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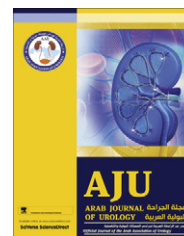


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### REVIEW

# Intracorporeal laser lithotripsy

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#### ABBREVIATIONS

URS, ureteroscopy;  
Ho:YAG, holmium:yttrium–aluminium–garnet; PCNL, percutaneous nephrolithotomy; FREDDY, frequency-doubled double-pulse Nd:YAG; EPS, endoscope-protection system

**Abstract Objectives:** To review the current literature on intracorporeal laser lithotripsy.

**Methods:** We searched PubMed for relevant reports up to January 2012, using the keywords ‘laser’, ‘lithotripsy’ and ‘intracorporeal’.

**Results:** We studied 125 relevant reports of studies with various levels of evidence. Efficient lithotripsy depends on the laser variables (wavelength, pulse duration and pulse energy) and the physical properties of the stones (optical, mechanical and chemical). The most efficient laser for stones in all locations and of all mineral compositions is the holmium yttrium–aluminium–garnet laser (Ho:YAG). The frequency-doubled double-pulse Nd:YAG laser functions through the generation of a plasma bubble. New laser systems, such as the erbium:YAG and the thulium laser, are under evaluation. Laser protection systems have also been developed for the novel digital flexible ureteroscopes. Although complications are rare, a high relevant clinical suspicion is necessary.

**Conclusions:** Laser lithotripsy technology is continuously developing, while the Ho:YAG laser remains the reference standard for intracorporeal lithotripsy.

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#### Introduction

During the last few decades the surgical treatment of urolithiasis has undergone tremendous advances as a result of improvements in technology [1,2]. Currently ureteroscopy (URS) is a precise, minimally invasive surgical intervention that can assess the entire collecting system to treat a stone using intracorporeal lithotripsy [1].

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The implication of laser technology in the development of lithotripter fibres has revolutionised intracorporeal lithotripsy. We searched PubMed (up to January 2012), using the keywords 'laser', 'lithotripsy' and 'intracorporeal'. From the 125 relevant articles of various levels of evidence, we present the most interesting and up-to-date findings.

### Laser lithotripsy variables

The efficient fragmentation of stones of diverse compositions and with minimal collateral tissue damage is primarily contingent on laser variables (wavelength, pulse duration and pulse energy) and the physical properties of the stones (optical, mechanical and chemical) [3]. The pulse duration governs the dominant mechanism in stone fragmentation, which is either photothermal or photoacoustic/photomechanical. Lasers with long pulse durations (i.e.  $> 10 \mu\text{s}$ ) induce a temperature rise in the laser-affected zone, with minimal acoustic waves [3]. Stone material is removed by means of vaporisation, melting, mechanical stress and/or chemical decomposition. Short-pulsed laser ablation (i.e.  $< 10 \mu\text{s}$ ), produces shock waves, and the resultant mechanical energy fragments the stones [3]. As stated in the European Association of Urology guidelines, the most efficient laser system for the treatment of stones in all locations and of all mineral composition is the holmium:yttrium–aluminium–garnet laser (Ho:YAG) [4].

### Ho:YAG laser efficacy

Kang et al. [5] investigated the effect of optical pulse duration on stone retropulsion during Ho:YAG laser lithotripsy. The dynamics of the recoil action of a calculus 'phantom' were monitored using a high-speed camera; the laser-induced craters were evaluated with optical coherent tomography. Bubble formation and collapse were recorded with a fast-flash photography system, and acoustic transients were measured with a hydrophone. The authors showed that shorter pulse duration produced more stone retropulsion than longer pulses at any given pulse energy. Regardless of pulse duration, higher pulse energy and larger fibres resulted in larger ablation volume and retropulsion ( $P < 0.05$ ). For shorter pulse duration, there was more rapid bubble expansion and higher amplitudes of the collapse pressure wave ( $P < 0.05$ ). Therefore, less retropulsion and equivalent fragmentation occurred when the Ho:YAG laser pulse duration increased.

Currently Ho:YAG laser lithotripsy has become the reference standard for both rigid and flexible URS (grade of recommendation: B) [4]. In a 3-year retrospective study on 188 patients treated with semi-rigid URS and Ho:YAG laser, the success rate was 92.7% at the time of URS and 96.7% at 3 months. The recorded fail-

ures were secondary to retropulsion of the stones (3.3%) [6]. Similar efficacy rates of Ho:YAG laser lithotripsy were reported in other studies [7]. A prospective study compared the Ho:YAG laser and pneumatic intracorporeal lithotripsy during URS [8]. The mean lithotripsy time was 24 min in the laser group and 19.8 min in the pneumatic group ( $P = 0.027$ ). The immediate stone clearance rate was higher in the laser group ( $P = 0.001$ ), while stone migration occurred only in the pneumatic group, in 16% of the patients.

For the treatment of impacted ureteric stones a recent study compared the Ho:YAG laser with the pneumatic lithotripter. The overall stone-free rates after a single URS were 97.5% and 80% in the laser and pneumatic groups, respectively ( $P = 0.03$ ). Auxiliary treatments were needed in 2.5% of the patients in the laser group and in 17.5% in the pneumatic group ( $P = 0.05$ ) [9]. Another recent randomised controlled trial compared three different lithotripters during semi-rigid URS for distal ureteric stones [10]. In particular, 69 patients undergoing URS were randomised to three groups, i.e. a LithoClast classic system (EMS SA, Nyon, Switzerland), the Ho:YAG laser and the LMA StoneBreaker™ pneumatic lithotripter (Cook Medical, Bloomington, IN, USA). The stone-free rates were 96%, 97% and 96.5%, respectively. Stone size and the placement of a second working wire were associated with a shorter fragmentation time ( $P < 0.01$ ).

The retrograde endoscopic approach to lower calyceal calculi and the use of the Ho:YAG laser represents one of the latest technological advances in endourology. Intracorporeal *in situ* renal lithotripsy is possible due to the possibility of using laser fibres with flexible ureteroscopes. The reported stone-free rates are 53–87% in various studies [11–13]. Therefore, flexible URS is a reasonable approach for lower-pole lithiasis, especially in obese individuals, patients on anticoagulation, concomitant ureteric calculi and bilateral occurrence [14]. Based on the available reports flexible URS has comparable efficacy to ESWL for the stones of  $< 15 \text{ mm}$  [15,16]. However, clinical experience with the last generation of ureterorenoscopes suggests a clinical advantage of flexible URS over ESWL. A recent study compared flexible URS with percutaneous nephrolithotomy (PCNL) for the stones of 1.5–2 cm [17]. The authors reported similar stone-free rates, both at initial treatment (89.3% vs. 92.8%, for URS vs. PCNL) and for additional intervention (94.6% vs. 97.6%, respectively). Complication rates did not differ statistically, except for the need for transfusion in the PCNL group. It was concluded that flexible URS has acceptable efficacy for medium-sized lower-pole stones. Lastly, a recent study investigated the role of the new digital flexible ureteroscopes in the improvement of lower-pole clearance rates [18]. When compared with standard flexible URS, lower calyx access

was better, with double the stone-free rate (31% vs. 69%).

Even for patients with renal stones of > 2 cm, flexible URS and Ho:YAG laser lithotripsy represent a favourable option for the selected patients [19]. Such cases include patients who did not consent to PCNL, patients on anticoagulation treatment that should not be discontinued, patients with morbid obesity, a solitary kidney, or chronic renal insufficiency [1]. Last, matrix renal stones present a management challenge. Although PCNL is the standard of therapy for large renal matrix stones, flexible URS and laser lithotripsy could also be used. Laser lithotripsy was used in conjunction with a ureteric access sheath to facilitate irrigation of the mucous matrix stone material [20].

### Non-Ho:YAG laser systems

Compared with the simple YAG laser, the rapid absorption in water (3 mm) and minimal tissue penetration (0.4 mm) of the Ho:YAG laser reduce thermal damage and improve the safety profile [4].

The frequency-doubled double-pulse Nd:YAG (FREDDY) laser functions through the generation of a plasma bubble [21]. On collapse of the bubbles a mechanical shock wave is generated, causing fragmentation of the stone. This mechanism of action is in contrast to the Ho:YAG laser, which causes stone destruction by vaporisation. The FREDDY laser presents an affordable and safe option for intracorporeal lithotripsy, but it does not fragment all stones of all compositions, and has no soft-tissue applications. Studies showed that *in vitro* stone fragmentation was significantly greater with the FREDDY laser than with the Ho:YAG laser, suggesting that the FREDDY might offer a low-cost alternative to the Ho:YAG laser [22]. However, stone retropulsion was significantly greater with the FREDDY laser than with the Ho:YAG laser. In a comparative study the Ho:YAG laser-induced damage to endourological tools was significantly higher than with the FREDDY or the flash-lamp pulsed-dye laser [23].

New lasers, such as the erbium:YAG, more effective and more innocuous than holmium, are currently under development [24]. Initial experiments with the erbium:YAG laser showed that it has a better efficiency of lithotripsy and more precise ablative and incision properties than the Ho:YAG laser, but the lack of adequate optical fibres currently limits its use [24,25]. In particular, the high-temperature water-absorption coefficient at the erbium:YAG laser wavelength of 2.94  $\mu\text{m}$  is  $\approx 30$  times higher than that of the holmium laser wavelength, at 2.12  $\mu\text{m}$ , which has translated to a two- to three-fold increase in efficiency for fragmenting stones [25]. Nevertheless, the erbium wavelength cannot be transmitted through the standard available silica fibres; special mid-infrared fibres are needed, and these fibres

are typically less flexible, more expensive and less bio-compatible than silica fibres.

Recent advances in laser technology have resulted in the commercial availability of the thulium laser, which has several potential advantages over other solid-state lasers such as the Ho:YAG [25]. The thulium fibre laser wavelength is tuneable and, when operated in the pulsed mode, it is capable of fragmenting urinary calculi. Furthermore, the thulium fibre laser-beam diameter is only 18  $\mu\text{m}$ , allowing easy coupling of the laser radiation into small-core optical fibres [25]. Such diminutive fibres have a great potential when used with flexible ureteroscopes, in particular in challenging cases, such as access to the lower-pole of the kidney.

### Technical and clinical implications

Classically, during Ho:YAG laser lithotripsy it is necessary to achieve contact with the stone surface [3]. Nevertheless, Chawla et al. [26] showed the validity of non-contact Ho:YAG laser stone fragmentation in an *in vitro* model. Adequate energy and a high frequency optimised the effectiveness of the 'popcorn' method. Settings of 1.0 J and 20 Hz were the most efficient, with a change in weight of - 18% per kJ.

Pressure waves from Ho:YAG lithotripsy are less than with other lithotripsy methods, yet some retropulsion occurs [27]. The duration of the laser pulse can influence shock wave generation and stone migration. A longer pulse width results in less stone movement after one shock and more energy delivery during repetitive shocks. Clinically, this might reduce the need for frequent and troublesome fibre readjustment, and lead to more efficient stone fragmentation. Another prospective multicentre study evaluated a series of reusable Ho:YAG laser optical fibres [28]. That study showed that reusable optical laser fibres were a more cost-effective option than the single-use variants. Also, it was found that fibres with a 365- $\mu\text{m}$  core provided more uses than the smaller 270  $\mu\text{m}$  variants.

Regarding the routine use of a stent, a prospective randomised trial compared unstented vs. routinely stented URS after Ho:YAG laser lithotripsy [29]. In all, 110 patients underwent uncomplicated URS laser lithotripsy. After the procedure, patients were randomised to an unstented or stented group (55 patients each). The stent was routinely placed for 3 weeks. The authors showed that uncomplicated URS laser lithotripsy could be safe without placing a ureteric stent. Patients without stents had a quicker procedure, and less pain and haematuria.

Although PCNL achieves better stone clearance for patients with large renal stones, flexible URS laser lithotripsy achieves acceptable treatment outcomes with a low risk of subsequent stone-related events or interventions [30]. Moreover, the lower relative cost of flexible

URS in these patients can have implications for the development of relevant treatment guidelines [31]. Recently, the use of the Ho:YAG laser in mini-PCNL has been studied [32]. A prospective study was conducted on 273 consecutive patients with staghorn renal stones, who were randomised to undergo multi-tract mini-PCNL with 30-W low-power or 70-W high-power Ho:YAG laser lithotripsy. The operation was significantly quicker in the high-power than in the low-power group (129.2 vs. 105.1 min). Recently, Sea et al. [33] determined the optimal Ho:YAG lithotripsy power settings to achieve maximum fragmentation, minimum fragment size and minimum retropulsion. The authors concluded that with a low pulse energy (0.2 J) there was less fragmentation and retropulsion, and small fragments were produced. At high pulse energy (2.0 J) there was more fragmentation and retropulsion, with larger fragments.

Cordes et al. [34] studied the destruction of stone-extraction baskets during *in vitro* lithotripsy with several lithotripsy methods. The direct application of laser pulses (wavelength 2.1  $\mu\text{m}$ ), irrespective of thickness and shape, led to melting of all wires of the stone-extraction basket in < 50 s. The pure kinetic-functioning lithotripters (electrokinetic-ballistic and pneumatic-ballistic) were not able to destroy any wire within the set time limit of 1 min. In contrast to baskets, newer stone-trapping devices seem to be more resistant to the laser energy [35,36]. In an *in vitro* study on the Accordion device (PercSys, Palo Alto, CA, USA), the Ho:YAG laser caused small perforations of the film of the device, without affecting the Accordion's stability and functionality.

Lastly, upper-tract urothelial carcinoma can be endoscopically managed with the laser [37]. The two commonly described laser sources for this procedure are the Ho:YAG and Nd:YAG. Both lasers achieve good haemostasis and the risk of stricture is less than with electro-fulguration. A ureteric stent is placed at the end of the procedure, and left until a 'second-look' repeat procedure is performed, usually at 6–12 weeks afterwards [37].

### Safety issues

Eye protection is required for the operators of the Ho:YAG laser, although at the energy levels used for the fragmentation of calculi the operator's cornea would be damaged only if it was positioned < 10 cm from the laser fibre [25]. Furthermore, laser fibres frequently damage flexible ureteroscopy components, e.g. the working channel, flexible component cable system, wires and fibre optical systems, during routine flexible URS [38]. The fracture of a laser fibre inside the ureteroscope can destroy the ureteroscopy's fibre-optic bundles that transmit images and light.

The clinical use of the protective FlexGuard sheath (LISA Laser Products, Germany) has been studied [39]. It significantly reduced the amount of force required to insert the laser fibre through the working channel. This reduction in force was protective against mechanical damage caused by laser fibre insertion. However, deployment of the sheath significantly diminished the rate of irrigant flow and the maximal deflection of the flexible ureteroscope.

A novel endoscope-protection system (EPS) against direct laser energy damage during URS has been developed. Xavier et al. [40] evaluated *in vivo* a novel EPS prototype that uses optical feedback from the sensor of a digital flexible ureteroscope to terminate the laser energy on retraction of the fibre. The EPS was highly effective and reliable, as no energy-based ureteroscope damage was recorded with slow and rapid retractions of the activated laser into the ureteroscope.

### Complications

The only true contraindication to laser lithotripsy is the presence of untreated UTI, because of the risk of urosepsis [25]. The laser is one of the safest intracorporeal lithotripters and the most significant complication of its use is the injury of the urothelial tissue adjacent to the treated stone. Well-known complications include a lost stone, ureteric perforation, extravasation and avulsion. As the depth of tissue penetration of the Ho:YAG laser is 0.4 mm, in the vast majority, injuries can be managed conservatively, although a ureteric stricture can be a chronic event.

The rate of development of subcapsular renal haematoma after URS with the Ho:YAG laser is low. In a prospective study of 2848 consecutive patients who underwent laser URS, 11 (0.4%) developed subcapsular renal haematoma after the operation [41]. All these patients were successfully treated conservatively. Chang et al. [42] described a case of a fatal gas embolism that occurred during URS with Ho:YAG laser lithotripsy under spinal anaesthesia. Although the correct crisis resolution protocols took place (reduction in the volume of air entrained, hydration, cardiopulmonary resuscitation) the patient died. Another extremely rare complication after Ho:YAG lithotripsy was the development of an intrarenal arteriovenous bleeding fistula, which was embolised [43].

In case of accidental laser fibre breakage, the detection of the radiolucent fibre remnants might become troublesome. A recent study evaluated a prototype of a radio-opaque laser fibre that was designed for lithotripsy with a Ho:YAG laser [44]. An optical-core gold-clad fibre prototype offered comparable performance to the commercially available fibre of the same optical core diameter. The radio-opaque property was con-

firmed *in vitro* and intracorporeally, thereby adding an additional safety feature to the laser treatment.

## Conclusions

The field of laser lithotripsy is advancing in two different directions, i.e. improvements to the existing Ho:YAG laser platform and the development of novel laser platforms. The most significant improvement in Ho:YAG laser lithotripsy will probably come from fibres with improved delivery. Indeed, the research into new fibres, more flexible, economic and long-lasting, is the future challenge.

## Conflict of interest

No conflict of interest to declare.

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