The evolution of lasers in urology

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***Abstract*:** The world's first laser was developed by Theodore Maiman in 1960. Over the course of the past five decades, this technology has evolved into a highly specialized entity, also finding a niche market in the field of urology. Lasers obtained from various lasing mediums producing amplified light of different wavelengths have been tested for urological applications. Today, these lasers are most commonly used in the surgical management of benign prostatic hyperplasia and as intracorporeal lithotripters. Other uses include ablation of various urologic tumors and incising strictures of the upper- and lower urinary tract. A continuous process of evolution of this technology is taking place, resulting in surgical lasers becoming ever safer, more effective, and more affordable.

***Keywords*:** ablation, laser, lithotripsy, penetration depth, thermal effects, vaporization, wavelength

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Introduction

In broad terms 'evolution' can be seen as changes in characteristics through successive generations, brought on by interactions with the environment. Variants of traits of the original become more common if they aid in survival of the entity: this is referred to as 'natural selection'.

The use of lasers in medicine is not new, and in urology they have been around for more than 40 years. Here too, a form of evolution is taking place. New, streamlined, safe and effective technology that can answer to growing demands is continuously being selected out, and the outdated and hazardous are condemned to history. However, every passing phase is an essential step towards the pinnacle of laser applications in urology.

Lasers: a short history and simplified physics

It was Albert Einstein who in 1917 first proposed the theory of 'stimulated emission': the process by which photons (a 'packet of light energy') with the correct amount of energy could disturb an excited atom and cause it to drop to a lower energy level, in turn leading to the creation of another identical photon. The original photon interacting with the atom, as well as the photon subsequently released will be discharged simultaneously and will therefore have an identical wavelength and direction of propagation [Einstein, 1917].

The concept of stimulated emission was the foundation on which subsequent laser development would be undertaken.

Development of the MASER ('microwave amplification by stimulated emission of radiation') was the first giant leap. Microwaves are electromagnetic waves with fairly long wavelengths (1 mm to 1 m). In 1954, Gordon and colleagues tested the first MASER where stimulated emission at microwave wavelengths (in this case 12.5 mm) was demonstrated in an oscillator [Gordon *et al.* 1954].

The step from MASER to LASER (light amplification by stimulated emission of radiation) took 3 years. The idea was to extend the principle of stimulated emission from the microwave wavelengths to much shorter wavelengths, also including the optical range or visible spectrum of around 390–750 nm. For this, one would need to build an optical oscillator that could generate coherent light by amplifying stimulated emission [Hecht, 2010]. Theodore Maiman was the first to succeed and in 1960 he built the first LASER using ruby crystals as an active medium [Maiman, 1960].

It is the active medium (also referred to as the lasing medium) in a laser that determines the wavelength (and therefore color) and frequency of the light that it emits. The wavelength and frequency are inversely proportional to one another.

In simple terms the design of a laser is basically that of a laser medium placed within an optical resonator, which is defined by two mirrors. Light at the characteristic laser wavelength receives amplification whenever it passes through the excited laser medium. The reflective surfaces of the optical resonator ensure many passes of the light beam through the medium, leading to repetitive amplification. Excitation energy is required for this amplification process and can be derived from an electrical current. A fraction of the amplified light inside the optical resonator escapes as a beam of light out of one or both mirrors.

Early lasers used gas as active medium: nitrogen (N), carbon dioxide (CO_2), helium (He) and neon (Ne). Liquids as medium soon followed: the so-called ‘dye lasers’, because the lasing agent is an organic dye [Gross and Herrmann, 2007]. Dye lasers have the advantage of being able to generate amplified light with a wider range of wavelengths. Some are even tunable. One of the earliest (1964) solid-state lasers utilized Nd:YAG (neodymium-doped yttrium aluminium garnet) as a medium; this is still popular today [Geusic *et al.* 1964].

A classification of laser output of particular practical importance in urology is that of pulsed wave (PW) *versus* continuous wave (CW). During CW operation the output of the laser is continuous and of constant amplitude. The clinical effect is a more controlled interaction with the tissue. PW operation on the other hand, delivers forceful bursts of laser energy, which is useful for stone fragmentation [Teichmann and Herrmann, 1994].

A basic understanding of the light-tissue interaction of lasers is required in order to fully appreciate important aspects such as penetration depth, thermal effects and reflection. These technical terms have major clinical significance. When laser light meets tissue, a percentage of the laser beam will be reflected. The reflected radiation is lost for the surgical purpose and may also cause unintended thermal damage to surrounding areas. Absorption is the most important interaction of laser light with tissue. A chromophore is required in order to achieve absorption: body chromophores accessible for laser light include blood, water and melanin. Absorbed laser light is converted to heat and depending on the amount of heat, the clinical effect will be tissue coagulation or vaporization. Absorption depth is dependent on the wavelength of the laser. Figure 1 illustrates the absorption spectrum of melanin, hemoglobin and water for specific laser wavelengths [Teichmann and Herrmann, 1994].

Over the course of the last four decades, many possible applications of lasers in urology have been investigated. This ‘trial and error’ era of the 1980s was a crucial step in the process of evolution of this technology. Every imaginable use was explored, with varying degrees of success

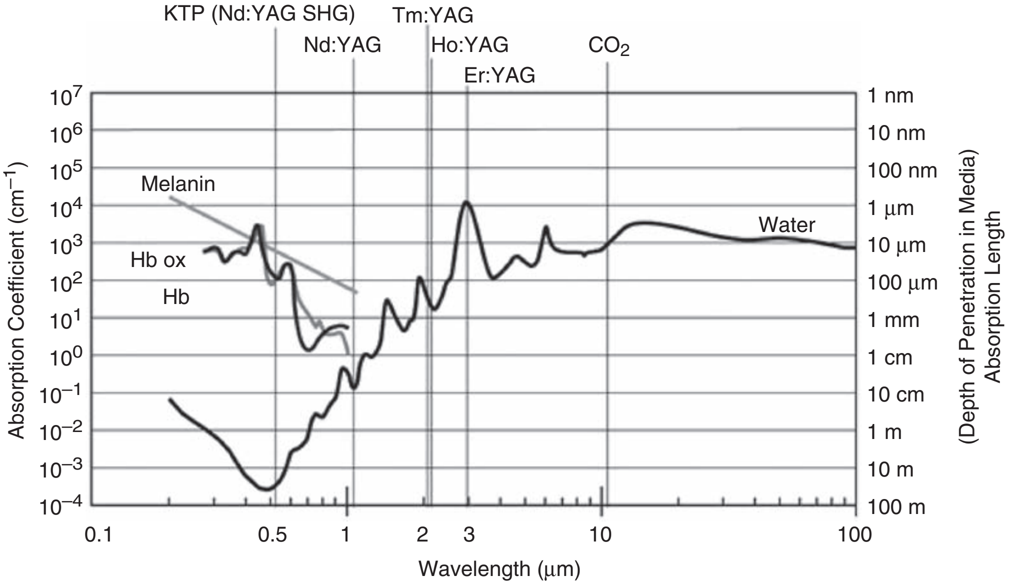

Figure 1. Absorption spectrum of melanin, hemoglobin and water for specific laser wavelengths [Teichmann and Herrmann, 2007].

and applicability. In the end, the safe and effective have remained, and are constantly being refined.

Today, the types of lasers most commonly used in urology include:

- Nd:YAG;
- Ho:YAG (holmium:YAG);
- Thu:YAG (thulium:YAG);
- CO_2 (carbon dioxide);
- KTP (potassium titanyl phosphate);
- LBO (lithium triborate);
- diode laser.

Laser applications in urology

Benign prostatic hyperplasia

The ability of the laser to ablate prostatic tissue with minimal hemorrhage has concentrated most of the interest in urologically applied lasers to benign prostatic hyperplasia (BPH) [Anson *et al.* 1994]. Despite tremendous advances in the surgical and minimally invasive treatment of BPH, transurethral resection of the prostate (TURP) is still considered the ‘gold standard’. The risks of TURP are always mentioned when discussing the reasons for seeking alternative treatment modalities for BPH. Bleeding certainly remains a concern, especially in patients on some form of anticoagulation (heparin, coumarin related compounds, antiplatelet agents) or those with prostates in excess of 60–80 g. On the other hand, with the availability of transurethral resection in saline (TURiS), the TURP syndrome is nowadays considered by many to be a relatively rare complication [Sarf *et al.* 2010].

Although removal of benign prostatic tissue using a laser was first described in 1986, it was only in 1990 that introduction of the ‘side-firing’ (deflecting device at the tip: 60–90°) laser prompted more widespread use of this modality. The Nd:YAG laser was initially the laser most commonly used and is also the one most extensively studied. One of the earliest techniques used for Nd:YAG laser treatment of BPH was called ‘visual laser ablation of the prostate’ (VLAP) [Norris *et al.* 1993]. This involves lasing prostatic tissue in a noncontact fashion to create an area of heat-induced coagulative necrosis that extends about 10 mm into the tissue. The method is reasonably simple to learn and perform, is safe in anticoagulated patients and carries no risk of the TURP syndrome. However, edema and prolonged sloughing of the coagulated tissue leads to irritative lower urinary tract syndrome (LUTS) and urinary retention requiring catheterization, often for long periods (3 months), in up to 30% of cases [Cowles *et al.* 1995].

Another approach in which the Nd:YAG laser can be used is the contact mode, which leads to real-time destruction of prostatic adenoma. A ‘contact tip’ converts laser light to heat, which induces vaporization and immediate creation of a cavity. As with VLAP, no tissue is available for histology, but this approach has the advantages of immediate relief of obstruction, early catheter removal and decreased postoperative LUTS and urinary retention. Tissue ablation advances slowly (so-called repetitive ‘painting’ of the surface that needs to be ablated) and it is therefore not suitable for prostates larger than 40 g. In addition the hemostatic effect is not as good as with VLAP [Floratos and de la Rosette, 1999].

Apart from VLAP and contact ablation, the Nd:YAG laser can also be used for performing interstitial laser coagulation (ILC) of the prostate. First described in 1993 by Hofstetter, the main feature of this method was preservation of the prostatic urethra and its urothelium [Hofstetter and Alvarez, 1993]. The procedure is performed by placing laser-diffusing fibers directly into the prostatic adenoma, either via the transurethral cystoscopic approach, or the perineal approach. Laser energy then produces coagulation necrosis within the adenoma, which subsequently undergoes atrophy [Perlmutter and Muschter, 1998]. As is the case with VLAP, this method is safe in anticoagulated patients, but substantial tissue edema also usually necessitates prolonged (7–21 days) postoperative catheterization. Retreatment rates are problematic: as high as 20% at 2 years, 41% at 3 years and 50% at 54 months. Several authors have concluded that this modality should probably be restricted to selected, high-risk patients. It can be safely performed with a combination of local anesthesia and intravenous sedation [Daehlin and Frugârd, 2007].

KTP laser, green light laser, frequency-doubled Nd:YAG laser and photoselective vaporization of the prostate (PVP) all refer to the same modality. Passing the Nd:YAG laser beam (wavelength 1064 nm, invisible) through a KTP crystal doubles the frequency and halves the wavelength (532 nm, visible green light). This wavelength is strongly absorbed by hemoglobin and therefore has a very short absorption depth in well-vascularized tissue such as the prostate [McAllister and Gilling, 2004]. It is used in a noncontact fashion, causes immediate vaporization of prostatic tissue and is a virtually bloodless procedure. Due to the limited absorption depth, necrosis of the tissue underlying the vaporized area, with subsequent edema, is not a problem. Some authors have reported discharging patients on the day of surgery without a catheter, even those with prostates sizes in excess of 100 g [Barber and Muir, 2004].

Application of the KTP laser has changed tremendously over the years. It started out as part of the 'hybrid technique' that involved VLAP with the Nd:YAG laser followed by bladder neck incision using the KTP laser at a low-power setting (34 W). The theory of these 'hybrid techniques' was that the additional KTP laser incisions would reduce the Nd:YAG laser's troublesome postoperative irritative symptoms and need for prolonged catheterization [Barber and Muir, 2004]. Further research was aimed at increasing the power output of the KTP laser, initially to 60 W. Although originally a pulsed wave laser, modifications to the system furthermore facilitated the delivery of pulses so rapidly that the effect of continuous wave delivery was created. All of these improvements heralded the 'high-power' era of KTP lasers: they were now being used for prostate vaporization independently from the Nd:YAG laser. Today, 'high-power' KTP laser prostatectomy refers to a power output of 80 W.

The 120 W lithium triborate (LBO) laser was the next step in the evolution of the 532 nm lasers. The aim with this system was to overcome the still relatively slow tissue ablation ability of the 'high-power' 80 W KTP, which leads to time-consuming procedures in patients with large prostate glands [Wosnitzer and Rutman, 2009]. Not only is energy transfer and tissue ablation faster and more efficient, but the working distance is also increased (working distance for KTP is 0.5 mm, for LBO it is up to 3 mm), making the LBO laser technically simpler to use. Unfortunately, a drawback of the higher power setting is a reduction in the hemostatic ability, as demonstrated in a recent study in an *ex vivo* model [Heinrich *et al.* 2010].

The Ho:YAG laser is a pulsed laser with a wavelength of 2140 nm. Some consider it to be the pinnacle of evolution of urological lasers: not only is it ideally suited for procedures on the prostate, but it is also extremely effective as an intracorporeal lithotriptor for most stones. In addition it can be used in the setting of ablation of urothelial tumors and incision of strictures of the upper and lower urinary tract [Kuntz, 2006]. The following features of the holmium laser make it such a useful instrument in prostate surgery:

- Absorption depth in the prostate is only 0.4 mm, creating a high energy density sufficient for vaporization.
- Dissipating heat causes simultaneous coagulation of small blood vessels to a depth of about 2 mm.
- This enables precise, char-free and virtually bloodless incision in prostatic tissue.

The holmium laser proceeded through many of the same 'evolutionary processes' as the some of its predecessors. Initially, it was also used in 'hybrid techniques' (VLAP with the Nd:YAG laser followed by creation of a tunnel and bladder neck incision with the Ho:YAG laser, to attempt shortening of the postoperative catheterization time) just like the early KTP lasers [Gilling and Frauendorfer, 1998]. The next step was prostate vaporization in the same 'painting' fashion as the Nd:YAG and KTP lasers. Although the procedure (called HoLAP, holmium laser ablation of the prostate) was easy to learn and effective, it was once again too time consuming when dealing with larger prostates. This led to the development of HoLRP (holmium laser resection of the prostate) which basically simulates traditional TURP [Gilling *et al.* 1996]. Chips of prostatic tissue are resected with an end-firing laser fiber and the chips are then removed via the urethra. This method is not only technically quite difficult to master, but operative times are still too long in patients with large adenomas. Refinement of the holmium laser technique and development of an efficient tissue morcellator led to HoLEP (holmium laser enucleation of the prostate)-finally size was no longer an issues. This procedure simulates open prostatectomy where the entire adenoma is removed at the level of the surgical capsule. The Ho:YAG laser ensures bloodless incision followed by blunt dissection using the cystoscope and laser fiber as an 'index finger' [Elzayat and Elhilali, 2006].

The Thu:YAG laser is the newest addition to the urologists laser armamentarium and use of this laser for BPH surgery was first published in 2005 [Xia *et al.* 2005]. This report described the so-called 'thulium laser resection of the prostate tangerine technique'. The next step was vaporesection (simultaneous resection of TURP-like chips and vaporization of tissue), which was proven to be safe and effective [Bach *et al.* 2009]. The final leaps came with 'Thu:YAG vapo-enucleation', followed by ThuLEP (thulium laser enucleation of the prostate) [Bach *et al.* 2010]. When compared with the holmium laser, thulium seems to deliver improved vaporization ability, ensuring smooth tissue incisions. This allows the surgeon to accurately remove the adenoma at the level of the surgical capsule, as this plane is easier distinguishable. Virtually any sized prostate can be removed transurethrally using this technique.

Diode lasers have been around for a long time, but their clinical application has thus far been limited when compared to the other lasers. There now seems to be some renewed interest in these lasers as an alternative to KTP or LBO for vaporization techniques. As mentioned previously, for KTP and LBO lasers power *versus* hemostasis is somewhat of a 'catch 22' situation: the increased power of the 120 W LBO certainly cuts down on operative times, but this is at the cost of hemostatic ability, which is much better when using the lower powered 80 W KTP system. However, lower power means longer duration of procedures. A recent report on a 980 nm diode laser device demonstrated better hemostasis during prostate vaporization when compared with a 120 W LBO laser. Unfortunately the diode laser was also associated with a higher incidence of complications such as postoperative irritative symptoms and epididymitis [Chiang *et al.* 2010].

Stones

Initial reports on the use of the pulsed dye laser for stone fragmentation appeared in 1987 [Dretler *et al.* 1987]. This was a very promising new technology enabling endoscopic fragmentation of more than 80–95% of stones and urothelial injury being rare. Drawbacks were very high initial costs and expensive disposables (coumarin dye), as well as trouble with fragmentation of notoriously 'hard' stones composed of calcium oxalate monohydrate (COM) and cysteine [Floratos and de la Rosette, 1999].

The FREDDY (frequency doubled double-pulse Nd:YAG) laser was the next step in laser lithotripsy, and consists of a KTP crystal incorporated into a Nd:YAG laser [Marks and Teichman, 2007]. This enables the laser to produce two pulses: a 20% green light component at 532 nm and an 80% infrared component at a wavelength of 1,064 nm. This combination works in synergy to enable highly effective stone fragmentation, mainly via a mechanical shockwave with very little thermal effects. Another major advantage is the extremely low risk of damage to the ureteral wall when using this laser [Yates *et al.* 2007]. Unfortunately the 'hard' types of calculi also present a challenge to this laser, as is the case with the pulsed dye lasers [Dubosq *et al.* 2006]. Another problem is that the FREDDY laser is only able to effectively fragment dark or colored stones that absorb the green wavelength. Some urologists later referred to it as the 50% laser because only about 50% of stones could be treated with it.

The alexandrite laser was introduced in 1991 and even though initial results were promising, there was never widespread acceptance of this laser for use as a lithotriptor [Pearle *et al.* 1998].

Owing to the high costs when investing in a urological laser, the ideal would be to have a system with applications in various pathological conditions. The drawback of the FREDDY lasers negligible effect on soft tissue is that it can be exclusively used for stone procedures. The use of the Ho:YAG laser in BPH surgery was discussed earlier and this laser has also become the one most commonly used for lithotripsy [Lee and Gianduzzo, 2009]. Fragmentation occurs through a photothermal effect and requires direct contact of the laser tip with the stone [Pierre and Preminger, 2007]. A major advantage is minimal retropulsion effects during stone fragmentation [Cinman *et al.* 2010]. What puts this laser 'at the top of the food chain' is its ability to fragment all types of stones, including cysteine, brushite and COM [Leveillee and Lobik, 2003]. The holmium laser can either reduce stones to tiny fragments that are easily cleared from the collecting system with outflow or irrigant, or larger stones can be broken up and fragments removed using baskets or grasping forceps [Bagley, 2002].

Other

As far as other applications of lasers in urology are concerned, none have evolved as far as in the case for the management of BPH and urolithiasis discussed above. The process of investigating the appropriateness of the use of a specific laser in a specific urological condition is ongoing, and in many of the instances that will be discussed, it is an exercise of re-evaluation and refinement. In most cases it is still 'a work in progress'.

Transitional cell carcinoma. Parsons was the first to experimentally use a pulsed ruby laser on an opened canine bladder [Anson *et al.* 1994]. In the setting of transitional cell carcinoma (TCC), the Ho:YAG and Nd:YAG lasers are the ones most frequently used for treating lesions located in the renal pelvis and ureter. The development of thin, flexible ureterorenoscopes as well as improvement of previously inadequate biopsy devices have helped establish lasers as a safe and effective option for managing these relatively uncommon but troublesome tumors [Bagley and Grasso, 2010]. The Nd:YAG laser coagulates tissue to a depth of several millimeters (5–10 mm) and is appropriate when dealing with large tumors. Direct contact of the laser fiber with the tumor is unnecessary and should be prevented, as this causes charring at the tip of the fiber with a resulting decrease in the effectiveness of the laser. The depth of penetration of the Ho:YAG laser is significantly less (0.4 mm), which makes this a much safer choice when dealing with small tumors in the ureter [Phillips and Landman, 2007].

Photodynamic therapy (PDT) for superficial TCC of the bladder is a diagnostic and treatment modality where laser light can be used. The PDT mechanism relies on *in situ* generation of toxic agents by the activation of a light sensitive drug (also called the 'photosensitizer') [Pinthus *et al.* 2006]. The drug is instilled into the bladder and thereafter activated cystoscopically by light of an appropriate wavelength. Diode lasers are popular here as they can be produced to match the desired wavelengths of most photosensitizer drugs (630–760 nm), but other light sources can also be used. The use of PDT in prostate cancer, renal cell carcinoma, and malignant lesions of the penis has been investigated [Stables *et al.* 1999; Pomer *et al.* 1995; Windahl *et al.* 1990].

Strictures of the upper and lower urinary tract. Reports on the use of an argon laser for the treatment of urethral strictures date back to 1978. Using the laser instead of a cold knife, in the same way as was initially described by Sachse [1978], seemed to be effective, but further follow up revealed a high recurrence rate of up to 70.1% at a mean of 15.2 months [Becker *et al.* 1995]. Other lasers that have also been investigated include the Nd:YAG, KTP and Ho:YAG lasers. There is still a lack of sufficient long-term data and therefore the role of lasers in the treatment of urethral strictures and also vesico-urethral strictures after radical prostatectomy has yet to be defined [Bader *et al.* 2010]. More recently, the Thu:YAG laser was investigated in this setting. Its penetration depth of only 0.3 mm should cause very little injury to surrounding tissue, making it an ideal instrument for optical urethrotomy [Wang *et al.* 2010].

Ureteropelvic junction (UPJ) obstruction can also safely be managed with endopyelotomy using the Ho:YAG laser. Results seem to be more or less similar to those achieved with the 'hot-wire balloon' [Lee and Gianduzzo, 2009]. The holmium laser is also effective in the minimally invasive treatment of ureterovesical anastomotic strictures after renal transplant as well as ureterointestinal anastomotic strictures after urinary diversion [Kristo *et al.* 2003].

Laser tissue soldering. Laser tissue soldering (LTS) has been used to obtain a watertight anastomosis in different tissues for more than 20 years. A diode, CO_2 or Nd:YAG laser can be used with albumin as a solder [Kirsch *et al.* 1995]. LTS relies on the photothermal properties of laser light. When performing LTS, laser energy is applied to a solder in conjunction with laser wavelength-specific chromophores to facilitate laser light absorption. The resultant temperature increase denatures the solder, which then forms a coagulum that increases the strength at the repair site [Lee and Gianduzzo, 2009]. In urology it has been successfully utilized in anastomosis of skin (hypospadias repair), bladder, urethra, renal pelvis (UPJ repair), as well as for vasovasostomy. In order to safely perform LTS, the laser power needs to be regulated: although higher power densities provide a stronger initial weld, there will be increased thermal damage to surrounding tissue which compromises tensile strength of the repair after a few days. Average soldering speed is around 1 minute per centimeter of incision length [Cooper *et al.* 2001].

Penis carcinoma. It is generally accepted that the risk of metastases is low for patients with penile squamous cell carcinoma exhibiting favorable histologic features (stages Tis Ta, T1, grades 1–2). Laser ablation is one of the organ-preserving therapeutic strategies that may be considered in these cases [Busby and Pettaway, 2005]. The CO_2 laser is often used in this setting. Some centers have combined it with the Nd:YAG laser to increase the depth of tissue necrosis in the tumor base [Windahl and Andersson, 2003].

Prostate carcinoma. The possibility of focal laser ablation (another term for interstitial laser coagulation) of localized prostate cancer has recently been investigated. Focal laser ablation of unresectable liver metastases and inoperable hepatocellular carcinoma has been studied more extensively. The Nd:YAG laser or diode laser can be used. An exciting recent innovation is the ability to monitor in real-time the lesion created by the laser using magnetic resonance imaging [Lindner *et al.* 2010].

Genital skin lesions. Condylomata accuminata can occur on the prepuce, glans, penile shaft and intra-urethrally. The CO_2 laser has been used since the late 1970s to vaporize multifocal, small lesions. For larger condylomata, coagulation with the Nd:YAG laser was later introduced. Intra-urethral lesions can be treated using the Nd:YAG or KTP laser [Stein, 1986]. Owing to the risk of dispersion of the oncogenic virus in the aerosol, laser vaporization of condylomata is not recommended in patients with HIV [Lee *et al.* 2001].

Future prospects

Current shortcomings of urological lasers include the high cost of the technology, relatively complex hardware and collateral injury to surrounding normal tissue [Pierre and Albala, 2007]. New lasers are continuously being developed: one of the more recent ones introduced for possible use in urology is the erbium:YAG (Er:YAG) laser. It operates at a wavelength of 2940 nm and can be used in all of the applications where the Ho:YAG laser is used. In an aqueous solution, this laser has a penetration depth of only 3 μm. Early studies seem to indicate that the Er:YAG laser may be slightly more effective than the holmium laser at breaking up stones [Fried, 2001]. Unfortunately there are still some unresolved issues: normal silica fibers cannot be used for this laser and the alternative materials are extremely expensive and potentially toxic. The hemostatic ability at this wavelength is also insufficient.

The year 2010 marks the 50th anniversary of the laser. This technology has changed and evolved tremendously over the course of five decades, but there is still ample room for improvement. During the next 50 years we can expect for even more applications of this versatile technology to be imagined, tested and eventually accepted.

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Conflict of interest statement

None declared.

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