Efficacy and safety of novel digital single-operator peroral cholangioscopy-guided laser lithotripsy for complicated biliary stones

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ABSTRACT

Background/study aims Laser lithotripsy can effectively fragment complicated biliary stones, but current cholangioscopes are limited by fragility, restricted mobility or moderate visual resolution. The efficacy and safety of a new digital single-operator peroral cholangioscope to guide laser lithotripsy were evaluated.

Patients and methods In this prospective single-center series, consecutive patients with complicated biliary stones, defined as impacted stones > 1.5 cm in size and wider than the more distal common bile duct, or stones that failed extraction by basket mechanical lithotripsy, underwent ERCP and SpyGlass DS peroral cholangioscope (Boston Scientific, Marlborough, United States)-guided laser lithotripsy. Stone clearance rate and incidence of adverse events were determined.

Results Seventeen patients (10 men, 7 women; median age 76 years) with a median biliary stone size of 2 cm underwent predominantly holmium:yttrium aluminum garnet laser lithotripsy, achieving a 94 % stone clearance rate over 1 median procedure. Lithotripsy was performed in 8 of 17 patients due to an impacted biliary stone. The remaining patients underwent lithotripsy due to prior failure of the basket mechanical lithotripter to capture or crush their stones. Post lithotripsy, 2 patients developed cholangitis and 1 patient with underlying COPD developed respiratory distress, all resolved with conservative management. There were no hemobilia, perforations, pancreatitis nor any deaths.

Conclusion SpyGlass DS peroral cholangioscopy-guided laser lithotripsy is an efficient and safe modality for management of complicated biliary stones.

Introduction

Impacted biliary stones wider in diameter than the distal common bile duct (CBD), and biliary stones failing removal by mechanical lithotripsy are considered complicated biliary stones, which are associated with lower clearance rates or require more invasive extraction techniques. Intracorporeal lithotripsy can facilitate fragmentation, but stone and duct visualization are important for accurate targeting. Current peroral cholangioscopes (POC) are limited by fragility, restricted mobility or moderate visual resolution. Recently, a novel digital single-operator POC, SpyGlass DS digital controller and catheter (Boston Scientific, Marlborough, United States), was introduced. With high-resolution integrated digital imaging, and 60 % wider field of view, superior visualization of the bile duct can be achieved compared to an earlier-generation device. We present early results of the efficacy and safety of this novel digital POC for guidance of laser lithotripsy of complicated biliary stones.

Patients and methods

This prospective series included consecutive consenting adult non-pregnant patients with either: 1) an impacted biliary stone > 1.5 cm in diameter and wider than the more distal CBD on endoscopic retrograde cholangiopancreatography (ERCP); or 2) a biliary stone that failed capture or crushing by basket mechanical lithotripsy (BML), from June 2015 to May 2016 at the Prince of Wales Hospital in Hong Kong. Patients with ongoing cholangitis or biliary pancreatitis, intrahepatic segmental stones, known history of biliary stricture, prior history of altered gastrointestinal/biliary anatomy, refractory bleeding tendencies (platelet count < 50,000 /mm^3 or International Normalized Ratio > 1.5 despite correction with platelet or fresh frozen plasma transfusions), and contraindications to endoscopy due to comorbidities were excluded.

The SpyGlass DS digital controller houses the video processor and light source as a single unit. On connection to the single-operator Spyscope DS cholangioscope, automatic white balance and light control with preset focus are available. Dedicated irrigation and aspiration channels ensure optimal visualization. POC-guided holmium:yttrium aluminum garnet (ho:YAG) laser lithotripsy was performed as follows. ERCP was performed with pre-procedural intravenous (IV) antibiotics, under conscious sedation with IV midazolam or diazemuls and meperidine, and with CO_2 insufflation. After cannulation and outlining of the stone and CBD by contrast, wire-guided biliary sphincterotomy (if not already performed) was followed by endoscopic papillary balloon dilation with a CRE dilation balloon (Boston Scientific, Marlborough, United States) to the diameter of the distal CBD. The single-use 10Fr cholangioscope would then be introduced through the working channel of a TJF 260 duodenoscope (Olympus Medical Systems, Tokyo, Japan), and into the CBD by free-hand technique under direct endoscopic vision to identify the biliary stone target. The 1.8Fr ho:YAG laser fiber (Lumenis, Yokneam, Israel) was inserted into the cholangioscope's 1.2-mm working channel for lithotripsy underwater and direct visualization with the following laser parameters: Energy 1.2 J, Rate 10 Hz, Power 12 W. When ho:YAG laser was not available, a 3Fr electrohydraulic laser (EHL) delivery fiber (Olympus Optical, Tokyo, Japan) was used in conjunction with the Lithotron EL 27 compact generator (Walz Elektronik, Rohrdorf, Germany) with the following power settings: Energy up to 950mJ, and automatic pulse frequency between 5 Hz and 60 Hz. Laser was applied until fragments of the target stone were no longer lumen filling, and could be dispersed with fluid irrigation (▶**Video 1**). Fragmented stones were then removed with conventional extraction devices, which may include BML to accelerate duct clearance at the discretion of the treating endoscopist. In cases where stone clearance was incomplete, a plastic biliary stent was inserted for biliary drainage until definitive stone clearance. Study outcomes were clinical success, defined as visualization, targeting and clearance of intended biliary stone, and the incidence of adverse events (AEs) as defined by Cotton *et al.* within 72 hours after the procedure [1]. Descriptive statistics were used to describe the results.

▶**Table 1** Patient and biliary stone characteristics, and clinical outcomes of SpyGlass DS POC-guided laser lithotripsy of complicated biliary stones.

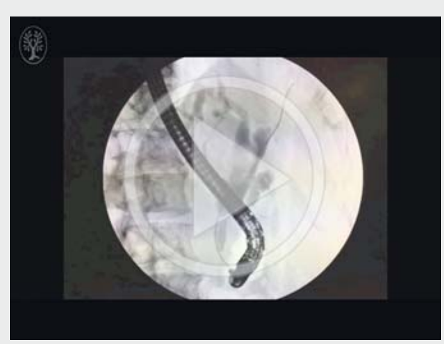
Parameter	n = 17
Patient characteristic (N = 17)	
– Median age (range), years	76 (45 – 88)
– Male:Female	10:7
Procedural indication	
– Impacted stone/stone duct size mismatch	8/17 (47 %)
– BML failure	9/17 (53 %)
Stone characteristic	
– Median stone size (range), cm	2 (1 – 4.5)
– Median number of stones per patient (range)	1 (1 – 10)
Stone location	
– Central intrahepatic duct	1/17 (6 %)
– Common hepatic/bile duct	15/17 (88 %)
– Cystic duct	1/17 (6 %)
Clinical outcome	
– Overall stone clearance	16/17 (94 %)
– Stone clearance at index laser lithotripsy session	10/16 (63 %)
– Median duration of procedure (range), minutes	90 (40 – 165)
Adverse event	
– Cholangitis	2/17 (12 %)

POC, peroral cholangioscope

Results

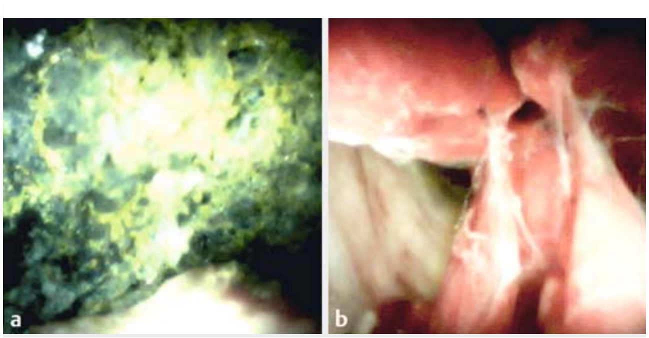
Seventeen patients (10 men, 7 women) with median age of 76 years (range: 45 – 88 years) consecutively underwent SpyGlass DS POC-guided laser lithotripsy of 19 complicated biliary stones (17 stones by ho:YAG laser, and 2 stones by EHL due to unavailability of ho:YAG laser) from June 2015 to May 2016 at the Prince of Wales Hospital (▶**Table 1**). Lithotripsy was performed on 8 of the 17 patients due to an impacted stone with a diameter > 1.5 cm, which was also wider than the distal CBD (▶**Fig. 1**). Nine of 17 patients underwent lithotripsy due to prior failure of the BML to capture or crush their stones. Median size of target biliary stone was 2 cm (range: 1 – 4.5 cm), with the majority of stones located along the common hepatic or common bile duct. One stone was at the central right intrahepatic duct and another at the cystic duct stump. Median number of stones was 1 (range: 1 – 10) per patient. Excellent visualization of stone permitting accurate laser targeting was achieved in all cases (▶**Fig. 2a**). Complete biliary stone clearance was successful in 94 % of patients (16/17) over a median of 1 endoscopic procedure (range: 1 – 3). Clearance of the target stone could be achieved at the index laser lithotripsy session in 10/16 (63 %) patients. Among these 10 cases, median duration of ERCP and laser lithotripsy, from duodenoscope intubation to withdrawal, was 90 minutes (range: 40 – 165 minutes). In the remaining 6 patients who required more than 1 endoscopic session, only 1 required additional laser lithotripsy for stone fragmentation. On χ^2 test, success of stone clearance at the index lithotripsy procedure was not associated with patient age, indication for lithotripsy, stone size or number of stones. BML was used to facil-

VIDEO 1



▶Video 1: ERCP and SpyGlass DS cholangioscopy-guided ho:YAG laser lithotripsy of an impacted biliary stone

▶ **Fig. 1** Cholangiogram during ERCP showing a large common hepatic duct stone, impacted against a more narrow common bile duct



▶ **Fig. 2** **a** Impacted biliary stone. **b** Newly diagnosed biliary stricture with thick papillary projections, as visualized by SpyGlass DS cholangioscope

itate clearance of lithotripsy fragmented stones in 75 % (12/16) of patients.

The 1 patient who did not have complete stone clearance had a 2-cm common hepatic duct stone and a new CBD stricture, visualized on cholangioscopy as thick papillary projections (▶ **Fig. 2b**), biopsied with Spybite (▶ **Video 2**). While stone visualization, laser targeting, and stone fragmentation was initiated, complete stone clearance was not performed in view of the need for a plastic biliary stent. Spybite biopsy results did not show malignant cells. Due to advanced age and patient comorbidities, no further investigations or interventions were performed. The patient remains well nearly 8 months after lithotripsy.

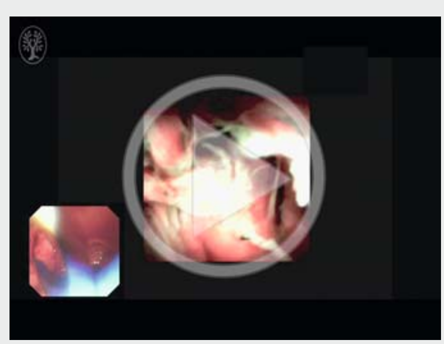
During the 72 hours after laser lithotripsy procedures, 2 of 17 patients developed cholangitis. One patient had a 3 cm stone impacted at the mid CBD, while the other had a 1-cm cystic duct stone which could not be captured with conventional extraction devices. With conservative management, both patients improved within 48 hours. The patient with concomitant biliary stone and stricture had underlying chronic obstructive pulmonary disease, and developed respiratory distress post-procedure managed by supplemental oxygen and chest physiotherapy. There were no incidents of hemobilia, perforations, or pancreatitis nor any deaths.

Discussion

We present one of the earliest clinical series on the role of a new digital single-operator POC to guide laser lithotripsy of complicated biliary stones, demonstrating a 94 % clinical success rate and good safety profile, even among our patients who were predominantly older than 75 years old.

We showed this technique effective for managing 2 categories of difficult biliary stones, namely cases of impacted stones larger than the more distal CBD and choledocholithasis failing conventional extraction by BML. Currently, individuals with stone/duct mismatch would be subjected to repeated ERCPs, as impacted large stones have lower BML clearance rates [2–4]. BML extraction of large stones also has a complication rate

VIDEO 2



▶ Video 2: ERCP and SpyGlass DS cholangioscopy-guided biopsy of common bile duct stricture, and ho:YAG laser lithotripsy of a common hepatic duct stone

▶ **Table 2** Comparison of select large series evaluating dual-operator POC, single-operator POC and ultraslim gastroscopes for laser lithotripsy of biliary stones.

First author (Year)	n	Biliary stone characteristics	Cholangioscopy and lithotripsy used	Index/Overall stone clearance rate	Adverse event rate
Moon (2009) [11]	18	Mean stone size 23.2 mm 89 % stones large or impacted	4.9 – 5 mm tip ultraslim gastroscope-guided EHL (56 %) and FREDDY laser (44 %)	NR/89 %	0 %
Tsuyuguchi (2011) [12]	122	Mean stone size 17 mm 43 % of stones Mirizzi syndrome 41 % of stones impacted	Olympus mother-baby system-guided EHL or flash-lamp-pumped dye laser	96 %[1]	No mortality
Chen (2011) [9]	66	Median stone size 19 mm 65 % of stones impacted	SpyGlass Direct Visualization System-guided EHL (83 %) or laser lithotripsy (17 %)	71 %/100 %	6 %
Patel (2014) [10]	69	Mean stone size 20.2 mm All patients failed at least endoscopic stone clearance once	SpyGlass Direct Visualization System-guided holmium:YAG laser lithotripsy	74 %/97 %	4 %
Navaneethan (2016) [8]	31	Mean stone size 14.9 mm 36 % of stones impacted 74 % failed conventional stone extraction	SpyGlass DS-guided laser lithotripsy[2]	87 %/100 %	NR

EHL, electrohydraulic lithotripsy; FREDDY laser, frequency doubled double pulse neodymium:YAG laser; NR, not reported specifically.
[1] Study did not separately report index versus overall stone clearance rates.
[2] Study did not specify type of laser lithotripsy used.

of 4 % to 5 % even among experienced endoscopists [5]. Recently, we demonstrated that SpyGlass DS POC-guided ho:YAG laser lithotripsy was effective for rescue of an impacted extraction stone and basket [6].

For stones refractory to BML, intracorporeal lithotripsy can be facilitated by a number of devices, such as the dual-operator mother-daughter system, the single-operator POC or ultraslim gastroscopes. The mother-daughter platform in general requires 2 experienced and coordinated operators. The daughter scope is fragile, and typically has only 2-way tip deflection. The SpyGlass POC (Boston Scientific, Marlborough, United States) has the advantages of requiring only a single operator, and the 4-way tip deflection can likely better facilitate cannulation of the papilla and central intrahepatic ducts, as well as allow more specific targeting of sites for biopsies, and stones for lithotripsy. While the first-generation device (SpyGlass Direct Visualization System) was limited by moderate visual resolution due to reliance on a 6000-pixel reusable optical probe, the second-generation device (SpyGlass DS), which is the POC that was evaluated in the current study, has a charged couple device for digital imaging and wider field of view. These devices are, however, single use. Ultraslim gastroscopes have also been used for POC. Biliary cannulation is, however, more challenging compared to the other devices, in part due to gastric looping, despite multiple techniques like overtubes or balloon anchors. Successful cannulation is, however, rewarded by the availability of narrow-band imaging, which permits more refined characterization of intraductal lesions.

A systematic review and meta-analysis on the efficacy of various forms of POC for difficult bile duct stones was recently published [7]. The larger case series of dual-operator POC, single-operator POC and ultraslim endoscope-guided laser lithotripsy are compared in ▶ **Table 2** [8 – 12]. Of note, our 94 % clearance rate is comparable to that reported by Navaneethan *et al.*, who evaluated the role of SpyGlass DS-guided laser lithotripsy in 31 patients with difficult biliary stones [8]. However, the stones in that series likely represented a lower risk and less complex group, as the mean patient age was younger at 62 years, the mean stone size was smaller at 1.4 cm, and there were fewer impacted stones (36 %) compared to our cohort. Further, that series did not specify the type of laser lithotripsy used (ho:YAG, FREDDY laser lithotripsy or EHL). The only patient in our study who did not achieve ductal clearance had a 2-cm CHD stone and a newly diagnosed CBD stricture, managed by partial stone fragmentation followed by stenting. He remains well nearly 8 months after stenting. There were no patients with concomitant biliary stone and strictures included in the other study [8]. Our results are also comparable to those of ho:YAG laser lithotripsy and EHL guided by the first-generation SpyGlass device [9 – 10].

Our AEs included 2 incidents of cholangitis, and a respiratory decompensation in a COPD patient, all of whom recovered after conservative measures. Cholangitis was likely related to a showering effect of fragmented stones throughout the biliary tree from lithotripsy. Due to endoscopic papillary balloon dilation, fluid injected for bile duct clearance may leak out across the papilla, accumulating in the stomach or distal digestive tract and contributing to aspiration risk or fluid overload. This highlights the importance of controlled use of irrigation during the procedure, suctioning of injected fluid washing out from the papilla, and consideration of using the cholangioscope's suction port to aspirate residual fluid in the biliary tree at the end of a procedure.

Overall, the 4-way 30° tip deflection and digital imaging of the novel SpyGlass DS cholangioscope enabled simple cannulation of the papilla, with successful localization, clear visualization, and precise targeting of stones throughout the biliary tree, including stones at the central right intrahepatic duct, cystic duct stump, and those proximal to a stricture, all sites associated with more difficult stone extraction. Depending on bile duct width, light diffusion can be variable, and light intensity should be adjusted. In contrast to an earlier study, we did not preload the ho:YAG laser lithotripsy fiber into the working channel of the SpyGlass DS cholangioscope before cannulation of the papilla [8]. Even without preloading, we rarely encountered resistance passing the laser fiber across the tip of the duodenoscope. By advancing the SpyGlass DS cholangioscope deeper into the biliary tree, the laser fiber can be carried forward into the distal bile duct as confirmed by fluoroscopy. A similar principle can be applied when advancing the Spybite forceps. Finally, laser lithotripsy may cause a drilling effect without immediate fragmentation, especially when the laser probe tip is too close to the stone surface. The fiber should be withdrawn to 1 mm to 2 mm away from the stone surface to achieve a better effect. Although our institution performs high-volume biliary endoscopy, the endoscopists involved had limited prior experience with this device. The high success rate reflects a quick learning curve, and likely generalizability to other centers. Limitations of our study included the small sample size, small number of endoscopists involved, and limited use of EHL. Nevertheless, our results comprise one of the earliest series showing high efficacy and safety of SpyGlass DS POC-guided laser lithotripsy for complex biliary stones. In the future, comparative studies evaluating this technique's efficacy as a first-line therapy for difficult biliary stones are warranted.

Competing interests

AYB Teoh is a consultant for Boston Scientific.

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