

Laser lithotripsy of difficult bile duct stones: results in 60 patients using a rhodamine 6G dye laser with optical stone tissue detection system

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Abstract

Introduction—Laser lithotripsy of bile duct stones has become a widely accepted endoscopic treatment modality for giant, impacted, or very hard stones. The procedure is usually carried out under direct endoscopic control in view of the potential risk of bile duct injuries in “blind” laser application.

Aims—To investigate the use of a rhodamine 6G laser lithotripter with an integrated optical stone tissue detection system (oSTDS).

Methods—From 1 September 1991 to 7 March 1997, 60 patients with giant or impacted common bile duct stones refractory to endoscopic papillotomy stone extraction, and mechanical lithotripsy were treated via the endoscopic retrograde route using a rhodamine 6G dye laser (595 nm, 2.5 µs, 80–150 mJ pp, Lithognost Telemit/Baasel Corp., Germany) with integrated oSTDS. In case of tissue contact oSTDS cuts off the laser pulse after 190 ns (transmission of 5–8% of the total pulse energy). 47 patients (78.3%) were subjected to x ray targeting (oSTDS) alone, five (8.3%) to choledochoscope targeting alone, and eight (13.3%) to both techniques.

Results—At the end of treatment 52 (87%) patients were completely stone-free. The only major complications included transient haemobilia, cholangitis, and pancreatitis in five patients. All five were successfully treated by conservative methods.

Conclusions—Laser lithotripsy using the described rhodamine 6G dye laser with oSTDS seems to be safe and effective and allows “blind” fragmentation of difficult common bile duct stones under radiological control only.

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Keywords: laser lithotripsy; stone tissue discrimination system; bile duct stones; cholangioscopy; endoscopic therapy; lithotripsy methods

Currently, about 90% of all patients with common bile duct stones are treated non-surgically using endoscopic sphincterotomy and stone extraction. Beyond that a high proportion of non-extractable concretions up to 2 cm in diameter are easily removed by mechanical lithotripsy, if the stone can be grasped with the lithotripsy basket. However, in about 10% of all

cases mechanical lithotripsy is cumbersome, time consuming, or ineffective.^{1–3} In such cases additional methods such as extracorporeal shock wave, intracorporeal electrohydraulic, or laser induced lithotripsy are required.^{4–7} For safety reasons most conventional laser lithotriptors are applied under direct endoscopic vision because of the potential risk of damage to the bile duct wall in the event of accidental pulse application.^{5–12} A new optical stone tissue detection system (oSTDS) automatically cuts off the emitted laser pulse, if no contact between fibre tip and stone is established by the detector.^{13–15} The mechanism of the system is based on the qualitative and quantitative analysis of the fluorescence which is transmitted back from the target with near light speed. By means of the oSTDS the laser pulse can be cut off 190 ns after its release. In case of misapplication only 5–8% of the total energy of the 2.5 µs (2500 ns) laser pulse is delivered until it is interrupted. After preliminary in vitro and animal experiments on the safety and efficacy of the laser system we reported our first clinical results in 18 patients treated with this lithotripter.¹⁶ The integrated stone tissue detection system with automatic pulse cut off not only increased safety during laser lithotripsy under unfavourable cholangioscopic viewing conditions but also allowed “blind” endoscopic retrograde lithotripsy implementing a “bare” laser fibre in a standard catheter which was introduced into the common bile duct by a transpapillary route. We report on our experience with this intelligent (“smart”) laser system in 60 patients with difficult common bile duct stones which had not been accessible to standard endoscopic retrograde methods. After an initial phase of cholangioscopic application of the laser system most of the patients recently referred for treatment have been treated under direct control of the stone tissue detection system and intermittent fluoroscopy using standard duodenoscopes and catheters via the endoscopic retrograde route.

Patients and methods

PATIENTS

From 1 September 1991 to 7 March 1997, 60 patients with difficult bile duct stones refractory to endoscopic sphincterotomy, stone extraction, or mechanical lithotripsy were treated using a rhodamine 6G dye laser with the integrated optical stone tissue detection system. The majority of patients (94%) had been referred from other hospitals. Most of our patients were women (68%, 41 patients); 32%

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(19 patients) were men. The average age was 71 (14) years (range 39–96 years). Additional gallstones were present in 18 patients (30%) with two patients exhibiting the sonographic or computed tomographic appearance of a sclero-atrophic cholecystitis. Of the 42 patients (70%) who had already undergone cholecystectomy, seven patients (12%) had also had bile duct stones surgically removed previously. In 78% of the patients jaundice and pruritus had been the principal symptoms in diagnosing the stones. Nearly two thirds of the patients (62%) reported pain in the upper abdomen and in one third (33%) there had been initial signs of cholangitis.

To determine the diameter and total number of stones suitable for laser lithotripsy (maximum diameter larger than 1 cm) the maximum diameter of the stones was measured in the retrograde cholangiogram prior to the laser lithotripsy and compared with the diameter of the distal end of the endoscope.

Solitary stones were present in 24 patients (40%). Thirty six patients (60%) had multiple stones. Table 1 presents the data on the number of stones in our patient population. An average of 3 (1.5) stones larger than 1 cm per patient was present. The calculated average size of all stones larger than 10 mm was 23 (10)

Table 1 Number of stones (≥ 10 mm) per patient

Number of stones	Number (%) of patients
Solitary stones	24 (40)
≥ 2	36 (60)
2	10
3	9
4	9
≥ 5	8
Mean (SD) per patient	3 (1.5)



Figure 1 Laser fragmentation of a biliary concrement using the rhodamine 6G dye laser *in vitro*.

Table 2 Treatment modalities

A	“Blind” laser lithotripsy using oSTDS/fluoroscopy Huibregtse catheter (65/78 sessions) Basket (3/78 sessions) Balloon catheter (8/78 sessions) Steerable catheter (2/78 sessions)	47 (78.3%) patients
B	Combined treatment: cholangioscopy plus oSTDS/fluoroscopy	8 (13.3%) patients
C	Cholangioscopy alone	5 (8.3%) patients

mm (range 10–60 mm). All patients had been given complete information on the procedure planned and had signed an informed consent form approved by the university’s ethics committee the day before the procedure.

LASER SYSTEM

A flashlamp pulsed rhodamine 6G dye laser with a wavelength of 595 nm (Lithognost, Telemite/Baasel Laser Technik, D-Starnberg) with a pulse length of 2.5 μ s was implemented. The pulse energy was measured at the distal fibre end by means of an integrated power meter before treatment and the laser was automatically calibrated. The maximum pulse energy applied was 150 mJ at the distal fibre end using a pulse repetition rate of 8 Hz which had proved favourable *in vitro* and in clinical testing.^{16, 17} The pulse energy was delivered via a 250 μ m (≤ 120 mJ pp) or a 300 μ m (150 mJ pp) flexible quartz step index fibre and applied in direct contact with the stone (fig 1).

OPTICAL STONE TISSUE DETECTION SYSTEM

The optical stone tissue detection (discrimination) system (oSTDS) works as follows: a small fraction of the energy of the laser pulse (about 1–2%) is used to induce specific fluorescence on the surface of the target in front of the distal fibre end and thus the oSTDS differentiates between stone material and tissue. The emitted fluorescence is transmitted back through the optical fibre and its intensity in a defined spectral range is analysed. If the light intensity detected within a time interval of 190 ns does not exceed a specific threshold, one can conclude that the fibre is not in contact with the stone and thus that the danger of energy being transferred to the bile duct wall is imminent. In this case, the laser pulse which has a relatively long duration of 2.5 μ s compared with the measuring interval (0.2 μ s), is automatically cut off by means of an optical switch (Pockel’s cell). A maximum of only 5–8% of the pulse energy can thus be misapplied. The effectiveness of oSTDS applied to the biliary system has been confirmed by our group, both *in vitro* and in animal experiments.^{14, 18}

ENDOSCOPIC EQUIPMENT AND APPLICATION TECHNIQUE

For the application under direct cholangioscopic vision both standard and prototype mother and babyscope systems were used (Olympus CHF B20/TJFM 20 and CHF B34Y/TJF 20), whereas standard duodenoscopes (Olympus JF1T20) and standard 7F catheter systems served for purely radiologically/oSTDS controlled fragmentation. Most of the radiological applications were performed with a standard endoscopic retrograde cholangiopancreatography (ERCP) catheter with a distal metal marking (PNB Medicals Denmark guiding catheter, Huibregtse catheter; see table 2) as used for the implantation of straight 10 or 12F biliary endoprotheses (fig 2). Furthermore, a standard 7F balloon catheter (Wilson & Cook, USA), a special 8F laser lithotripsy basket constructed by our technical endoscopy workshop,



Figure 2 Standard duodenoscope with metal marked 7F plastic catheter, distal metal marking, and central laser fibre.



Figure 3 Side flushing system (Tuohy-Borst adapter, William-Cook, Europe) for coaxial irrigation of the laser fibre via a standard 7F ERCP catheter.

and a steerable catheter were applied in individual cases. The duration of laser application was limited to 60 minutes.

After successful stone disintegration, fragments as well as smaller stones located cranially to the obstructing stone were extracted by means of standard lithotripsy baskets or by balloon catheters. If necessary, an additional mechanical lithotripsy or—in the case of a large stone mass (generally concrements larger than 3.5 cm) and initial successful laser induced fragmentation—extracorporeal shock wave lithotripsy was applied (Piezolith, Richard Wolf GmbH, Knittlingen, Germany) to speed up further disintegration.

During laser lithotripsy under cholangioscopic vision continuous rinsing was applied coaxially to the fibre light guide via the instrumentation channel of the cholangioscope. For “blind” laser lithotripsy using standard catheters under intermittent fluoroscopy the catheter was continuously perfused with the rinsing

solution containing 50% saline and 50% water soluble non-ionic contrast medium (Omnipaque, Schering, Berlin, Germany). For cholangioscopic applications about 150–500 ml of saline and for radiologic applications 50–150 ml of diluted contrast medium were used. The proximal end of the guiding catheter was sealed against saline leakage using a Tuohy-Borst adapter (William Cook Europe, Bjaevershov, Denmark; fig 3). The fluid surrounding the stone was necessary for effective propagation of the laser induced shock waves.

STATISTICAL ANALYSIS

Statistical analyses were performed using the software packages StatView SE + Graphics and StatView 4.0 for Apple Macintosh (Abacus Corp., California, USA). The results were presented as mean (SD) or median and/or range. Mean values were compared using the χ^2 test for categorical variables and the Wilcoxon rank sum test for continuous variables. A p value of less than 0.05 was considered to be statistically significant.

Results

In total 104 laser lithotripsy sessions were carried out in 60 patients (mean 1.8 (1.0) per patient, range 1–4); 47 (78.3%) had x ray targeting (oSTDS) alone, five (8.3%) had choledochoscope targeting alone, and eight (13.3%) had both techniques (figs 4, 5, and 6). A quarter of the laser applications (26/104, 25%) were carried out cholangioscopically. The remaining 78 treatments (75%) were performed under oSTDS and fluoroscopic control exclusively.

For blind laser application in the bile duct the standard ERCP catheter with a metal marking at its distal tip and a concentrically guided fibre was applied in 86% of cases. In 4% a balloon catheter and in 10% the special lithotriptor basket were used to achieve better centring of the laser fibre onto the stone. In two cases (3%) a steerable catheter was used (table 2). Significantly fewer laser pulses were needed in visually controlled application of the laser fibre as compared with fluoroscopic/oSTDS application (cholangioscopic application: 1723 (1438) pulses total/1540 (1250) pulses with confirmed stone contact; fluoroscopic application: 2526 (2087) pulses total/2017 (1976) pulses with confirmed stone contact). Concerning the number of pulses per patient needed for stone treatment, the difference between the two application modes proved to be statistically significant ($p < 0.05$). This was the case with both the total number of pulses and the number of pulses with positive stone recognition. The number of misapplied pulses was 183 (266) pulses when the cholangioscopic application technique was implemented, and 509 (463) pulses when the oSTDS/fluoroscopic technique was applied. Therefore, about three times as many laser pulses were automatically interrupted by the stone tissue discrimination system in blind application compared with the cholangioscopic application mode.

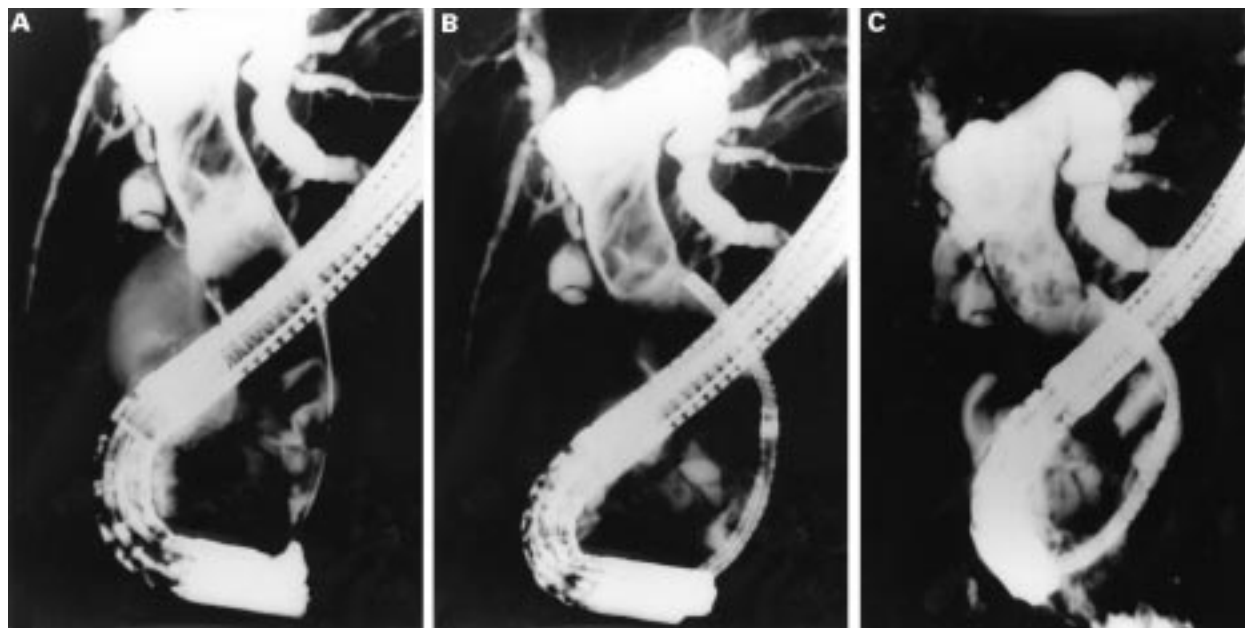


Figure 4 Laser lithotripsy under direct cholangioscopic vision using a mother and babyscope system before (A), during (B), and after (C) treatment (see Ell et al¹⁶; reprinted with permission).

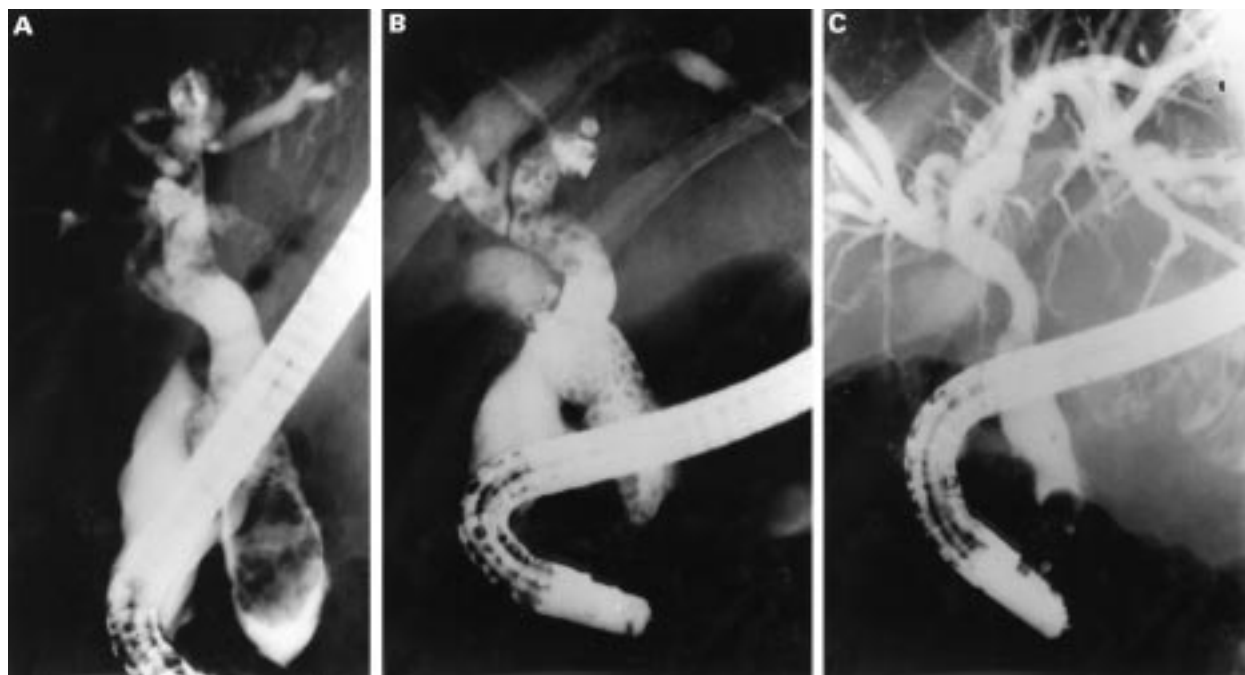


Figure 5 Blind laser application of giant common bile duct stones before (A), during (B), and after (C) treatment using the standard ERCP catheter with distal metal marking under control of the oSTDS and intermittent fluoroscopic control.

Successful stone fragmentation could be achieved in all patients (100%). In 70/104 treatment sessions (67%) the fragmentation result was excellent or good, in 30 sessions the success was moderate, and in four of the 104 laser sessions lithotripsy was insufficient. In two of the four cases with poor fragmentation results (both in the blind application group) insufficient lithotripsy could be attributed to inadequate positioning of the laser fibre on the stone.

STONE CLEARANCE RATE

At the end of the treatment period 52 (87%) of the 60 patients were completely free of stones.

In eight patients (13%) only partial stone clearance could be achieved. In three of these patients failure to achieve complete clearance was due to postoperative or postinflammatory stenoses in the right hepatic duct, in the hepatic bifurcation, and in the distal common bile duct. In these three patients surgical revision was carried out at the same time in order to resolve the underlying anatomical problem. One patient underwent hemihepatectomy, another a resection of the hilum of the liver, and a third a revision of the common bile duct because of a pre-existing choledochobulbostomy. In a fourth patient with anastomotic

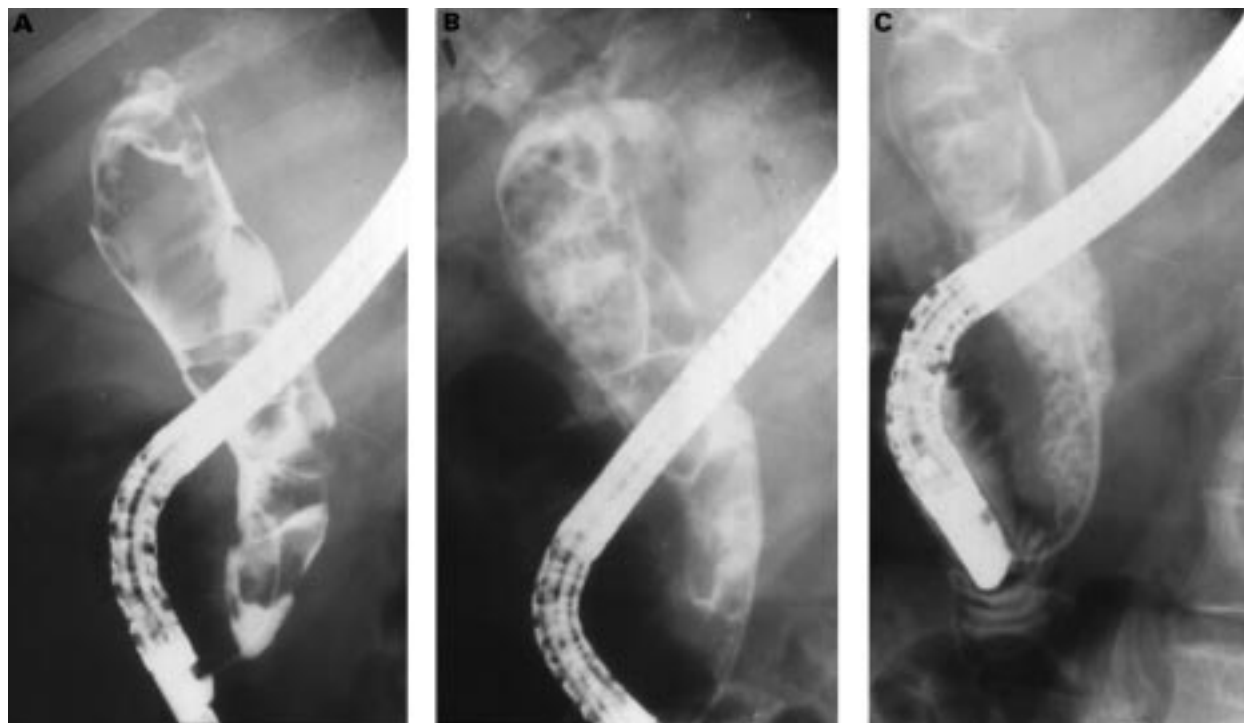


Figure 6 Blind laser application of giant common bile duct stones before (A), during (B), and after (C) treatment using the standard ERCP catheter with distal metal marking under control of the oSTDs and intermittent fluoroscopic control.

stricture of a biliodigestive anastomosis complete clearance of stones was not possible despite endoscopic accessibility. A fifth patient with an S shaped dilatation and distal stenosis of the common bile duct could not be entirely freed of stones. Three elderly patients refused further treatment after initial successful fragmentation of the concretions, partial clearance of the duct, and temporary stent impantation.

COMPLICATIONS

Relevant complications occurred in five of the 60 patients (8%), and in five of 104 treatment sessions (5%). In one fully anticoagulated patient with a prosthetic mitral valve a transient haemobilia with a decrease in haemoglobin from 13.5 to 11.0 g/l and cholangitis occurred which did not require blood transfusion or any further intervention except reinsertion of a nasobiliary catheter. Two further cases of cholangitis, one case of pancreatitis, and another mild haemobilia occurred as the only major complications two days after sphincterotomy, and mechanical and laser lithotripsy. All five patients could be treated conservatively with no consecutive symptoms and none died.

RECURRENCES

In one patient multiple intrahepatic and extrahepatic concretions up to 4 cm in size which were again partly resistant to mechanical lithotripsy had developed two years after successful laser lithotripsy. Due to the failure of mechanical lithotripsy of the impacted concretion the patient was successfully treated by endoscopic retrograde laser lithotripsy and fragment extraction a second time.

Discussion

In 1986 our group reported on the first successful endoscopic retrograde laser lithotripsy in humans by means of a flashlamp pulsed millisecond neodymium YAG laser.^{5 19 20} The effect was at that time thermo-mechanical. With the development of microsecond pulsed dye laser systems which allow the formation of plasma induced shock waves laser lithotripsy has become a commonly accepted modality for the treatment of difficult bile duct stones and has proved its effectiveness in a number of clinical trials.^{8-12 16 21}

Electrohydraulic intracorporeal lithotripsy (EHL) using 4.5 and, more recently, 3.0F probes represents an effective treatment option for the endoscopic removal of difficult common bile duct stones.^{1 6 22 23} However, EHL requires continuous visual control of the fragmentation procedure because of the high pulse energies reaching up to the range of Joules. As bile duct perforations have been described in both animal experiments and in clinical applications after only a few pulses were fired with the EHL probe in contact with the bile duct wall,^{1 22 24} the use of cholangioscopes plus continuous saline rinsing are mandatory. This is usually achieved by means of a nasobiliary catheter which is introduced into the bile duct before additional placement of the babyscope beside the catheter. Although EHL is equally as effective as laser lithotripsy with regard to stone fragmentation, this procedure is cumbersome.

Extracorporeal shock wave lithotripsy (ESWL) is another treatment modality for large bile duct stones.^{3 25} Different single centre studies have shown the efficacy of the treatment. To our knowledge there currently exist

only two trials comparing ESWL and laser lithotripsy as modalities for treatment of difficult common bile duct stones refractory to mechanical lithotripsy. In these two studies the success rate of laser lithotripsy was 96% and 82% respectively compared with 72% and 53% for ESWL.^{26, 27}

So far, conventional laser systems have mostly been used under direct cholangioscopic control. The reason for this lies in the potential risk of perforation in case of direct tissue contact as shown in animal experiments.^{14, 18, 28, 29} A new optical stone tissue detection system integrated into a rhodamine 6G dye laser allows immediate interruption of the laser pulse in case of suspected tissue contact. The pulse can be cut off up to 190 nanoseconds after its release. By this time only 8% of the energy of the 2.5 microsecond pulse has been released. In vitro and animal experiments have shown the high reliability of this optical feedback control system with incorrect recognition amounting to only 5/21 000 pulses applied directly to the gall bladder wall of a rabbit.¹⁸ In the present study we showed the clinical effectiveness of the system for laser induced fragmentation of difficult bile duct stones and its safety even when only the bare laser fibre is introduced into the common bile duct in a standard metal marked ERCP catheter via standard duodenoscopes. The first nine patients were treated under direct cholangioscopic control, as in vitro and animal tests to adapt the oSTDS to biliary application were still underway. Subsequently, patients were treated mainly under intermittent x ray guidance and control by the oSTDS. The next four patients were treated using the cholangioscopic and fluoroscopic application mode to gather experience in the x ray controlled application. From that time on we primarily treated patients using the easier blind application technique. Four patients had to undergo consecutive cholangioscopic fragmentation of stones, as the degree of stone disintegration under fluoroscopic/STDS control had been poor or insufficient.

All patients included in our study had so called difficult, mostly giant bile duct stones which had been refractory to endoscopic sphincterotomy, stone extraction, and mechanical lithotripsy. The successful laser induced fragmentation in all our patients and the complete stone removal rate of 87% at the end of the treatment confirm the clinical efficiency of the system. In the two patients with unsuccessful positioning of the laser fibre onto the stone, changes in the anatomy of the biliary system were found to be the underlying disease, thus favouring a surgical solution after failure to achieve complete stone clearance.

Neuhaus *et al*³⁰ reported on 38 patients treated mainly under direct cholangioscopic vision via the percutaneous transhepatic route because of inadequate endoscopic retrograde access or incomplete stone fragmentation. On average Neuhaus *et al* applied about twice as many pulses as we did and had a longer treatment time (20–115 minutes, mean 70 minutes) compared with our peroral approach without ESWL (Neuhaus *et al* used a mean number

of 5320 pulses and a mean of 1.3 sessions). We usually terminated laser lithotripsy treatment after 60 minutes. To speed up stone clearance we additionally applied ESWL in 21 patients (35%) with a large stone mass after initially successful laser lithotripsy.

The average stone size in the population of Neuhaus *et al* was comparable to ours (mean 28 mm (range 8–52 mm) versus a mean of 22 mm (range 10–60 mm) in our study). However, like most other authors they took into account only the largest stone, whereas we included all stones larger than 10 mm in our determination of the mean stone size. In the studies by Ponchon *et al*¹¹ and Cotton and colleagues⁸ the mean stone size was somewhat smaller (mean of 18 mm with a lower number of laser pulses applied (Ponchon *et al* used 350–3000 pulses).

Later studies using the rhodamine 6G dye laser and percutaneous transhepatic access plus cholangioscopic lithotripsy showed somewhat better results than previous studies with less experience in the use of the coumarin dye laser in which endoscopic retrograde access to the bile duct was chosen. The percutaneous stone clearance rates vary from 80 to 97%.^{8, 11, 12, 30, 31}

Percutaneous transhepatic lithotripsy of gallstones is however reserved for cases with an anatomically difficult or impossible endoscopic access or with inadequate fragmentation via the endoscopic-retrograde route. Furthermore, both percutaneous transhepatic cholangioscopy and endoscopic retrograde mother and babyscopy always mean an increased effort concerning equipment, preparation, and overall time of the procedure and often costs. It was therefore our aim to investigate the safety of transpapillary laser lithotripsy using standard duodenoscopes. The laser fibre is directed onto the stone under fluoroscopic guidance in a metal marked ERCP catheter and the microsecond laser pulses are applied under the control of an optical stone tissue discrimination system. This procedure is the easiest one concerning equipment and application. In special cases we used a balloon catheter, a special lithotripter basket, or a steerable catheter for better centring of the fibre onto the stone. These instruments were also used in combination with standard duodenoscopes, as they routinely serve for diagnostic procedures, papillotomy, or stone extraction in the treatment of bile duct concretions.

However, a significantly higher number of pulses were interrupted in the case of the blind application mode compared with pulse application under direct cholangioscopic vision (331 versus 183 pulses). This fact and the potential damage in the animal experiments in cases of direct tissue contact confirm the need for an STDS for this application mode.

Apart from conservatively managed bleeding in two patients, one of whom was fully anticoagulated because of an artificial heart valve, no laser induced relevant complications occurred. Two cases of cholangitis could also be managed conservatively, indicating that the procedure is not only effective but also safe.

As a perspective for a wider proliferation of laser lithotripsy a new pulsed solid state laser system with a piezoacoustic stone tissue detection system is currently under investigation.^{32 33} In initial in vitro experiments this frequency doubled double pulse Q switched neodymium YAG laser (FREDDY) achieved a fragmentation efficiency comparable to that of the rhodamine 6G dye laser at about one third of the cost. The results of animal experiments in which the stone tissue discrimination system was implemented are promising. The first clinical applications in five patients with choledocholithiasis who were treated under direct cholangioscopic control yielded a stone free bile duct after the first treatment session in all cases. Further clinical experience in a larger number of patients has to be awaited before a conclusive clinical assessment of the system is possible.

As mechanical lithotripsy of stones larger than 2 cm in diameter is often cumbersome and time consuming,^{34 35} laser lithotripsy may be a suitable instrument complementing endoscopic sphincterotomy and stone extraction for large stones even without mechanical lithotripsy. The question of whether laser lithotripsy without papillotomy will become a reality, thus providing the means to avoid possible complications of 6–10% and a mortality rate of 0.5–1.5%, as well as preserving the intact papillary muscle in young patients, is currently open. Balloon dilatation could be a viable partner for laser lithotripsy to avoid endoscopic papillotomy.^{36–39}

Part of the study was presented at Digestive Disease Week in Washington, DC, 10–16 May 1997 (abstract no. 1827). Preliminary results in 18 patients have been published previously (*Gastrointest Endosc* 1993;39:755–62).

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