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## **Laser lithotripsy**

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**INTRODUCTION** – Gallstone disease continues to be a major health problem throughout the world, affecting approximately 10 to 20 percent of the Caucasian population [1]. (See "Epidemiology of and risk factors for gallstones"). Ten percent of patients also have gallstones in their biliary ductal system which, in most cases, can be removed endoscopically [2].

A variety of methods have been devised for extracting stones that are not easily removable using standard methods (ie, a retrieval basket or a balloon). As a general rule, these involve methods to crush or fragment the stone (known as lithotripsy). Examples include mechanical, electrohydraulic, and extracorporeal shock wave lithotripsy [3]. (See "Endoscopic management of bile duct stones: Standard techniques and mechanical lithotripsy").

More recently, lithotripsy has been accomplished using laser light [4]. This topic review will discuss the theoretical background, equipment, indications, technique, and clinical effectiveness of laser lithotripsy. Standard methods for removing gallstones within the biliary system are discussed separately. (See "Endoscopic management of bile duct stones: Standard techniques and mechanical lithotripsy").

**THEORETICAL BACKGROUND** – Only a few months after the discovery of a new form of stimulated emission in 1960, laser (light amplification of stimulated emission of radiation) devices that were based upon laser light were introduced into the medical arena. Laser light is monochromatic, coherent, and collimated, creating a narrow beam of energy suitable for therapeutic applications in many medical specialties [5]. Laser-tissue interactions produced by medical lasers primarily involve photocoagulation, photothermal ablation (vaporization), and photochemical ablation.

In the field of gastroenterology, these phenomena have been used for a number of applications including palliation of advanced gastrointestinal cancer, curative ablation of early carcinoma or high-grade dysplasia in patients with Barrett's esophagus, and treatment of bleeding peptic lesions or angiodysplasias [6]. (See appropriate topic reviews.) Photodisruption induced by ultrashort pulses of laser light is also gaining wider attention as an effective treatment for intraductal gallstones (show picture 1).

**Laser lithotripsy** – The underlying principle of laser lithotripsy is the generation of a high-energy shock wave capable of fragmenting intraductal gallstones (show picture 2). The original continuous-wave lasers (eg, cw-Nd:YAG) were inefficient for stone fragmentation because they caused drilling effects in the gallstones and thermal melting instead of lithotripsy. In addition, cw-lasers emit radiation energy over a long period of time, which may lead to increasing temperatures on the stone surface and surrounding



tissue [5].

In contrast, pulsed laser systems reduce the risk of thermal injury significantly since power peaks may reach the gigawatt range (10 billion W), but only for fractions of a second [7]. This is accomplished by using a small amount of energy delivered during an extremely short pulse duration. Two categories of lasers are used for laser lithotripsy, both of which can achieve these objectives (see below):

- Flashlamp-pumped pulsed dye lasers (eg, coumarine dye, rhodamine-6G dye)
- Pulsed solid-state lasers (eg, q-switched neodymium:YAG [8], alexandrite, holmium:YAG [9-11])

Flashlamp-pumped dye lasers are usually operated at pulse durations within the microsecond-range while q-switched solid-state lasers are operated at pulse durations within the nanosecond range. Thus, pulsed systems are most efficient at fragmenting stones and reducing the risk of injury to surrounding tissues.

**Generation of a shock-wave** – Focusing the laser light to a power density of >100 billion W/cm<sup>2</sup> achieves so-called "nonlinear optical effects" in which electrons are torn away from their atomic nuclei and matter is transformed into a plasma state (a gaseous collection of ions and free electrons) at the stone surface and within adjacent fluid. The plasma expands at supersonic speed, inducing a spherical shock wave. Oscillation of the plasma bubble (cavitation) may cause further mechanical effects, such as tensile or compressive waves directed at the stone. This transformation of optical energy into mechanical energy is commonly called "optical breakdown" [7,12].

**Tissue effects** – Laser-induced shock waves are ideally supposed to hit gallstones precisely within the biliary tree without affecting the biliary epithelium. However, in clinical practice, stone targeting under direct vision or fluoroscopic control can be difficult or impossible due to anatomic variations, bouncing fragments, or floating debris.

Although nonlinear optical breakdown does not cause significant thermal energy exposure to the bile duct wall, potential hazards exist during laser lithotripsy [13]. Several in vitro and in vivo animal studies have demonstrated that deep penetration or perforation can occur if the laser fiber has perpendicular contact with bile duct (show picture 3). The extent of damage does not seem to differ depending upon laser systems (dye lasers versus solid-state lasers) or laser fibers (bare fiber versus optomechanical coupling) [8,9,14], but is clearly worsened with increasing pulse energies and exposure time. Direct tissue contact should be avoided during laser lithotripsy.

**EQUIPMENT** – As mentioned above, lasers used for lithotripsy are pulsed solid-state lasers (eg, q-switched neodymium:YAG [8], alexandrite, holmium:YAG [9-11]) or flashlamp-pumped pulsed dye lasers (eg, coumarine dye, rhodamine-6G dye). Optical fiber delivery systems of laser light are constantly being improved [15]. Both systems have advantages and disadvantages with regard to efficiency, tissue side effects, light transmission fibers, maintenance, and costs [5,16]. The costs of these systems is substantial (approximately \$100,000).

The most commonly used lasers were the coumarine dye laser (Candela Laser



Corporation, Massachusetts USA), operated at pulse energies up to 140 mJ with repetition rates up to 10 Hz, pulse duration 2.4  $\mu$ s, transmitted through a 200  $\mu$ m bare quartz fiber [17-19], and the rhodamine 6G dye laser (Lithognost, Telemit/Baasel Lasertechnik, Starnberg, Germany), operated at pulse energies up to 150 mJ, pulse repetition rates up to 10 Hz, pulse duration of 2.5  $\mu$ s, with flexible quartz fibers of 250 to 300  $\mu$ m in direct contact with the stone [20-24].

**Stone tissue detection systems** – The rationale for a stone tissue detection system (STDS) is to provide laser systems with a "feedback" mechanism to avoid accidental laser radiation to the biliary epithelium during laser lithotripsy [25]. One such system (Lithognost, Telemit Electronic, München, Germany) is based upon spectroscopic analysis of backscattered light. The system (referred to as an optical STDS) uses a small fraction of laser pulse energy (1 to 2 percent) to induce characteristic fluorescent radiation at the surface of the target, which can be used to differentiate the stone from surrounding tissue.

The fluorescent light travels back through the same laser fiber that emitted it. Its intensity in a spectral range is subsequently analyzed. The STDS senses that the fiber is not in contact with the stone if the intensity of the backscattered light is below a predefined threshold value approximately 190 ns after the onset of the laser pulse. The laser pulse (which has a long pulse duration of 2.5  $\mu$ s compared with the measuring interval of 0.2  $\mu$ s) is then automatically cut off by a fast optical switch. Thus, a maximum of only 5 to 8 percent of laser pulse energy could be misapplied, minimizing tissue absorption and possible injury [20,23,26].

Current versions of the optical STDS are coupled to a rhodamine 6G dye laser. More recently, a new piezoacoustic STDS (paSTDS) coupled to a frequency-doubled Nd:YAG laser has been proposed, but awaits further evaluation [16,27].

**INDICATIONS** – Gallstone disease is frequent in most populations throughout the world [1]. Despite advances in the treatment of gallstones, the incidence of clinically apparent common bile duct stones has not declined in recent years. The development of endoscopic sphincterotomy in 1974 revolutionized the ways in which common bile duct stones were treated by permitting stone extraction from the bile duct with the Dormia basket or balloon catheters via a therapeutic side-viewing endoscope [2,28].

Large stones lodged within the bile duct require fragmentation before they can be removed endoscopically. This has been traditionally accomplished using mechanical lithotripsy, which is successful in approximately 90 percent of patients [3]. In the remaining 10 percent, gallstones resist conventional fragmentation due to size (>2 cm), consistency (eg, bilirubin stones), anatomical position (eg, impaction), or accessibility (eg, intrahepatic stones) [18,29]. Shock wave technology circumvents many of these limitations. Shock waves can be generated outside the bile duct (extracorporeal shock wave lithotripsy) and within the bile duct using electrohydraulic or laser technology [30-33].

**Electrohydraulic lithotripsy** – Electrohydraulic lithotripsy (EHL) is the least expensive approach to stone fragmentation because of the relatively low cost of the lithotripter machine (approximately \$10,000). However, it has not gained wide acceptance due to the inherent risk of bile duct damage [14]. The risk of bile duct damage is in part due to



the lack of an STDS for EHL; control of the shock waves depends upon visual guidance only [34].

The development of thinner (7Fr), steerable, and more durable choledochoscopes (eg, ERCP-Scope, Polydiagnost, Pfaffenhofen, Germany) may renew interest in this approach [35,36]. The miniscopes can be used via the working channel of a standard duodenoscope and permit targeting of bile duct stones even in awkward locations (show picture 4). (See "Electrohydraulic lithotripsy in the treatment of bile and pancreatic duct stones").

**Extracorporeal shock wave lithotripsy** – Extracorporeal shock wave lithotripsy (ESWL) is technically challenging and cost-intensive. The original machines required patients to be placed under general anesthesia while the procedure was performed with patients immersed in a water bath. Third generation machines do not need a water bath or general anaesthesia, making ESWL more practical. (See "Nonsurgical treatment of gallstone disease").

Despite this advance, ESWL still has a number of limitations. Several treatment sessions are required and complete ductal clearance is not always achieved, particularly with large or intrahepatic stones [18,37].

**Laser lithotripsy** – As discussed above, the main advantage of laser lithotripsy is that it permits precise targeting, thereby reducing the risk of bile duct injury. Only laser lithotriptors can be coupled to a stone tissue detection system (STDS). In addition, laser lithotripsy may be suitable in a multitude of unusual clinical situations. Laser-induced shock waves have been used successfully to disintegrate intraductal stones that had become impacted in a Dormia basket [38], to perform lithotripsy under solely fluoroscopic control in patients who have undergone a Billroth II gastrectomy [39], and to manage Caroli's disease [40]. Giant gallstones entrapped in the duodenal bulb (Bouveret's syndrome) could be fragmented non-invasively [41,42], albeit this approach can be complicated by distal gallstone ileus [43].

Laser lithotripsy of pancreatic duct stones is still in its infancy [44]. Preliminary reports advocate the use of pancreatoscopic laser lithotripsy in selected groups of patients [45].

**TECHNIQUE** – Staff using medical lasers should have formal training in laser safety involving all aspects of the biological effects and hazards of laser irradiation. Laser safety regulations should be enacted and thoroughly followed. Those interested in using lasers should attend training courses teaching laser principles including basic laser physics, laser tissue interaction, discussions of the clinical speciality field, and receive hands-on experience.

During laser operation, a laser warning sign should be posted at the door and the door should be kept closed. Laser eye protectors should be available at all times.

Prior to inserting the optical fiber into the endoscopic delivery system, the laser should be adjusted and calibrated for output power and then placed in the off or stand-by mode. The laser fiber should be secured to the endoscope to prevent inadvertent dislodgement.

**Hepatobiliary access** – The biliary tree can be accessed by two different routes: peroral



or transhepatic [29,35,46]. Peroral retrograde endoscopy with a side-viewing therapeutic duodenoscope (or less commonly with a forward viewing gastroscope) is considered the standard approach to the bile duct for the performance of stone fragmentation (show picture 4) [4,18-20,23,47,48]. No randomized studies have been performed that directly evaluate stone fragmentation and ductal clearance rates depending upon the route of hepatobiliary access. However, in certain clinical settings, only the percutaneous transhepatic approach can permit successful access to the bile duct (eg, Billroth II gastrectomy situations) or to the stones (eg, giant stones in a tortuous biliary system, stones above severe biliary strictures and intrahepatic stones) [22,26,49].

Although the percutaneous transhepatic approach has been increasingly used, it is still considered to be more invasive and time-consuming compared to the peroral approach. Because of the inherent risk of complications associated with the creation of a cutaneobiliary fistula (eg, subcapsular liver hematoma, hemobilia, biliary infection), the percutaneous approach should be limited to cases not amenable to retrograde procedures [50].

**Fragmentation procedure** – Stone targeting and laser-induced disintegration can be performed under fluoroscopic or direct visual (endoscopic) control. The originally described fluoroscopy-guided laser lithotripsy had a multitude of technical problems [17]. Because the procedure was performed blindly, the prerequisites for effective shock wave lithotripsy (perpendicular positioning of the laser beam to the stone and bathing in the irrigation fluid) could not always be achieved. In addition, there were reports of bile duct injury (eg, hemobilia).

The newer devices permitted adjustment of the laser fiber by providing an acoustic signal, which indicated that the fiber was in contact with the stone or tissue. However, these were not always reliable [26].

The development of mother-baby endoscopy allowed for visual control during laser lithotripsy. However, a major limitation to this approach is that it requires two dedicated and experienced endoscopists and fragile equipment [35,50]. This limitation may be improved with the emergence of steerable 9Fr/7Fr miniscopes, which can be passed through the working channel of a standard endoscope [36,37]. However, regardless of the device used, the view is often obscured during stone disintegration due to floating fragments and sludge formation. Adequate flushing is more easily achieved during the percutaneous compared to the peroral approach [17,18]. (See "Cholangioscopy and pancreatoscopy" and see "Percutaneous transhepatic cholangioscopy").

As described above, laser-induced lithotripsy coupled with an automatic stone tissue detection system permits stone fragmentation by means of fluoroscopy-assisted targeting, as in conventional ERCP, in a blind although intelligent fashion [20,23,25,26]. On average, one-third of laser pulses are delivered to the stone or its fragments due to the automatic cut-off of laser energy [25]. It is possible that combined application of lithotripsy under visual control with stone tissue discrimination systems may further improve the therapeutic laser intervention with regard to safety and efficacy [18,23].

**CLINICAL EFFECTIVENESS** – Few studies have directly compared the efficacy and safety of different lithotripsy techniques. In most series, the combined use of extracorporeal and intracorporeal lithotripsy methods achieved disintegration rates of



nearly 100 percent and ductal clearance rates of approximately 90 to 95 percent without serious procedure-related complications [3,24,51]. The combined extra-/intrahepatic approach has also been successful for more than 90 percent of intrahepatic stones [48]. ESWL has advantages compared to other approaches for treatment of intrahepatic stones, which are more difficult to treat than extrahepatic stones [3,47,52]. On the other hand, laser lithotripsy appears to be superior to ESWL in achieving clearance of extrahepatic stones while requiring fewer sessions [22,24].

The largest experience with laser lithotripsy has been in Europe, where it is used routinely by at least three groups [20,26,47]. The Erlangen/Wiesbaden group prospectively evaluated laser lithotripsy in 60 patients with giant or impacted common bile duct stones that were refractory to mechanical lithotripsy [20,23]. In most patients (78 percent), laser application and stone disintegration was monitored by fluoroscopy only. At the end of treatment, 87 percent of patients were stone free. Side effects (hemobilia, pancreatitis, and cholangitis) occurred in five patients, but could be treated conservatively [16].

The Ludwigshafen group evaluated 30 patients treated with laser lithotripsy with STDS (19 who had extrahepatic and 11 who patients had intrahepatic stones) [47]. Initial treatment was performed under fluoroscopic guidance but switched to choledochoscopic guidance if the stone could not be adequately approached. Successful stone fragmentation was achieved in 17 of the 19 patients (90 percent) with extrahepatic stones (only one required choledochoscopy), and 7 of the 11 patients with intrahepatic stones (64 percent), although choledochoscopy was required in nine (90 percent). Thus, 24 of the 30 patients (80 percent) were stone free after treatment with laser lithotripsy alone.

The Düsseldorf group recruited 38 patients with bile duct stones (mean number 3.6/mean diameter 25 mm) of which 37 were successfully treated by laser lithotripsy in 1.3 sessions, lasting 15 to 115 minutes without major complications [26]. Stone disintegration was achieved under fluoroscopic targeting or the limited visual control provided by miniscopes.

A Japanese group applied flashlamp-excited dye laser lithotripsy successfully to 12 of their patients with impacted biliary stones via a small choledochoscope [53]. No adverse effects were reported [53]. Surgeons from the University of Texas were able to clear the biliary system from difficult-to-treat stones in a single therapeutic session by means of the holmium:YAG laser lithotripter [54].

**Conclusions** – The available data suggest that laser lithotripsy combined with STDS is highly effective and safe for the fragmentation and extraction of difficult-to-treat gallstones. However, the enormous costs of today's laser lithotriptors will limit their routine use to a few centers specialized in the treatment of gallstone disease.



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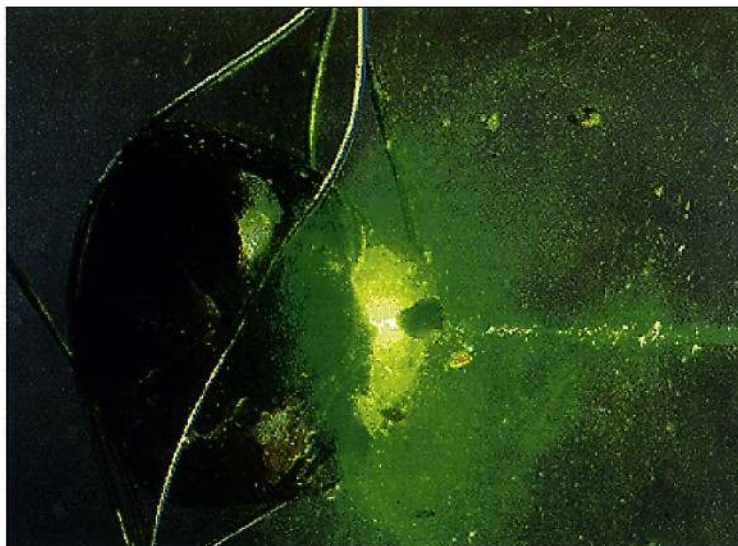


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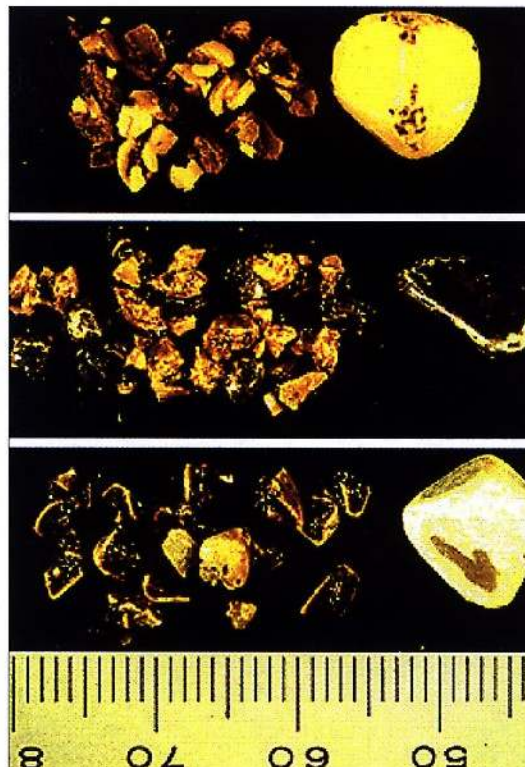
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**Laser lithotripsy** A large stone grasped with a basket under direct exposure of the laser beam. A greenish "plasma" is seen generating shock-waves to break up the surface of the stone. Reproduced with permission from Berlien, Laser und Medizin-Technologie gGmbH (LMTB), Berlin from H, Muller, G. Angewandte Lasermedizin: Lehr- und Handbuch für Praxis und Klinik, ecomed verlagsgesellschaft 1990.

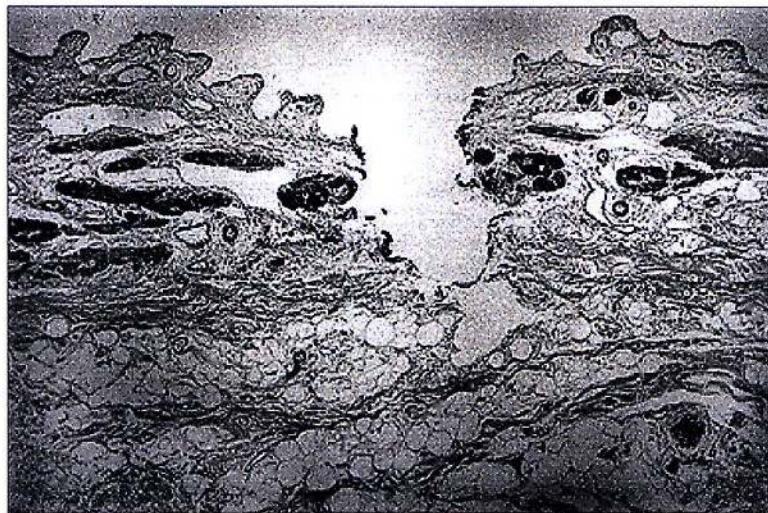




**A cholesterol stone before and after in-vitro laser lithotripsy**

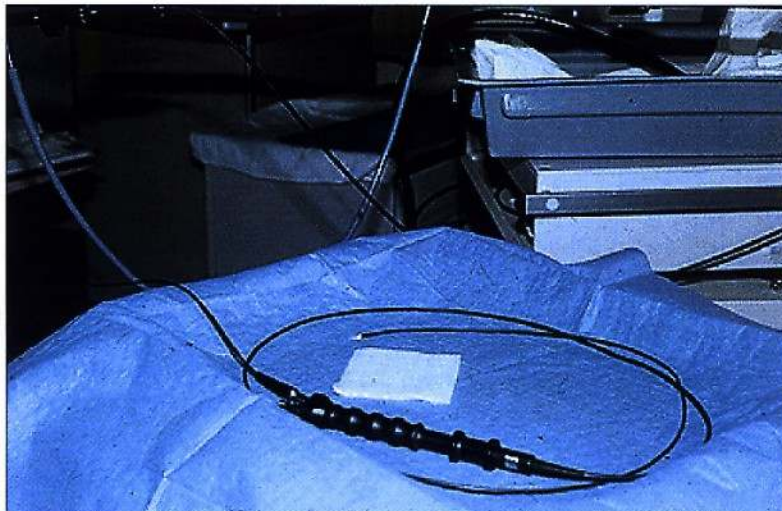
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**In-vitro experiments on human gallbladders with direct perpendicular exposure of the gallbladder mucosa** The laser fiber tip has creating a narrow channel penetrating the wall up to the serosa. (From Lingenfelser, TH, Routschka, A, Grossman, T, et al. Flashlamp exited pulsed dye laser and electrohydraulic lithotripsy: In vitro study on tissue effects. J Stone Dis 1993; 5:118. Copyright © 1993 Futrua Publishing Company, Inc.)





**Miniscope (choledochoscope)** A choledochoscope can be introduced via the working channel of a therapeutic side-viewing duodenoscope for retrograde access to the biliary system. The system can be worked by one endoscopist and one endoscopy nurse only. Courtesy of Thomas Lingenfelser, MD, PhD.