

Advances in laser technology and fibre-optic delivery systems in lithotripsy

Nathaniel M. Fried^{1,2*} and Pierce B. Irby²

Abstract | The flashlamp-pumped, solid-state holmium:yttrium–aluminium–garnet (YAG) laser has been the laser of choice for use in ureteroscopic lithotripsy for the past 20 years. However, although the holmium laser works well on all stone compositions and is cost-effective, this technology still has several fundamental limitations. Newer laser technologies, including the frequency-doubled, double-pulse YAG (FREDDY), erbium:YAG, femtosecond, and thulium fibre lasers, have all been explored as potential alternatives to the holmium:YAG laser for lithotripsy. Each of these laser technologies is associated with technical advantages and disadvantages, and the search continues for the next generation of laser lithotripsy systems that can provide rapid, safe, and efficient stone ablation. New fibre-optic approaches for safer and more efficient delivery of the laser energy inside the urinary tract include the use of smaller-core fibres and fibres that are tapered, spherical, detachable or hollow steel, or have muzzle brake distal fibre-optic tips. These specialty fibres might provide advantages, including improved flexibility for maximal ureteroscope deflection, reduced cross section for increased saline irrigation rates through the working channel of the ureteroscope, reduced stone retropulsion for improved stone ablation efficiency, and reduced fibre degradation and burnback for longer fibre life.

The introduction of percutaneous renal surgery using ultrasonic lithotripsy in the late 1970s and early 1980s was the first minimally invasive technology for kidney stone surgery^{1–3}. This technique remains the preferred method for management of large (>1.5 cm) renal and upper ureteral stones owing to the associated high stone-free rates and reduced need for auxiliary procedures. However, potential complications of ultrasonic lithotripsy include haemorrhage, injury to the kidney or adjacent structures, urine leakage, infection, and risks associated with a general anaesthetic⁴.

In the mid 1980s, the introduction of shock wave lithotripsy (SWL) by a team in Germany represented a novel, noninvasive outpatient technology to treat stones^{5,6}. Although SWL was initially offered for treatment of stones of all sizes, its use in the USA is now usually limited to opaque, upper ureteral and renal stones <20 mm in diameter⁷. SWL is contraindicated in some patients based on stone composition, location, patient size, and comorbidities. Additionally, potential complications of SWL include renal haematoma, incomplete fragmentation, and ureteral obstruction from stone fragments⁸. Stone-free rates with SWL do not generally exceed 80–85%⁹. Overall, SWL is a low-risk, well-tolerated procedure that requires a low level

of technical expertise and is associated with favourable reimbursement in the USA. Lithotripter technology is expensive, meaning that very few hospitals own the treatment devices and/or have them in a fixed facility. Thus, for economic reasons to maximize utilization, in the USA, these machines are largely owned and operated by independent enterprises that bring the device to given health facility locations on a fixed schedule. Therefore, SWL access is an elective procedure for patients whose acute treatment needs have been temporized or for whom the stone condition is stable. Required scheduling is commonly on the order of a week or more depending on the availability of the mobile unit.

The last notable advance in minimally invasive stone management occurred with the development of miniature rigid and flexible fibre-optic ureteroscopes in the 1990s¹⁰. With further incorporation of digital optics and the advent of early laser lithotripsy techniques, these instruments can now be inserted into the upper urinary tract to engage stones in the vast majority of locations. The inherent miniaturization and flexibility of current-generation 200–270 µm laser fibres means that they can be used within the narrowest internal channels of the smallest modern rigid and flexible ureteroscopes, and can, therefore, access all locations of the upper urinary tract.

¹Department of Physics and Optical Science, University of North Carolina at Charlotte, Charlotte, NC, USA.

²McKay Department of Urology, Carolinas Medical Center, Charlotte, NC, USA.

*e-mail: nmfried@uncc.edu

<https://doi.org/10.1038/s41585-018-0035-8>

Key points

- The holmium:yttrium–aluminium–garnet (YAG) laser is currently the gold standard for laser lithotripsy during flexible ureteroscopy because it can be used to effectively treat all stone compositions.
- The frequency-doubled, double-pulse YAG (FREDDY) laser has been tested as a more compact and efficient solid-state laser than the initial dye lasers for short-pulse lithotripsy, but the FREDDY laser is not effective for all stone compositions.
- The erbium:YAG laser has been tested for efficient ablation of urinary stones, but a suitable mid-infrared optical fibre delivery system is not available for this procedure.
- The thulium fibre laser (TFL) is the most promising alternative to holmium for lithotripsy owing to its use of a more suitable TFL wavelength, smaller fibres, and potential for using a smaller, less expensive laser system; however, clinical studies are needed to assess this new technology.
- TFL promotes the development of novel miniature fibre-optic delivery systems, including tapered, ball tip, hollow steel tip fibres, and muzzle brake fibre-optic tips, which can reduce both fibre burnback or degradation and stone repulsion without sacrificing laser ablation rates.

By the late 1990s, the holmium:yttrium–aluminium–garnet (YAG) laser had emerged as the dominant tool for laser lithotripsy. This modality is able to destroy all stone compositions, with stone-free rates approaching 95% in experienced hands, depending on stone size, location, and patient anatomy¹¹.

Other modalities of ureteroscopic intracorporeal lithotripsy have been developed, such as electrohydraulic (EHL) and pneumatic fragmentation^{12,13}, but these procedures have limited utility. Compared with modern laser lithotripsy, EHL technology developed during the 1980s has largely been discontinued owing to poor fragmentation efficacy, increased risk of injury to adjacent tissue, and the high costs of probe replacement¹⁴. Pneumatic probes can only be used in conjunction with rigid endoscopes and are, therefore, limited to treatment of stones located in the lower ureter. The flexibility of laser fibres means that they can be used in both flexible and rigid instruments and can, therefore, access stones at any location in the upper urinary tract.

The availability of relatively inexpensive ureteroscopic laser lithotripsy instruments has broadened such that most community hospitals now own the necessary equipment or can rent such technology at short notice. This time frame is in contrast to the 1-week notice period typically necessary to schedule use of SWL in a patient who has potentially competing indications for each modality. Surgical technique and experience required for ureteroscopy with or without laser lithotripsy exceed that of SWL. Younger, recently trained urologists in the USA, who have typically experienced a large volume of procedures during their residency, perform ureteroscopy more readily than their more senior counterparts, who might prefer to use SWL as a first-line treatment option. As such, over the past 15 years, the relative precedence has gradually changed in favour of ureteroscopy over SWL¹⁵.

The evolution of laser lithotripsy

Since the 1960s, researchers and clinicians have tested several lasers for lithotripsy, including ruby, neodymium:YAG, and carbon dioxide lasers. All of these were operated in continuous-wave mode but had little success,

partly owing to excessive collateral thermal damage to soft tissues and limitations in fibre-optic delivery systems¹⁶. In the 1980s, the first successful pulsed laser lithotripsy system, the short-pulse dye laser, with a wavelength of 504 nm and pulse duration of ~1 µs, was commercialized by Candela Laser Corporation following development at the Wellman Center for Photomedicine at Massachusetts General Hospital¹⁷.

However, within just 10 years of the introduction of the short-pulse dye laser, the long-pulse, infrared holmium:YAG laser with a wavelength of 2100 nm had become the gold-standard modality for laser lithotripsy^{18–20}. The small size and flexibility of laser fibres have resulted in the exclusive use of this instrument for urinary stone fragmentation in conjunction with modern ureteroscopes^{21,22}. Laser lithotripsy is usually carried out within the ureteral lumen, where the majority of stones become lodged and obstructive as they move down from the kidney. As ureteroscopes have become smaller, advances in fibre-optic and digital technology have enabled the development of miniaturized laser fibres, which have become an essential tool for successful minimally invasive stone surgery, effectively reducing the stone to tiny spontaneously passable particles (<2 mm fragments) known as — literally — ‘dust’. As urologists become more experienced in the use of ureteroscopic laser lithotripsy, the same miniaturized tools are being used for more technically ambitious procedures, such as retrograde intrarenal surgery (RIRS), which can be used to manage moderate-to-large stones within the internal space in lieu of extracorporeal shock wave lithotripsy (ESWL) or invasive percutaneous surgery. Thus, ureteroscopic laser lithotripsy is now the primary surgical management option for the majority of patients presenting with urinary stones at advanced medical centres in the USA that have embraced the most effective, rather than the most convenient, treatment modalities. The number of such cases performed in the USA has been rising, currently approaching 300,000 cases annually, owing to the increasing incidence of stone disease in general and to the increasing experience in using the technique¹⁵.

In this Review, we discuss advances in laser technology as the potential next generation of lasers for use in lithotripsy and compare this new technology with the current generation of laser lithotripsy technologies. We also consider how new laser technologies might enable the use of novel optical fibre delivery systems for more efficient and safer delivery of the laser energy from the laser to the stone inside the urinary tract.

Laser lithotripsy sources**Holmium:YAG laser**

The holmium:YAG laser is the clinical gold standard for laser lithotripsy because it is able to fragment stones of a wide variety of compositions and is cost-effective in comparison with other lasers and technologies. From both a scientific and technical perspective, the holmium laser also has several desirable characteristics for use in general urology. First, the holmium infrared laser wavelength of 2,100 nm is strongly absorbed by water. A substantial amount of water can be present in the pores, fissures, and lamellations of the stone surface owing to

the urine environment and saline irrigation during laser lithotripsy²³. This water absorbs infrared laser energy, causing microexplosions during thermal expansion and vaporization of the water. This mechanical phenomenon of microexplosions is a component of the ablation mechanism, in addition to direct infrared laser absorption and thermal decomposition of the stone material^{23,24}. The optical absorption of near-infrared laser radiation for dry stones is noted to be relatively independent of stone type²⁵. Strong water absorption at the holmium wavelength translates into an intermediate optical penetration depth of about 400 μm (REF.²⁶). This property enables the laser to also be used for multiple soft tissue incision and coagulation applications²⁷. The holmium laser is a compromise between the ultraprecise erbium:YAG laser, which uses a wavelength of 2,940 nm for tissue ablation and incision, and the deep volumetric heating provided by the neodymium:YAG laser, which uses a wavelength of 1,064 nm for thermal coagulation and haemostasis²⁸. The holmium laser can be used for a variety of applications, which is desirable to urologists who seek a single laser system for treating various indications, such as urinary stones and BPH.

Second, the holmium laser wavelength can be delivered through conventional, low-hydroxyl (OH^-) silica optical fibres²⁹ (FIG. 1). Silica fibres are robust with desirable thermal, mechanical, and chemical properties, which enables transmission of high laser power for stone ablation, short bend radii for use inside the working channel of flexible ureteroscopes, sterilization for medical use, and resistance to corrosion in the fluid environment of the urinary tract. Silica is also a biocompatible material, making it safe for biomedical use²⁹. Furthermore, silica fibres are mass produced for use in telecommunications and industrial applications, making them

affordable as a disposable, single-use, medical fibre-optic delivery system²⁹.

Third, the flashlamp pumping scheme for the holmium:YAG laser is inexpensive in comparison to other diode-pumped laser systems, which makes the laser cost-effective for surgery. Although the initial capital cost of a low-power holmium laser is relatively low by medical device standards, the need for a high-voltage power supply, internal water cooling system, replacement flashlamps, and use of bulk optics makes the laser apparatus fairly complex and potentially costly to maintain over its lifetime³⁰.

Holmium laser technology has been available for over two decades, but modest improvements in the technology have taken two different directions. In one direction, smaller, lower power (20 W), more compact tabletop holmium laser modules dedicated specifically to laser lithotripsy have been developed to save space in the operating room and for direct integration with other ureteroscope components, such as monitors, illumination, and imaging systems, into a single console. In the other direction, larger, more powerful, and more expensive holmium lasers with progressively higher laser output powers (from 30 W originally and now up to 120 W) have been incrementally developed, primarily for use in laser enucleation of the prostate during treatment of BPH. The ability of these high-power holmium lasers to operate at increased pulse rates in contrast to the more conventional, low-power holmium laser lithotriptors has also enabled treatment of kidney stones in a 'dusting' mode with low pulse energy (0.2 J) and high pulse rate (50–80 Hz) as an alternative to conventional 'fragmentation' mode with high pulse energy (0.6–1.0 J) and low pulse rate (5–10 Hz)³¹.

The introduction of very-high-power (100 and 120 W) holmium lasers for lithotripsy has raised concerns about the potential for unintended collateral thermal damage to soft tissues within the urinary tract caused by overheating of the saline from direct absorption of the infrared laser energy^{32–35}. Several studies have addressed this concern and reported that high temperatures capable of thermally coagulating and irreversibly damaging soft urinary tissues typically occur only in extreme circumstances, such as the use of high laser power in the urinary tract with minimal or no saline irrigation or when the ureter is obstructed and impedes sufficient saline irrigation^{32–35}. Nevertheless, when normal saline irrigation rates are applied, the constant flow seems to be sufficient to prevent overheating of fluids in the urinary tract^{32–35}.

Further advances in holmium laser lithotripsy have involved the manipulation of the laser temporal pulse profile to reduce stone retropulsion via two different approaches. First, the laser pulse has been modified from its standard 350 μs pulse length up to 700 μs by delivering two pulses together or by stretching the laser pulse even further, up to ~1,500 μs (REFS^{36–40}). Second, delivery of a short, low-energy pulse to create a vapour bubble before delivery of a longer, higher energy pulse has been used to both reduce stone retropulsion and increase ablation rates^{41,42}. This mode is referred to as 'Moses Tech' because the laser-induced vapour bubble

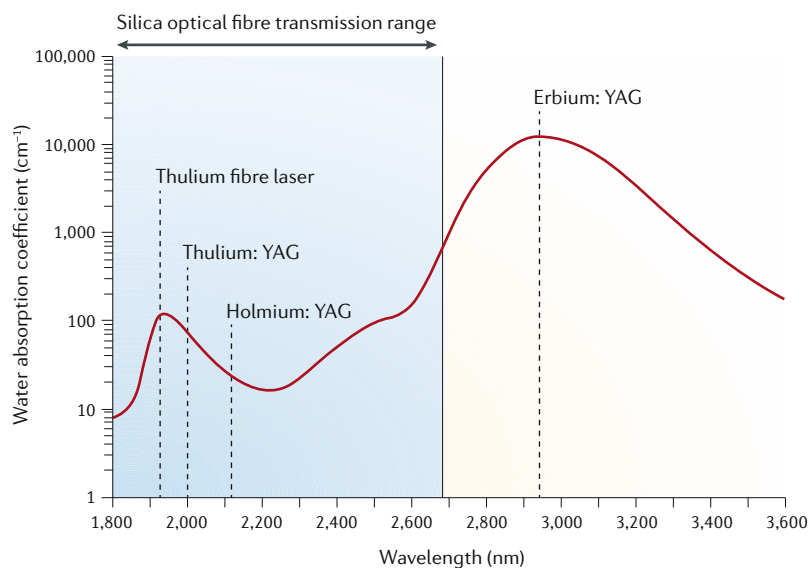


Fig. 1 | Water absorption coefficient as a function of laser wavelength in the mid-infrared spectrum. The common mid-infrared laser wavelengths include thulium fibre laser at 1,908 and 1,940 nm, thulium:yttrium–aluminium–garnet (YAG) at 2,010 nm, holmium:YAG at 2,100 nm, and erbium:YAG at 2,940 nm. Laser energy delivery through conventional low-hydroxyl (OH^-) silica optical fibres is limited to wavelengths <~2,700 nm owing to increasing OH^- absorption in the mid-infrared spectrum.

created during the initial pulse effectively ‘parts the water’ (commonly referred to as the Moses Effect in the field of laser–tissue interactions), enabling the subsequent pulse to be more efficiently delivered to the stone for enhanced ablation⁴³. This concept, proposed over two decades ago⁴¹, has been provided as an option on commercial high-power holmium clinical laser systems since 2017 (REF.⁴²).

Alternatives to the holmium laser

Despite widespread adoption of holmium laser technology for lithotripsy, several fundamental limitations of this technology remain. Potential alternatives are associated with various advantages and disadvantages compared with current holmium laser technology and have varying levels of potential for use as a next-generation laser lithotripter.

FREDDY laser

The frequency-doubled, double-pulse YAG (FREDDY) laser represents a more compact, user-friendly, less expensive, solid-state laser alternative to the short-pulse dye lasers originally introduced for lithotripsy^{44–49}. The FREDDY laser operates with a short pulse of about 1 μ s and emits laser energy at both 532 and 1,064 nm wavelengths, and the laser has been tested in both preclinical and clinical studies for lithotripsy^{44–49}. Similar to the dye laser, the short pulse of the FREDDY laser provides a photomechanical mechanism of stone ablation, first by generating a plasma and then depositing subsequent laser energy into the plasma to create a shock wave for fragmenting the kidney stone^{44–49}.

This photomechanical approach provides a better safety profile for avoiding accidental soft tissue damage to the ureter or kidney wall than the holmium laser because soft tissues are elastic and can readily absorb the shock-wave with minimal damage^{44–49}. This effect is in contrast to the holmium laser, which operates with a long pulse duration (350–1,500 μ s) and primarily via a photothermal laser–tissue interaction mechanism. Although complications are rare, the holmium laser poses more substantial safety concerns than the FREDDY laser owing to the potential for unintended soft tissue heating and thermal coagulation, as well as damage to soft tissues and ureteroscopic devices (such as stone baskets) through misdirection of the laser output^{14,50–56}. However, the FREDDY laser is limited by its inability to efficiently fragment some of the harder stone compositions, including cysteine and calcium oxalate monohydrate stones^{48,49}. The FREDDY laser is also limited for use only on stones, unlike the holmium laser, which can provide a multiple-use laser platform for both soft tissue ablation and coagulation applications, for example, treatment of BPH^{48,49}.

Erbium:YAG laser

The flashlamp-pumped, solid-state erbium:YAG laser has also been tested in the laboratory as an alternative to the holmium laser for lithotripsy^{57–60}. The erbium laser wavelength of 2,940 nm matches a larger water absorption peak in tissue than the holmium laser wavelength of 2,120 nm, resulting in much stronger absorption of the laser energy²⁶ (FIG. 1). The increased stone absorption and

higher water absorption at this wavelength translate, in part, into improved laser ablation of kidney stones^{57,60}. However, the major limitation of the erbium laser is the lack of a suitable fibre-optic delivery system; the standard, low-OH⁻ silica optical fibres currently used for holmium laser lithotripsy cannot be used at the longer, erbium laser wavelength because silica is not transparent beyond \sim 2,700 nm owing to strong absorption by the OH⁻ component in silica (FIG. 1).

Several specialist optical fibres, including hollow silica waveguides and sapphire, germanium oxide, fluoride, and chalcogenide fibres, are commercially available for transmission of mid-infrared erbium:YAG and/or carbon dioxide laser wavelengths. Some of these fibres have been tested for lithotripsy^{61–64} but are all inferior to silica fibres owing to their higher cost, poor biocompatibility, worse mechanical and chemical properties, and/or lower flexibility⁵⁸. Thus, overall, the main limitation preventing use of the erbium laser in flexible ureteroscopic laser lithotripsy is the lack of a suitable optical fibre delivery system that is robust, inexpensive, flexible, and biocompatible⁵⁸.

Ultrashort-pulse femtosecond lasers

Use of ultrashort-pulse femtosecond lasers for plasma-mediated laser lithotripsy has been reported, with potential benefits including minimal stone retropulsion and creation of very small, dust-sized stone particles⁶⁵. In general, plasma-mediated ablation is appealing because the process is independent of laser wavelength and tissue optical properties and enables ultraprecise tissue ablation⁶⁶. However, femtosecond laser technology is limited by several major issues that prevent its use in laser lithotripsy. First, the high peak power that is generated from a femtosecond pulse results in catastrophic damage to the optical fibre, preventing the use of a fibre delivery system to transmit the laser energy to the stone. Second, although femtosecond lasers can operate at high pulse rates (kHz to MHz), tissue ablation rates are low, at <0.1 μ m depth per laser pulse⁶⁶, making these lasers inefficient for rapid removal of bulk tissues. For laser lithotripsy, in which ultrahigh precision is unnecessary, plasma-mediated ablation rates are too low and treatment times too long for femtosecond lasers to be useful clinically. Finally, the technology is considerably more expensive than conventional flashlamp-pumped, solid-state lasers, such as holmium:YAG and erbium:YAG, costing in the order of US\$100,000s, versus \$10,000s+ for holmium and erbium lasers.

Thulium fibre lasers

Background. Continuous-wave, diode-pumped, solid-state thulium:YAG lasers have been introduced as a potential alternative to the holmium:YAG laser for soft tissue applications in urology, including treatment of BPH⁶⁷. However, it should be emphasized that the thulium:YAG laser should not be confused with the thulium fibre laser, as the former is a solid-state laser, whereas the latter is a fibre laser.

Fibre lasers are one of the latest laser technologies to be developed. In these lasers, a chemically doped silica optical fibre is used as the gain medium instead of a bulk solid-state crystal (as used in holmium:YAG,

thulium:YAG, and erbium:YAG lasers). The light originates within the core of a small optical fibre and is pumped by another laser source, such as a diode laser, and then the light emitted from the fibre laser can be coupled into a separate, conventional, disposable, low-OH⁻ silica surgical fibre. The primary advantage of fibre lasers in general is their ability to deliver high power output from a small fibre core, resulting in high intensity or brightness⁶⁸. The most common fibre lasers are made of silica fibres doped with ytterbium, erbium, and thulium, which emit at wavelengths of 1,075 nm, 1,550 nm, and 1,940 nm, respectively⁶⁸. The mid-infrared fibre laser wavelengths are especially useful for laser ablation applications in surgery such as lithotripsy, as these wavelengths target water absorption peaks in tissue, thus providing a rapid increase in temperature within a small tissue depth, sufficient for efficient and precise tissue ablation.

Initial experimental studies of mid-infrared fibre lasers in surgery were limited to very-low-power lasers (just a few watts) emitting either in continuous-wave or short-pulse (nanosecond) modes at wavelengths near 1,940 nm and 2,940 nm water absorption peaks for tissue ablation and coagulation^{68–72}. The limited power output and continuous-wave operation mode were suboptimal for most surgical applications because high intensities and pulsed operation are necessary for thermal confinement of the energy and efficient tissue ablation. Additionally, the use of a 2,940 nm wavelength was limited by the inability to use standard, low-OH⁻ silica fibres, as is also the case in erbium:YAG lasers.

However, considerable progress has been made in the development of high-power thulium fibre lasers (TFL), which operate near a major water absorption peak in tissue at 1,940 nm (FIG. 1). This wavelength can be delivered through standard silica fibres, similar to those currently used with holmium:YAG ($\lambda = 2,120$ nm) and thulium:YAG ($\lambda = 2,010$ nm) lasers in urology. The first experimental use of high-power TFLs in urology reported ablation of soft tissues and urinary stones at 40 W and 110 W (REFS^{73–75}). Since then, TFL studies have been reported for liver, brain, skin, dental, endobronchial, and lithotripsy applications^{76–83}. TFL is one of the most promising new laser technologies for lithotripsy and could offer several potential advantages compared with the current gold standard holmium laser.

Laser wavelength. The TFL operates with primary emission wavelengths of 1,908 nm and 1,940 nm, which more closely match a water absorption peak than that of the holmium laser at 2100 nm (REFS^{26,84,85}) (FIG. 1). Absorption of infrared energy by water is believed to have a major role in stone ablation, in addition to direct absorption of laser energy by the stone material, as near-infrared absorption spectra by dry stones are similar for different stone compositions^{23–25}. The water absorption coefficient is $\mu_a = 120$ cm⁻¹ for TFL, $\mu_a = 60$ cm⁻¹ for thulium:YAG, and $\mu_a = 25$ cm⁻¹ for holmium:YAG lasers²⁶ (FIG. 1). These values result in absorption of TFL energy that is twice that of thulium:YAG and fourfold to fivefold higher than holmium:YAG lasers. This higher water absorption

directly translates into lower tissue ablation thresholds⁸⁶. TFL ablation thresholds for the most common stone compositions encountered in the clinic, calcium oxalate monohydrate and uric acid, have each been reported to be fourfold lower for TFL than holmium:YAG^{87,88}. Thus, a lower TFL pulse energy can be used for equivalent stone ablation, or equivalent pulse energy can be used for more efficient stone ablation. This improved efficiency is notable because the holmium laser energy and/or power cannot be increased to compensate for its reduced efficiency without also translating into increased stone retropulsion, which can result in the urologist wasting time pursuing the stone through the urinary tract and associated complications.

Preliminary studies have shown that use of lower TFL pulse energies than the holmium laser results in smaller laser-induced vapour bubble dimensions (1 mm versus 5 mm)⁸⁹, which translates into an improved safety profile, as the effective working distance between fibre tip and tissue directly correlates with this bubble diameter⁹⁰. For example, TFL-induced damage to the nitinol stone baskets that are frequently used during ureteroscopic laser lithotripsy procedures has been reported at working distances up to 1.0 mm from the fibre tip⁹⁰, whereas holmium laser-induced damage has been observed at working distances up to 5 mm (REFS^{52–55}), meaning that the TFL has a better safety profile.

Spatial beam profile. The primary advantage of fibre lasers is the ability to achieve high intensity or high brightness because the light originates within the small (18–25 μ m) core of the thulium-doped silica optical fibre, which is about 100 times smaller in diameter than a solid-state, holmium:YAG laser crystal. This TFL property provides a near single-mode, Gaussian spatial beam profile that is more uniform and symmetrical than the multimodal beam typically produced by the holmium:YAG laser⁹¹.

The multimode beam profile of the holmium laser prohibits coupling of high laser power into small-core fibres (<200 μ m) without risking overfilling of the input fibre core and launching of energy into the fibre cladding, which can directly damage the proximal fibre end⁹¹. Holmium laser beams are typically limited to large diameters (275–500 μ m)⁹¹, which are suboptimal for the increased flexibility and irrigation flow needed for complex ureteroscopy procedures. Several approaches have been explored for reducing proximal fibre failure during coupling of holmium laser energy into small-core fibres^{91,92}. These approaches have included ferrule designs that absorb or direct excess energy away from the fibre cladding, and thicker fibre claddings that prevent laser heating of the metal connector and consequent spallation^{91,92}. However, designs that redirect or absorb laser energy at the proximal fibre connector can result in wasteful loss of laser energy and inefficient fibre coupling.

Furthermore, the holmium laser generates heat, which in turn produces thermal lensing in the laser rod that can alter the spatial beam profile and lead to misalignment of the beam with the proximal fibre end, potentially causing fibre damage⁹³. Differences between individual manufacturers result in considerable variability of holmium laser optics, fibres, and fibre connector

components, which has been addressed in several studies comparing commercial fibres for holmium laser lithotripsy^{93–96}. Holmium laser lithotripsy fibres have been known to fail during procedures owing to extreme bending, distal fibre tip degradation and/or burnback, and proximal fibre tip failure^{93–96}. Furthermore, holmium laser ablation rates typically decrease after delivery of only a few laser pulses owing to fibre damage, thus increasing the probability that the surgical fibres will either need to be replaced or their distal tips recleaved during a procedure⁹⁷. Reflection of laser energy at the proximal connector end also increases the probability of proximal fibre destruction and damage to the laser system⁹⁸. As further evidence of this limitation, small (<300 µm-core) fibres have high reported rates of connector end failures during holmium laser lithotripsy, likely owing to overflow of the laser beam at the fibre connector⁵¹. Laser blast shields are frequently incorporated into the laser system as a precaution in order to prevent potential damage to the laser optics⁹³.

Multi-use holmium fibres are available as an option to reduce the costs associated with single-use fibres; however, multi-use fibres still experience cumulative laser-induced damage with repeated use⁹⁹. TFL lithotripsy using an improved spatial beam profile has been reported to reduce laser-induced damage to the proximal fibre tip surface compared with the holmium laser, potentially enabling fibres to be used for longer periods, but exactly how long remains to be studied further¹⁰⁰.

The small, uniform TFL beam also enables focusing of high power into smaller lithotripsy fibres (50–150 µm core) than is possible with the holmium laser (≥200 µm core)^{101–103}. Use of smaller fibres during laser lithotripsy provides several important advantages during flexible ureteroscopy, including increased cross-sectional area within the ureteroscope working channel for saline irrigation (for improved visibility and safety) as well as enabling maximal deflection of the flexible ureteroscope for improved access to the lower pole of the kidney¹⁰². Smaller fibres can also spur development of smaller ureteroscopic instruments, such as integrated fibres and baskets and miniature ureteroscopes^{104,105}. Multiple reports have also shown that stone retropulsion decreases with decreasing fibre diameter^{36–38,47,106–109}, so use of smaller fibres might further contribute to improved ablation efficiency by reducing the likelihood of stone retropulsion.

Laser pulse repetition rate. The diode-pumped TFL enables more flexibility in the choice of laser operating parameters than conventional flashlamp-pumped, solid-state lasers. For example, the low-power holmium:YAG laser is limited to operation at pulse rates <30 Hz owing to potential overheating and catastrophic thermal damage to the laser rod¹¹⁰. The vast majority of the white light from the flashlamp used to pump the laser crystal does not contribute to laser operation but is instead wasted in the form of heat, requiring bulky and expensive water cooling systems to prevent thermally induced damage to the laser rod. As a result of this pumping scheme, the wall-plug efficiency of holmium:YAG lasers is typically <1–2% (with 98–99% of energy wasted as heat). Although high-power holmium:YAG lasers capable of operation at pulse

rates up to 80 Hz are now available, the increased power is generated by implementation and packaging of multiple laser rods and cavities within the laser system at substantial added complexity and expense (FIG. 2; TABLE 1), rather than a major breakthrough in holmium laser technology.

By contrast, the diode-pumped TFL is efficient, with a wall-plug efficiency of ~12%, enabling air cooling and laser operation at pulse rates up to 2000 Hz. Such high pulse rates are probably unnecessary, and TFL lithotripsy studies have reported pulse rates only up to 500 Hz (REF.¹¹¹). This capability to operate at high pulse rates enables the TFL to be operated with more flexible parameters than the holmium laser, for use in dusting mode, with low pulse energy compensated by high pulse rates and production of small stone fragments during the procedure.

The combination of an air-cooled laser with increased wall-plug efficiency results in a smaller overall form factor for the laser (TABLE 1). High-power (50 W), compact, tabletop versions of the TFL have been manufactured and tested (FIG. 2) with higher average power output than tabletop versions of the holmium laser (50 W versus 20 W)^{112–115}. Preliminary studies directly comparing this second-generation TFL technology with the current 120 W holmium laser using equivalent laser parameters have demonstrated that the TFL provides twofold to fourfold higher stone ablation rates than the holmium laser, as well as reduced stone retropulsion^{112–114}



Fig. 2 | Comparison of lasers for lithotripsy. An air-cooled, tabletop, quasi-continuous-wave thulium fibre laser with 50 W average power, 500 W peak power, and pulse rates up to 2000 Hz is shown on the left. A high-power, 120 W holmium:yttrium–aluminium–garnet (YAG) laser, capable of pulse rates up to 80 Hz, for stone dusting applications is on the right.

Table 1 | Comparison of experimental thulium fibre laser and clinical holmium:YAG laser

Characteristic	Thulium fibre laser	Holmium:YAG laser
Model	Urolase	P120H
Manufacturer	IPG Medical	Lumenis
Wavelength	1,940 nm	2,100 nm
Dimensions (width × length × height)	55 cm × 46 cm × 29 cm	47 cm × 116 cm × 105 cm
Weight	35 kg	245 kg
Cooling system	Air	Water
Peak power	500 W	NA
Average power	50 W	120 W
Pulse rate	1–2000 Hz	5–80 Hz
Pulse energy	0.2–6.0 J	0.2–6.0 J
Pulse width	0.2–12 ms	Adjustable
Mode	Fragmentation and dusting	Fragmentation and dusting
Fibre delivery	Silica (≥150 μm)	Silica (≥200 μm)
Price	NA	~US\$200,000

NA, not applicable; YAG, yttrium–aluminium–garnet.

(TABLE 2). The increased wall-plug efficiency can also enable TFL operation at higher average power than the holmium laser, while still using a standard 110 V electrical outlet, which could eliminate problems associated with limited availability of electrical and cooling requirements when transporting the laser between operating rooms. Furthermore, the fibre laser architecture not only eliminates water cooling requirements but also means that no bulk optics (such as lenses and mirrors) are required, so contamination and misalignment of optics caused by poor handling or vibration shocks during transportation are also eliminated.

Laser fibre-optic delivery systems

Novel fibre-optic delivery systems

A robust, flexible, biocompatible, and affordable fibre-optic delivery system is required to deliver energy from the laser system through the working channel of a flexible ureteroscope inside the upper urinary tract. The near-single-mode TFL spatial beam profile enables transmission of higher laser power into smaller optical fibres than the holmium:YAG laser¹⁰¹. This property has in turn stimulated the development of a variety of different fibre-optic delivery systems with customized distal fibre tips for potential use in flexible ureteroscopy with the TFL (FIG. 3), although some of these fibre tip designs are experimental and still in the early stages of development.

Small-diameter fibres. The TFL can be used with standard low-OH⁻ silica optical fibres that are similar in composition to the holmium laser fibres currently used in the clinic. However, the near-single-mode TFL spatial beam profile enables focusing of the laser beam down to ~25 μm, much smaller than can be achieved using the holmium laser. This small beam can easily be coupled into 50, 100, or 150 μm core fibres, providing several benefits over standard holmium fibres, which are ≥200 μm core^{101–103}. First, the use of a small fibre diameter increases the radiant exposure or irradiance on the stone surface, meaning that reduced laser pulse energies of ~35 mJ can be used for stone ablation, compared with typical holmium pulse energies of ≥200 mJ used in the clinic. Second, the small fibres are more flexible with shorter bend radii than larger fibres, and can, therefore, be inserted into the working channel of the ureteroscope under maximum deflection and are less likely to break inside the working channel or damage the ureteroscope. Smaller fibres have also been reported to reduce stone retropulsion without sacrificing stone ablation rates^{36–38,47,106–109}. They can also

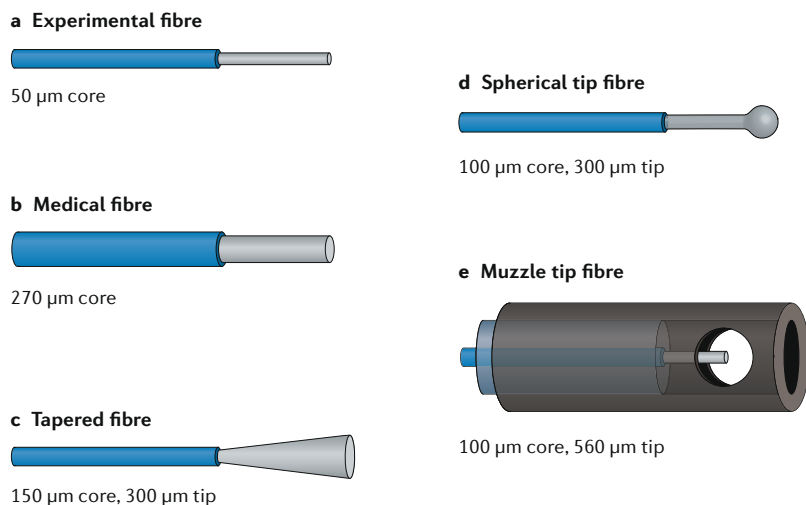


Fig. 3 | Fibre-optic tip designs. **a** | Miniature experimental fibre with 50 μm core, 65 μm cladding, and 85 μm jacket. **b** | Standard clinical holmium fibre with 270 μm core, 320 μm cladding, and 465 μm jacket. **c** | Tapered optical fibre with 150 μm core tapered to a 300 μm tip. **d** | Spherical tip fibre with 100 μm core trunk fibre and 300 μm spherical ball tip. **e** | Muzzle brake fibre-optic tip design, comprising a 100 μm core fibre recessed a distance of 500 μm inside a 560 μm diameter hollow metal tip, with 275 μm side holes, also centred a distance of 500 μm from the fibre end. The hollow metal tip (not shown) is similar in design to the muzzle brake tip but without the side holes.

Table 2 | Summary of preclinical studies comparing experimental thulium fibre laser and holmium:YAG laser

Year	Study	Laser parameters	Sample	Results	Refs
2010	Low pulse energy comparison	TFL: 70 mJ and 10 Hz Ho: 70 mJ and 3 Hz	UA and COM	TFL: 5–10 × higher ablation rates than Ho	123
2011 2013	Ablation thresholds, ablation rates, and stone retropulsion	TFL: 35 mJ and 400 Hz Ho: 550 mJ and 10 Hz	UA, COM, and PoP	TFL: 4 × lower ablation threshold than Ho	8288
2016	Proximal fibre tip damage	TFL: 35 mJ and 14 W Ho: 600 mJ and 3.6 W	NA	TFL: no damage up to 14 W Ho: damage at 3.6 W	100
2016	Ablation rates and stone retropulsion at high pulse energies	TFL: 1–3 J and 3–30 W Ho: 1–3 J and 3–30 W	COM and Bego	TFL: 1.3–2.3 × higher ablation rate and lower retropulsion than Ho	112
2016 2017	Ablation rates and stone retropulsion at variable energies, pulse rates, and average powers	TFL: 0.2–5 J, 6–80 Hz, and 3.6–50 W Ho: 0.2–5 J, 6–80 Hz, and 3.6–50 W	COM and Bego	TFL: 2–4 × higher ablation rate and lower retropulsion; 29–75% of Ho for equivalent pulse energies	113,114

Bego, Begostone; COM, calcium oxalate monohydrate; Ho, holmium:yttrium–aluminium–garnet (YAG) laser; NA, not applicable; PoP, plaster of Paris; TFL, thulium fibre laser; UA, uric acid.

be more easily integrated with other ureteroscopic tools, such as stone baskets¹⁰⁴, to create miniature multipurpose tools without sacrificing valuable cross-sectional space within the ureteroscope for irrigation or other instruments.

However, the use of smaller fibres also presents challenges. Increased distal tip degradation and burnback rates have been reported in smaller fibres (200–50 µm) than the rates seen with fibres >200 µm (REF.⁹⁸). Some fibres can be thinner than a human hair and are, therefore, difficult to see and less rigid than larger fibres, making insertion through the ureteroscope working channel more challenging. However, these limitations could potentially be addressed by selecting a fibre jacket or buffer that is nominally larger and more rigid to offset some of the diminished mechanical properties that small-core fibres experience.

Reverse tapered fibre-optic tips. One approach to reduce the distal fibre tip degradation and burnback that are unique to the TFL is the use of tapered optical fibres on the distal or output end. Normally, tapered fibres are used on the input or proximal end of a fibre to provide a larger fibre core for coupling a non-uniform, multimodal laser beam (such as from a holmium laser) into the fibre¹¹⁶. However, tapered proximal fibre tips are limited in that they produce higher order modes (more optical path lengths are supported within the fibre core), some of which are more likely to leak into the fibre cladding than lower order modes, lead to a poorer fibre output beam profile, and potentially damage the fibre¹¹⁶. As the TFL emits a more uniform spatial beam profile than the multimode output from a holmium laser, the tapered fibre tip can instead be used on the output or distal end of the fibre in a reverse manner. The large taper then acts as a more robust fibre tip than a typical nontapered distal fibre tip, similar to using a larger trunk fibre, decreasing the intensity of the laser beam across the large surface area of the fibre tip and reducing fibre tip degradation and burnback¹⁰².

Spherical tip fibres. Spherical tip fibres are commercially available for use in the clinic with the holmium:YAG laser during lithotripsy^{96,117}. One benefit of the distal spherical tip is that it provides a smoother surface than a sharp bare tip fibre, enabling initial damage-free insertion through the working channel of the ureteroscope. However, holmium spherical tip fibres are also still relatively large, with a 270 µm core and 450 µm outer diameter. The improved TFL spatial beam profile again enables miniaturization of spherical tip fibres to 100 µm core and 300 µm outer diameter¹¹⁸. The spherical tip also acts as a lens, focusing the laser beam and potentially extending the noncontact working distance between fibre tip and stone surface, in contrast to the diverging beam observed from the output end of a bare fibre. However, this focusing effect is stronger in air than in saline owing to the larger refractive index mismatch between glass and air (1.5 versus 1.0) than between saline and air (1.3 versus 1.0), so such benefits have not been observed in laboratory studies¹¹⁸. Spherical tip fibres have also been observed to rapidly degrade during laser lithotripsy in contact mode, especially when using high-power laser parameters, meaning that other than serving its initial purpose of damage-free insertion through the working channel of the ureteroscope, the spherical tip eventually becomes worn down to something resembling a bare fibre tip with continued use during the procedure.

Detachable fibre-optic tips. The distal fibre tip is typically destroyed instantaneously during lithotripsy owing to the high ablative temperatures experienced when the fibre is in direct contact with or in close proximity to the stone surface⁹⁸. This damage can mean that the entire optical fibre must be disposed of during or after a procedure unless fibre cleaving tools are readily available. Alternatively, the ability to instead preserve and reuse the trunk fibre and fibre connector and dispose of only a short section of the distal tip could result in considerable cost savings per lithotripsy procedure. A prototype disposable fibre tip has been reported, which uses a miniature twist-lock, spring-loaded attachment

mechanism (<1 mm diameter) and is produced using off-the-shelf spring components. This approach could potentially provide a cost-effective method to customize and exchange fibre tips for a specific procedure, thus enabling improved personalized care¹¹⁹.

Muzzle brake fibre-optic tips. A design using a bare distal fibre tip recessed within a hollow steel tip has been tested for reducing bare fibre tip degradation and burnback¹²⁰. However, use of the hollow tip resulted in increased stone retropulsion and reduced stone ablation rates¹²⁰. In an attempt to balance acceptable stone ablation rates, reduce fibre tip degradation, and reduce stone retropulsion, a fibre-optic muzzle brake tip has been reported¹²¹. A muzzle brake or recoil compensator is commonly used in ballistics to reduce the recoil of a gun by redirecting gaseous vapours laterally instead of axially along the bore during firing of the gun. A similar approach has been reported using a prototype muzzle brake fibre-optic tip (a stainless-steel tip with circumferential holes) to manipulate the laser-induced vapour bubble. This design not only reduces stone retropulsion but also additionally protects the recessed bare fibre tip from degradation and burnback¹²¹.

The advantages and disadvantages of small, large, tapered, ball, hollow metal, and muzzle brake fibre-optic tips are based on key characteristics desired in an ideal laser lithotripsy fibre. These characteristics include but are not limited to sufficient flexibility to enable maximal ureteroscope deflection for access to the lower pole of the kidney, small diameter to enable sufficient saline irrigation and remove stone debris for visibility and safety, reduction in stone retropulsion so the urologist does not have to waste time pursuing the stone in the urinary tract, reduction in fibre tip degradation and/or burnback to improve the longevity of the fibre-optic delivery system, and sufficient stone ablation rate to minimize procedure time (TABLE 3).

Future developments

The current clinical gold standard holmium:YAG laser is cost-effective in treating all stone compositions during lithotripsy procedures. Predicting the future of the laser lithotripsy field is difficult, but consideration of and extrapolation from past developments in holmium technology might offer some clues. For example, the output power from holmium laser lithotripters has steadily increased over the past two decades (from 20 to 120 W), and the size and cost of such lasers have also increased correspondingly owing to limited wall-plug efficiency of about 1–2%. The next generation of holmium lasers will

probably operate at continually increasing output powers (>120 W) and pulse rates (>80 Hz), enabling increased flexibility, especially for stone dusting approaches. Continued experimentation with and optimization of laser temporal pulse shaping should also result in further reduced stone retropulsion, translating into more efficient procedures. Such higher-power holmium lasers will become progressively more expensive, as observed from examining past trends of the cost of low-power (20–30 W) holmium lasers, which cost ~\$50,000, compared with the cost of the newest high-power (120 W) holmium lasers, at ~\$200,000.

Development of a fundamentally new type of laser technology, such as the TFL, might disrupt this trend. For example, over the past decade, TFL output power has increased rapidly from 70 W to 500 W peak power, while the TFL has also become smaller, shrinking from a console to a tabletop version (FIG. 2). Wall-plug efficiency has doubled from 6% to 12%, in part owing to smaller diode pump laser components and newer, more efficient pump schemes, enabling convenient air cooling instead of water cooling. These advances have occurred without an increase in production costs, so TFL technology should remain cost competitive.

Laboratory studies directly comparing the TFL and high-power holmium laser at equivalent laser parameters have demonstrated that the TFL was more efficient for lithotripsy in both dusting and fragmentation modes, providing two to four times faster stone ablation than the holmium laser as well as reduced stone retropulsion^{113,114} (TABLES 1, 2). The superior in-vitro performance of the TFL versus holmium laser for efficient lithotripsy, as well as the potential for delivery of various novel fibre designs, portends interesting potential developments in stone management. Initial clinical studies with the TFL have been conducted in Europe¹²², and results of planned multicentre trials will determine the feasibility and acceptability of the TFL as an alternative to the holmium laser.

Conclusions

The flashlamp-pumped, solid-state, infrared holmium:YAG laser is currently the clinical gold standard for lithotripsy during ureteroscopy owing to its cost-effective treatment of all stone compositions. However, this technology, which is approaching 30 years in clinical use, has several technical limitations. The holmium wavelength does not match a water absorption peak in tissue, its multimode beam profile prevents coupling of high power into small (<200 µm core) fibres, and an inefficient pumping scheme currently limits operation

Table 3 | Comparison of standard and experimental fibre-optic tips for use in laser lithotripsy

Property	Small	Large	Taper	Spherical	Steel	Muzzle
High flexibility	Yes	No	Yes	Yes	Yes	Yes
High irrigation	Yes	No	Yes	Yes	Yes	Yes
Low retropulsion	Yes	No	No	No	No	Yes
Low burnback	No	Yes	Yes	No	Yes	Yes
High ablation	Yes	Yes	Yes	Yes	No	Yes

to low pulse rates (5–80 Hz) and requires a high-voltage power supply and water cooling. Several lasers have been tested as potential alternatives to holmium for lithotripsy, including FREDDY, erbium:YAG, and femtosecond lasers. However, they are subject to limitations in fibre-optic delivery and cannot be used on all stone types or for multiple applications. The TFL is a fundamentally different type of laser. The TFL wavelength more closely matches a water absorption peak in tissue for twofold to fourfold more efficient stone ablation than holmium, the near-single-mode TFL beam profile enables coupling of high power into flexible and small (50–150 µm core) silica fibres, and the TFL architecture enables high pulse rates up to 2,000 Hz and a more efficient pumping scheme,

enabling availability of a high-power, compact, tabletop, air-cooled laser system. Furthermore, this technology enables use of novel fibre delivery systems, including miniature, tapered, spherical, hollow steel, and muzzle brake distal fibre-optic tips, which can provide increased irrigation rates through the working channel of a flexible ureteroscope, improved ureteroscope deflection, and reduced fibre tip degradation or burnback and stone repulsion without sacrificing stone ablation rates. Only clinical studies with direct comparison to holmium laser will demonstrate whether a next-generation laser lithotripsy system can replace the holmium laser.

Published online: 08 June 2018

1. Fernstrom, I. & Johansson, B. Percutaneous pyelolithotomy. A new extraction technique. *Scand. J. Urol. Nephrol.* **10**, 257–259 (1976).
2. Alken, P., Hutschenreiter, G., Gunther, R. & Marberger, M. Percutaneous stone manipulation. *J. Urol.* **125**, 463–466 (1981).
3. Segura, J. W. et al. Percutaneous removal of kidney stones: review of 1,000 cases. *J. Urol.* **134**, 1077–1081 (1985).
4. Ghani, K. R. et al. Trends in percutaneous nephrolithotomy and outcomes in the United States. *J. Urol.* **190**, 558–564 (2013).
5. Chaussy, C. et al. The use of shock waves for the destruction of renal calculi without direct contact. *Urol. Res.* **4**, 175 (1976).
6. Chaussy, C. et al. First clinical experience with extracorporeally induced destruction of kidney stones by shock waves. *J. Urol.* **127**, 417–420 (1982).
7. Assimos, D. et al. Surgical management of stones: AUA/Endourological Society Guideline. *American Urological Association* <http://auanet.org/guidelines/surgical-management-of-stones-aua/endourological-society-guideline-2016> (2016).
8. Lee, F. J. & Yeh, H. T. in *Smith's Textbook of Endourology* (ed. Smith, A.) 612–623 (Wiley, 2012).
9. Matlaga, B. R., Jansen, P., Meckley, L. M., Byrne, T. W. & Lingeman, J. E. Treatment of ureteral and renal stones: a systematic review and meta-analysis of randomized, controlled trials. *J. Urol.* **188**, 130–137 (2012).
10. Grasso, M. & Bagley, D. A 7.5/8.2 F actively deflectable, flexible ureteroscope: a new device for both diagnostic and therapeutic upper urinary tract endoscopy. *Urology* **43**, 435–441 (1994).
11. Scales, C. D. et al. Comparative effectiveness of shock wave lithotripsy and ureteroscopy for treating patients with kidney stones. *JAMA Surg.* **149**, 648–653 (2014).
12. Denstedt, J. D. & Clayman, R. V. Electrohydraulic lithotripsy of renal and ureteral calculi. *J. Urol.* **143**, 13–17 (1990).
13. Sun, Y. et al. Pneumatic lithotripsy versus laser lithotripsy in the endoscopic treatment of ureteral calculi. *J. Endourol.* **15**, 587–590 (2001).
14. Sofer, M. et al. Holmium: YAG laser lithotripsy for upper urinary tract calculi in 598 patients. *J. Urol.* **167**, 31–34 (2002).
15. Oberlin, D. T., Flum, A. S., Bachrach, L., Matulewicz, R. S. & Flury, S. C. Contemporary surgical trends in the management of upper tract calculi. *J. Urol.* **193**, 880–884 (2015).
16. Dretler, S. P. Laser lithotripsy: a review of 20 years of research and clinical applications. *Lasers Surg. Med.* **8**, 341–356 (1988).
17. Dretler, S. P., Watson, G., Parrish, J. A. & Murray, S. Pulsed dye laser fragmentation of ureteral calculi: initial clinical experience. *J. Urol.* **137**, 386–389 (1987).
18. Johnson, J. P., Oz, M. C., Chuck, R. S. & Treat, M. R. Comparison of methods for transcatheter fragmentation of gallstones. *Surg. Endosc.* **3**, 7–10 (1989).
19. Spindel, M. L. et al. Comparison of holmium and flashlamp pumped dye lasers for use in lithotripsy of biliary calculi. *Lasers Surg. Med.* **12**, 482–489 (1992).
20. Bagley, D. & Erhard, M. Use of the holmium laser in the upper urinary tract. *Tech. Urol.* **1**, 25–30 (1995).
21. Matlaga, B. R. Contemporary surgical management of upper urinary tract calculi. *J. Urol.* **181**, 2152–2156 (2009).
22. Scales, C. D. et al. Practice variation in the surgical management of urinary lithiasis. *J. Urol.* **186**, 146–150 (2011).
23. Hardy, L. A., Irby, P. B. & Fried, N. M. Scanning electron microscopy of real and artificial kidney stones before and after Thulium fibre laser ablation in air and water. *Proc. SPIE 10468 Therapeutics and Diagnostics in Urology*. 10468 <https://doi.org/10.1117/12.2285069> (2018).
24. Chan, K. F. et al. Holmium:YAG laser lithotripsy: a dominant photothermal ablative mechanism with chemical decomposition of urinary calculi. *Lasers Surg. Med.* **25**, 22–37 (1999).
25. Roggan, A., Bindig, U., Wäsche, W. & Zgoda, F. *Action Mechanisms of Laser Radiation in Biological Tissues* (eds Berlien, H. P. & Muller, G. J.) 87 (Springer, 2003).
26. Hale, G. M. & Querry, M. R. Optical constants of water in the 200 nm to 200 µm wavelength region. *Appl. Opt.* **12**, 555–563 (1973).
27. Razvi, H. H., Chun, S. S., Denstedt, J. D. & Sales, J. L. Soft-tissue applications of the holmium:YAG laser in urology. *J. Endourol.* **9**, 387–390 (1995).
28. Welch, A. J., van Gemert, M. J. C., Star, W. M. & Wilson, B. C. in *Optical-Thermal Response of Laser-Irradiated Tissue* (eds Welch, A. J. & van Gemert, M. J. C.) 27–64 (Springer, 1995).
29. Harrington, J. A. *Infrared Fibers and their Applications* (SPIE, 2004).
30. Scholle, K., Lamrini, S., Koopmann, P. & Fuhrber, P. in *Frontiers in Guided Wave Optics & Optoelectronics* (ed. Pal, B.) 471–500 (IntechOpen, 2010).
31. Dauw, C. A. et al. Contemporary practice patterns of flexible ureteroscopy for treating renal stones: results of a worldwide survey. *J. Endourol.* **29**, 1221–1230 (2015).
32. Molina, W. R. et al. Influence of saline on temperature profile of laser lithotripsy activation. *J. Endourol.* **29**, 235–239 (2015).
33. Buttice, S. et al. Temperature changes inside the kidney: what happens during holmium:yttrium-aluminum-garnet laser usage? *J. Endourol.* **30**, 574–579 (2016).
34. Aldoukhi, A. H., Ghani, K., Hall, T. L. & Roberts, W. W. Thermal response to high-power holmium laser lithotripsy. *J. Endourol.* **31**, 1308–1312 (2017).
35. Wollin, D. A. et al. Effect of laser settings and irrigation rates on ureteral temperature during holmium laser lithotripsy, an in vitro model. *J. Endourol.* **32**, 59–63 (2018).
36. Finley, D. S. et al. Effect of holmium:YAG laser pulse width on lithotripsy retropulsion in vitro. *J. Endourol.* **19**, 1041–1044 (2005).
37. Kang, H. W. et al. Dependence of calculus retropulsion on pulse duration during Ho:YAG laser lithotripsy. *Lasers Surg. Med.* **38**, 762–772 (2006).
38. Kalra, P., Le, N. & Bagley, D. Effect of pulse width on object movement in vitro using Ho:YAG laser. *J. Endourol.* **21**, 228–231 (2007).
39. Bader, M. J. et al. Impact of pulse duration on Ho:YAG laser lithotripsy: fragmentation and dusting performance. *World J. Urol.* **33**, 471–477 (2015).
40. Wollin, D. A. et al. Variable pulse duration from a new Holmium:YAG laser: the effect on stone comminution, fibre tip degradation, and retropulsion dusting model. *Urology* **103**, 47–51 (2017).
41. Trost, D. U. S. Laser pulse format for penetrating an absorbing fluid. US Patent US5321715A (1994).
42. Elhilali, M. M., Badaan, S., Ibrahim, A. & Andonian, S. Use of the Moses technology to improve holmium laser lithotripsy outcomes: a preclinical study. *J. Endourol.* **31**, 598–604 (2017).
43. Vogel, A. & Venugopalan, V. Mechanisms of pulsed laser ablation of biological tissues. *Chem. Rev.* **103**, 577–644 (2003).
44. Zorcher, T., Hochberger, J., Schrott, K. M., Kuhn, R. & Schafhauser, W. In vitro study concerning the efficiency of the frequency-doubled double-pulse Neodymium:YAG laser (FREDDY) for lithotripsy of calculi in the urinary tract. *Lasers Surg. Med.* **25**, 38–42 (1999).
45. Delvecchio, F. C. et al. In vitro analysis of stone fragmentation ability of the FREDDY laser. *J. Endourol.* **17**, 177–179 (2003).
46. Ebert, A., Stangle, J., Kuhn, R. & Schafhauser, W. The frequency-doubled double-pulse Neodymium:YAG laser lithotripter (FREDDY) in lithotripsy of urinary stones. First clinical experience. *Urologe A.* **42**, 825–833 (2003).
47. Marguet, C. G. et al. In vitro comparison of stone retropulsion and fragmentation of the frequency doubled, double pulse nd:yag laser and the holmium:yag laser. *J. Urol.* **173**, 1797–1800 (2005).
48. Dubosq, F. et al. Endoscopic lithotripsy and the FREDDY laser: initial experience. *J. Endourol.* **20**, 296–299 (2006).
49. Yates, J., Zabbo, A. & Pareek, G. A comparison of the FREDDY and holmium lasers during ureteroscopic lithotripsy. *Lasers Surg. Med.* **39**, 637–640 (2007).
50. Santa-Cruz, R. W., Leveille, R. J. & Krongrad, A. Ex vivo comparison of four lithotripters commonly used in the ureter: what does it take to perforate? *J. Endourol.* **12**, 417–422 (1998).
51. Althunayan, A. M., Elkoushy, M. A., Elhilali, M. M. & Andonian, S. Adverse events resulting from lasers used in urology. *J. Endourol.* **28**, 256–260 (2014).
52. Cordes, J., Lange, B., Jocham, D. & Kausch, I. Destruction of stone extraction basket during an in vitro lithotripsy—a comparison of four lithotripters. *J. Endourol.* **25**, 1359–1362 (2011).
53. Cordes, J., Nguyen, F., Lange, B., Brinkmann, R. & Jocham, D. Damage of stone baskets by endourologic lithotripters: a laboratory study of 5 lithotripters and 4 basket types. *Adv. Urol.* **632790**, 1–6 (2013).
54. Bader, M. J. et al. Impact of collateral damage to endourologic tools during laser lithotripsy—in vitro comparison of three different clinical laser systems. *J. Endourol.* **25**, 667–672 (2011).
55. Freiha, G. S., Glickman, R. D. & Teichman, J. M. Holmium:YAG laser-induced damage to guidewires: experimental study. *J. Endourol.* **11**, 331–336 (1997).
56. Honeck, P., Wendt-Nordahl, G., Hacker, A., Alken, P. & Knoll, T. Risk of collateral damage to endourologic tools by holmium:YAG laser energy. *J. Endourol.* **20**, 495–497 (2006).
57. Teichman, J. M. et al. Erbium:YAG versus holmium:YAG lithotripsy. *J. Urol.* **165**, 876–879 (2001).
58. Fried, N. M. Potential applications of the erbium:YAG laser in endourology. *J. Endourol.* **15**, 889–894 (2001).
59. Chan, K. F. et al. Erbium:YAG laser lithotripsy mechanism. *J. Urol.* **168**, 436–441 (2002).

60. Lee, H., Kang, H. W., Teichman, J. M., Oh, J. & Welch, A. J. Urinary calculus fragmentation during Ho:YAG and Er:YAG lithotripsy. *Lasers Surg. Med.* **38**, 39–51 (2006).
61. Iwai, K. et al. Erbium:YAG laser lithotripsy by use of a flexible hollow waveguide with an end-scaling cap. *Appl. Opt.* **42**, 2431–2435 (2003).
62. Yang, Y., Chaney, C. A. & Fried, N. M. Erbium:YAG laser lithotripsy using hybrid germanium/silica optical fibres. *J. Endourol.* **18**, 830–835 (2004).
63. Raif, J., Vardi, M., Nahlieli, O. & Gannot, I. An Er:YAG laser endoscopic fibre delivery system for lithotripsy of salivary gland stones. *Lasers Surg. Med.* **38**, 580–587 (2006).
64. Qiu, J. et al. Comparison of fluoride and sapphire optical fibres for Er:YAG laser lithotripsy. *J. Biophotonics* **3**, 277–283 (2010).
65. Qiu, J. et al. Femtosecond laser lithotripsy: feasibility and ablation mechanism. *J. Biomed. Opt.* **15**, 028001 (2010).
66. Niemz, M. H. ed., *Laser-tissue Interactions: Fundamentals and Applications* 3rd Edition (Springer, 2007).
67. Xia, S. J. et al. Thulium laser versus standard transurethral resection of the prostate: a randomized prospective trial. *Eur. Urol.* **53**, 382–389 (2008).
68. Jackson, S. D. & Lauto, A. Diode-pumped fibre lasers: a new clinical tool? *Lasers Surg. Med.* **30**, 184–190 (2002).
69. Pierce, M. C., Jackson, S. D., Dickinson, M. R. & King, T. A. Laser-tissue interaction with a high-power 2 μm fibre laser: preliminary studies with soft tissue. *Lasers Surg. Med.* **25**, 407–413 (1999).
70. Sumiyoshi, T. et al. High-power continuous-wave 3- and 2 μm cascade Ho³⁺:ZBLAN fibre laser and its medical applications. *IEEE J. Sel. Top. Quantum Electron.* **5**, 936–943 (1999).
71. Pierce, M. C., Jackson, S. D., Dickinson, M. R., King, T. A. & Sloan, P. Laser-tissue interaction with a continuous wave 3 μm fibre laser: preliminary studies with soft tissue. *Lasers Surg. Med.* **26**, 491–495 (2000).
72. El-Sherif, A. F. & King, T. A. Soft and hard tissue ablation with short-pulse high peak power and continuous thulium-silica fibre lasers. *Lasers Med. Sci.* **18**, 139–147 (2003).
73. Fried, N. M. High-power laser vaporization of the canine prostate using a 110Watt Thulium fibre laser at 1.91 μm . *Lasers Surg. Med.* **36**, 52–56 (2005).
74. Fried, N. M. & Murray, K. E. High-power thulium fibre laser ablation of urological tissues at 1.94 μm . *J. Endourol.* **19**, 25–31 (2005).
75. Fried, N. M. Thulium fibre laser lithotripsy: an in vitro analysis of stone fragmentation using a modulated 110W Thulium fibre laser at 1.94 μm . *Lasers Surg. Med.* **37**, 53–58 (2005).
76. Polder, K. D., Harrison, A., Eubanks, L. E. & Bruce, S. 1,927 fractional thulium fibre laser for treatment of nonfacial photodamage: a pilot study. *Dermatol. Surg.* **37**, 342–348 (2011).
77. Weiss, E. T. et al. 1927nm fractional resurfacing of facial actinic keratosis: a promising new therapeutic option. *J. Am. Acad. Dermatol.* **68**, 98–102 (2013).
78. Tunc, B. & Gulsoy, M. Tm:Fibre laser ablation with real-time temperature monitoring for minimizing collateral thermal damage: ex vivo dosimetry for ovine brain. *Lasers Surg. Med.* **45**, 48–56 (2013).
79. Guney, M., Tunc, B. & Gulsoy, M. Investigating the ablation efficiency of a 1940nm thulium fibre laser for intraoral surgery. *Int. J. Oral Maxillofac. Surg.* **43**, 1015–1021 (2014).
80. Gesierich, W., Reichenberger, F., Fertl, A., Haeussinger, K. & Sroka, R. Endobronchial therapy with a thulium fibre laser (1940 nm). *J. Thorac. Cardiovasc. Surg.* **147**, 1827–1832 (2014).
81. Alagha, H. Z. & Gulsoy, M. Photothermal ablation of liver tissue with 1940nm thulium fibre laser: an ex vivo study on lamb liver. *J. Biomed. Opt.* **21**, 015007 (2016).
82. Demirkan, I., Sarp, A. S. K. & Gulsoy, M. Ceramic bracket debonding with Tm:fibre laser. *J. Biomed. Opt.* **21**, 065007 (2016).
83. Pal, D., Ghosh, A., Sen, R. & Pal, A. Continuous-wave and quasi-continuous wave thulium-doped all-fibre laser: implementation on kidney stone fragmentation. *Appl. Opt.* **55**, 6151–6155 (2016).
84. Jansen, E. D., van Leeuwen, T. G., Motamedi, M., Borst, C. & Welch, A. J. Temperature dependence of the absorption coefficient of water for midinfrared laser radiation. *Lasers Surg. Med.* **14**, 258–268 (1994).
85. Lange, B. I., Brendel, T. & Huttmann, G. Temperature dependence of light absorption in water at holmium and thulium laser wavelengths. *Appl. Opt.* **41**, 5797–5803 (2002).
86. Schomacker, K. T., Domankevitz, Y., Flotte, T. J. & Deutsch, T. F. Co:MgF₂ laser ablation of tissue: effect of wavelength on ablation threshold and thermal damage. *Lasers Surg. Med.* **11**, 141–151 (1991).
87. Blackmon, R. L., Irby, P. B. & Fried, N. M. Comparison of holmium:YAG and thulium fibre laser lithotripsy: ablation thresholds, ablation rates, and retropulsion effects. *J. Biomed. Opt.* **16**, 071403 (2011).
88. Blackmon, R. L. *Thulium Fibre Laser Lithotripsy*. Thesis, UNC Charlotte (2013).
89. Hardy, L. A., Kennedy, J. D., Wilson, C. R., Irby, P. B. & Fried, N. M. Analysis of Thulium fibre laser induced vapor bubbles for ablation of kidney stones. *J. Biophotonics* **10**, 1240–1249 (2017).
90. Wilson, C. R., Hardy, L. A., Irby, P. B. & Fried, N. M. Collateral damage to the ureter and nitinol stone baskets during thulium fibre laser lithotripsy. *Lasers Surg. Med.* **47**, 403–410 (2015).
91. Griffin, S. Fibre optics for destroying kidney stones. *Biophotonics International* **11**, 44–47 (2004).
92. Nazif, O. A., Teichman, J. M. H., Glickman, R. D. & Welch, A. J. Review of laser fibres: a practical guide for urologists. *J. Endourol.* **18**, 818–829 (2004).
93. Marks, A. J., Mues, A. C., Knudsen, B. E. & Teichman, J. M. H. Holmium:YAG lithotripsy proximal fibre failures from laser and fibre mismatch. *Urology* **71**, 1049–1051 (2008).
94. Knudsen, B. E. et al. Performance and safety of holmium:YAG laser optical fibres. *J. Endourol.* **19**, 1092–1097 (2005).
95. Mues, A. C., Teichman, J. M. & Knudsen, B. E. Evaluation of 24 holmium:YAG laser optical fibres for flexible ureteroscopy. *J. Urol.* **182**, 348–354 (2009).
96. Akar, E. C. & Knudsen, B. E. Evaluation of 16 new Holmium:Yttrium-Aluminum-Garnet laser optical fibres for ureteroscopy. *Urology* **86**, 230–235 (2015).
97. Lee, H. et al. Effect of lithotripsy on holmium: YAG optical beam profile. *J. Endourol.* **17**, 63–67 (2003).
98. Mues, A. C., Teichman, J. M. H. & Knudsen, B. E. Quantification of holmium:yttrium aluminum garnet optical tip degradation. *J. Endourol.* **23**, 1425–1428 (2009).
99. Knudsen, B. E., Pedro, R., Hinck, B. & Monga, M. Durability of reusable holmium:YAG laser fibres: a multicenter study. *J. Urol.* **185**, 160–163 (2011).
100. Wilson, C. R., Hardy, L. A., Irby, P. M. & Fried, N. M. Microscopic analysis of laser-induced proximal fibre tip damage during Holmium:YAG and Thulium fibre laser lithotripsy. *Opt. Eng.* **55**, 046102 (2016).
101. Scott, N. J., Cilip, C. M. & Fried, N. M. Thulium fibre laser ablation of urinary stones through small-core optical fibres. *IEEE J. Sel. Top. Quantum Electron.* **15**, 435–440 (2009).
102. Blackmon, R. L., Irby, P. B. & Fried, N. M. Thulium fibre laser lithotripsy using tapered fibres. *Lasers Surg. Med.* **42**, 45–50 (2010).
103. Blackmon, R. L. et al. Thulium fibre laser ablation of kidney stones using a 50 μm core silica optical fibre. *Opt. Eng.* **54**, 011004 (2015).
104. Wilson, C. R., Hutchens, T. C., Hardy, L. A., Irby, P. B. & Fried, N. M. A miniaturized, 1.9F integrated optical fibre and stone basket for use in thulium fibre laser lithotripsy. *J. Endourol.* **29**, 1110–1114 (2015).
105. Kennedy, J. D., Wilson, C. R., Irby, P. B. & Fried, N. M. Miniature ureteroscope tip designs for use in Thulium fibre laser lithotripsy. *Proc. SPIE 10038, Therapeutics and Diagnostics in Urology*. <https://doi.org/10.1117/12.2247822> (2017).
106. White, M. D., Moran, M. E., Calvano, C. J., Borhan-Manesh, A. & Mehlhaff, B. A. Evaluation of retropulsion caused by holmium:YAG laser with various power settings and fibres. *J. Endourol.* **12**, 183–186 (1998).
107. Lee, H. et al. Stone retropulsion during holmium:YAG lithotripsy. *J. Urol.* **169**, 881–885 (2003).
108. Lee, H. et al. Dependence of calculus retropulsion dynamics on fibre size and radiant exposure during Ho:YAG lithotripsy. *J. Biomechan. Eng.* **126**, 506–515 (2004).
109. Sea, J. et al. Optimal power settings for holmium:YAG lithotripsy. *J. Urol.* **187**, 914–919 (2012).
110. Struve, B. & Huber, G. Properties and medical applications of nearIR solid-state lasers. *J. Phys. IV* **1**, C7-3–C7-6 (1991).
111. Hardy, L. A., Wilson, C. R., Irby, P. B. & Fried, N. M. Rapid thulium fibre laser lithotripsy at pulse rates up to 500Hz using a stone basket. *IEEE J. Sel. Top. Quantum Electron.* **20**, 138–141 (2014).
112. Zamyatina, V. et al. Super pulse thulium fibre laser for lithotripsy (abstract 28). *Lasers Surg. Med.* **48**, 10 (2016).
113. Glybochko, P. et al. Comparison between the possibilities of holmium and thulium laser in lithotripsy in vitro. *Eur. Urol.* **16**, e391–e392 (2017).
114. Dymov, A. et al. Thulium lithotripsy: from experiment to clinical practice. *J. Urol.* **197**, e1285 (2017).
115. Hardy, L. A., Gonzalez, D. A., Irby, P. B. & Fried, N. M. Fragmentation and dusting of large kidney stones using a compact, air-cooled, high peak power, 1940nm, Thulium fiber laser. *Proc. SPIE 10468, Therapeutics and Diagnostics in Urology 2018 10468* <https://doi.org/10.1117/12.2285082> (2018).
116. Clarkin, J. P., Timmerman, R. J. & Shannon, J. H. Shaped fibre tips for medical and industrial applications. *Proc. SPIE 5317, Optical Fibers and Sensors for Medical Applications IV 5317* <https://doi.org/10.1117/12.540734> (2004).
117. Shin, R. H. et al. Evaluation of a novel ball tip holmium laser fibre: impact on ureteroscopy performance and fragmentation efficiency. *J. Endourol.* **30**, 189–194 (2016).
118. Wilson, C. R., Hardy, L. A., Kennedy, J. D., Irby, P. B. & Fried, N. M. Miniature ball tip optical fibres for use in Thulium fibre laser ablation of kidney stones. *J. Biomed. Opt.* **21**, 18003 (2016).
119. Hutchens, T. C., Blackmon, R. L., Irby, P. B. & Fried, N. M. Detachable fibre optic tips for use in thulium fibre laser lithotripsy. *J. Biomed. Opt.* **18**, 38001 (2013).
120. Hutchens, T. C., Blackmon, R. L., Irby, P. B. & Fried, N. M. Hollow steel tips for reducing fibre burnback during Thulium fibre laser lithotripsy. *J. Biomed. Opt.* **18**, 78001 (2013).
121. Hutchens, T. C., Gonzalez, D. A., Irby, P. B. & Fried, N. M. Fibre optic muzzle brake tip for reducing fibre burnback and stone retropulsion during Thulium fibre laser lithotripsy. *J. Biomed. Opt.* **22**, 18001 (2017).
122. Martov, A. G. et al. Initial experience in clinical application of thulium laser contact lithotripsy for transurethral treatment of urolithiasis. *Urologia* <https://doi.org/10.18565/urology.2018.1.112-120> (2018).
123. Blackmon, R. L., Irby, P. B. & Fried, N. M. Holmium:YAG ($\lambda = 2120\text{ nm}$) versus thulium fibre laser ($\lambda = 1908\text{ nm}$) lithotripsy. *Lasers Surg. Med.* **42**, 232–236 (2010).

Author contributions

N.M.F. researched data for the article and wrote the manuscript. P.B.I. contributed to the discussion of content and reviewed and edited the manuscript before submission.

Competing interests

N.M.F. is a consultant at IPG Medical Corporation (Marlborough, Massachusetts, USA) and is currently funded by a research grant from the National Institutes of Health (Bethesda, Maryland, USA). P.B.I. declares no competing interests.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.