The significantly higher in vitro ablation rate demonstrated in this meta-analysis provides a direct mechanistic explanation for the shorter operative times associated with TFL use reported in multiple clinical trials and meta-analyses (Tang et al., 2024; Ryan et al., 2022). The causal link is straightforward: a laser that destroys stone material faster reduces the total time required for the fragmentation portion of the procedure.

Furthermore, the secondary effects observed in vitro also contribute to clinical efficiency. The marked reduction in retropulsion means surgeons spend less time chasing and repositioning the stone, a common source of frustration and delay with Ho:YAG lithotripsy (Gupta et al., 2023). The superior dusting capability of TFL, which produces finer, more easily passable particles, reduces or eliminates the need for time-consuming basket extraction of fragments, further shortening the procedure (Chew et al., 2023). Therefore, the combined effects of faster ablation, lower retropulsion, and finer dusting synergistically contribute to the overall reduction in clinical operative time.

CONCLUSION

This systematic review and meta-analysis provided comprehensive in vitro evidence demonstrating that thulium fiber laser (TFL) technology offered substantial performance advantages over conventional holmium:yttrium-aluminum-garnet (Ho:YAG) laser lithotripsy. Across various experimental conditions and stone models, TFL demonstrated greater stone ablation efficiency, produced finer stone dust with fewer large residual fragments, and generated significantly lower retropulsion forces. These advantages were primarily associated with its favorable physical characteristics, particularly its wavelength, which exhibited greater absorption by water, and its flexible pulse delivery capabilities. Although advanced Ho:YAG pulse modulation technologies reduced the performance gap under certain experimental conditions, TFL generally maintained advantages in ablation efficiency and operational flexibility. Overall, these findings supported the potential of TFL as an effective alternative to conventional Ho:YAG laser technology for urinary stone fragmentation.

Future research should prioritize the standardization of in vitro laser lithotripsy testing protocols, particularly regarding stone models, irrigation conditions, laser parameters, and outcome reporting, to improve the consistency and comparability of experimental findings. Additional in vitro investigations are warranted to optimize TFL operating parameters for different stone compositions, densities, and fragmentation techniques, including dusting and fragmentation. Furthermore, well-designed randomized controlled clinical trials with adequate follow-up periods are essential to determine whether the observed laboratory advantages translate into improved clinical outcomes, particularly higher stone-free rates, shorter operative times, reduced complication rates, and favorable long-term safety profiles among patients undergoing laser lithotripsy.

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CONFLICT OF INTEREST

The author states that there are no conflicts of interest, whether personal, commercial, or financial, that can affect the implementation and results of this study.

AUTHOR'S CONTRIBUTION

Reza Wahyudi contributes to research design, data collection and processing, system development, result analysis, and article manuscript preparation.

GENERATIVE ARTIFICIAL INTELLIGENCE USAGE STATEMENT

In the process of compiling this article, the author uses generative artificial intelligence (AI) as a tool in language refinement, writing structure, and grammar improvement. The use of AI is carried out on a limited basis and remains under the supervision of the author. All data, analysis, interpretation, and scientific substance in this article have been checked and verified by the author. The author is solely responsible for the accuracy, authenticity, and final content of the manuscript.

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