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

Nathaniel M. Fried1,2* 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 surgery1–3. 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 stones5,6. 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.
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 retropulsion 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 anatomy. Other modalities of ureteroscopic intracorporeal lithotripsy have been developed, such as electrohydraulic (EHL) and pneumatic fragmentation, 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 replacement. 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 SWL.

**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 systems. 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 Hospital.

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. 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.

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 technique.

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 lithotripsy. 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. The optical absorption of near-infrared laser radiation for dry stones is noted to be relatively independent of stone type. Strong water absorption at the holmium wavelength translates into an intermediate optical penetration depth of about 400 μm. This property enables the laser to also be used for multiple soft tissue incision and coagulation applications. 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 hemostasis. 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 fibres. 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 use. 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 system.

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 lifetime.

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).

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. 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. Nevertheless, when normal saline irrigation rates are applied, the constant flow seems to be sufficient to prevent overheating of fluids in the urinary tract.

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. 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. 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 uptake 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 ablation. This concept, proposed over two decades ago, has been provided as an option on commercial high-power holmium clinical laser systems since 2017 (REF 45).

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 lithotriptor.

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. The FREDDY laser operates with a short pulse of about 1 μs 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. 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.

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 shockwave with minimal damage. This effect is in contrast to the holmium laser, which operates with a long pulse duration (350–1,500 μs) 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. 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. 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.

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. 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 energy (FIG. 1). The increased stone absorption and higher water absorption at this wavelength translate, in part, into improved laser ablation of kidney stones. 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 ~2,700 nm owing to strong absorption by the OH− component in silica.

Several specialist optical fibres, including hollow silica waveguides and 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 but are all inferior to silica fibres owing to their higher cost, poor biocompatibility, worse mechanical and chemical properties, and/or lower flexibility. 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 biocompatible.

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 particles. In general, plasma-mediated ablation is appealing because the process is independent of laser wavelength and tissue optical properties and enables ultraprecise tissue ablation. 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 µm depth per laser pulse, 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 BPH. 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, etc.).
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 brightness. 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, respectively. 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 short-pulse (nanosecond) modes at wavelengths near (just a few watts) emitting either in continuous-wave or a small tissue depth, sufficient for efficient and precise tissue 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. 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 (λ = 2,120 nm) and thulium:YAG (λ = 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, whereas holmium laser-induced damage has been observed at working distances up to 5 mm, 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 μm) core of the holmium-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 laser.

The multimode beam profile of the holmium laser prohibits coupling of high laser power into small-core fibres (<200 μm) without risking overfilling of the input fibre core and launching of energy into the fibre cladding, which can directly damage the proximal fibre end. Holmium laser beams are typically limited to large diameters (275–500 μm), 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. 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. 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 damage. 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. 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. 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 procedure. Reflection of laser energy at the proximal connector end also increases the probability of proximal fibre destruction and damage to the laser system. 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 connector. Laser blast shields are frequently incorporated into the laser system as a precaution in order to prevent potential damage to the laser optics.

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 use. 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 further.

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). 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 kidney. Smaller fibres can also spur development of smaller ureteroscopic instruments, such as integrated fibres and baskets and miniature ureteroscopes. Multiple reports have also shown that stone retropulsion decreases with decreasing fibre diameter, 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 rod. 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). 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.

**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.
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.

| 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 x length x height) | 55 cm x 46 cm x 29 cm | 47 cm x 116 cm x 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.

**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 laser. 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. 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. They can also
be more easily integrated with other ureteroscopic tools, such as stone baskets\textsuperscript{104}, 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 \textsuperscript{105}. 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 fibre\textsuperscript{106}. 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 fibre\textsuperscript{106}. 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 burnback\textsuperscript{107}. Spherical tip fibres. Spherical tip fibres are commercially available for use in the clinic with the holmium:YAG laser during lithotripsy\textsuperscript{108,109}. 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 diameter\textsuperscript{110}. 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 studies\textsuperscript{111}. 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 surface\textsuperscript{112}. 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
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 burnback. However, use of the hollow tip resulted in increased stone retropulsion and reduced stone ablation rates. 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 reported. 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 burnback.

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 (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 Europe, 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>
<thead>
<tr>
<th>Property</th>
<th>Small</th>
<th>Large</th>
<th>Taper</th>
<th>Spherical</th>
<th>Steel</th>
<th>Muzzle</th>
</tr>
</thead>
<tbody>
<tr>
<td>High flexibility</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>High irrigation</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Low retropulsion</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Low burnback</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>High ablation</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
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 fiberoptic 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 kHz 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 muzzled 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 retropulsion without sacrificing stone ablation rates. Only clinical studies with direct comparison to holmium laser will demonstrate whether this next-generation laser lithotripsy system can replace the holmium laser.

Published online: 08 June 2018
El-Sherif, A. F. & King, T. A. Soft and hard tissue.
Fried, N. M. & Murray, K. E. High-power thulium fibre.
Tunc, B. & Gulsoy, M. Tm:Fibre laser ablation with.
osmotic abdominal schemes.
Nature reviews | Urology
Reviews
NATURE REVIEWS | UROLOGY
© 2018 Macmillan Publishers Limited, part of Springer Nature. All rights reserved.
| Urology
J. Urol.