

Peroral Cholangiopancreatography with the SpyGlass® System: What do we Know 10 Years Later

Pedro Pereira, Armando Peixoto, Patrícia Andrade, Guilherme Macedo

Gastroenterology Department,
Centro Hospitalar de São João;
Oporto WGO Training
Center;
Porto Medical School,
University of Porto,
Porto, Portugal

Address for correspondence:

Armando Peixoto

Gastroenterology Department,
Centro Hospitalar de São João,
Porto, Portugal
armandoafp5@gmail.com

ABSTRACT

Smaller endoscopes and catheters have been developed that permit direct visualization of the bile and pancreatic ducts (cholangioscopy and pancreatoscopy, respectively). These endoscopes and catheters are passed through the working channel of a standard therapeutic duodenoscope during endoscopic retrograde cholangiopancreatography (ERCP). The SpyGlass Direct Visualization System (Boston Scientific Corp, Natick, MA, USA) is currently the most widely used and studied device. Cholangioscopy with intraductal lithotripsy has become an established modality in the treatment of difficult biliary lithiasis. When used in the evaluation of indeterminate biliary strictures by experienced endoscopists in recognizing intraductal pathology, it increases the diagnostic yield of tissue sampling. Pancreatoscopy is complementary to other imaging modalities in the evaluation of intraductal papillary mucinous neoplasms of the pancreas and is emerging as a sole or adjunctive therapy to extracorporeal shock wave lithotripsy for the treatment of main pancreatic duct stones. It remains investigational in the diagnosis of pancreatic adenocarcinoma. Complications specific to the performance of cholangiopancreatography include cholangitis, which is related to intraductal fluid irrigation.

Key words: cholangioscopy – pancreatoscopy – biliary strictures – pancreatic duct strictures.

Abbreviations: EHL: Electrohydraulic lithotripsy; ERCP: Endoscopic retrograde cholangiopancreatography; ESWL: Extracorporeal lithotripsy by shock waves; ET: Endoscopic therapy; EUS: Endoscopic ultrasound; IPMN: intraductal papillary mucinous neoplasm; LL: Laser lithotripsy; MDCT: Multi-detector computed conventional tomography; MPD: Main pancreatic duct; MRCP: Magnetic resonance cholangiopancreatography; MRI: Magnetic resonance imaging; POCPS: Peroral cholangiopancreatography; PSC: Primary sclerosing cholangitis

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is a valuable tool in the assessment and treatment of biliary and pancreatic diseases. However, one of its limitations is the suboptimal definition of the fluoroscopic image in the diagnosis of pancreatic and biliary duct diseases. The introduction of peroral cholangiopancreatography (POCPS) offers the possibility to overcome this problem by allowing direct visualization of the biliary and pancreatic ducts and detect abnormalities that may not be detectable by cholangiography.

In 1970, Rosch et al. [1] and Urakami [2] independently described two different endoscopic methods for peroral cholangioscopy. Since then, several systems have been introduced; however, widespread adoption of POCPS has been hindered by technological obstacles until recently [3]. Since then, these systems were refined due to advances in endoscopic technique, scope, design and functionality.

With the introduction of the SpyGlass® system (Boston Scientific Corp., Natick, MA, USA), it is reasonable to think that this technique will soon become universally adopted for the evaluation and treatment of biliary and pancreatic tract diseases. In fact, the cholangiopancreatography with SpyGlass® has demonstrated promising results in an international multicenter study [3], and was approved by the US Food and Drug Administration in 2009 for diagnostic and therapeutic applications during endoscopic procedures in the pancreatobiliary system [4].

Until now, cholangioscopy with the SpyGlass® system was shown to be an effective therapeutic and diagnostic tool [5, 6]. Potential diagnostic applications include: the evaluation of

Received: 20.02.2017

Accepted: 10.04.2017

indeterminate strictures in patients with or without primary sclerosing cholangitis (PSC), study of undetermined filling defects in bile ducts seen in MRCP or ERCP imaging, biopsy of lesions after nondiagnostic ERCP, preoperative precise location and extension of bile intraductal tumors, visual evaluation and biopsy to evaluate post-transplant biliary stenosis, diagnosis of intraductal mucinous neoplasms, assessment for cytomegalovirus, fungal and parasitic infections, and study of patients with hemobilia [5, 6]. As a therapeutic tool, cholangioscopy can be used to treat biliary stones that have failed extraction with conventional ERCP techniques, can be an alternative to surgery in patients with type II Mirizzi syndrome, allows placement of stents in the cystic duct, photodynamic therapy of cholangiocarcinoma and photocoagulation with argon in cases of intraductal mucinous neoplasia [5, 6].

In the context of pancreatic diseases, diagnostic and therapeutic indications for pancreatoscopy include chronic pancreatitis, pancreatic stones, tumors of the pancreatic duct and diagnosis of autoimmune pancreatitis.

In this review, we shall discuss technical issues of the use of SpyGlass® system and explore the main diagnostic and therapeutic applications to date.

TECHNICAL ISSUES

SpyGlass® was introduced in 2006 and was designed to solve many of the problems related to old systems that limited its regular utilization in clinical practice. One important advantage of the SpyGlass® system is that it requires only one operator, in contrast with the “mother-daughter” system composed of a “mother” duodenoscope and a “daughter” cholangioscope, each with its respective control handles, requiring two endoscopists, or an endoscopist with a trained assistant [7]. The system comprises a reusable fiber optic probe with an average use of about 8 to 10 times (direct probe SpyGlass® display; Boston Scientific Corp) that contains a 6,000 pixel image package surrounded by about 225 light transmitting fibers, and a disposable delivery catheter (SpyScope®, Boston Scientific Corp.) [8, 9]. The delivery catheter has a four-way deflected direction, an outer diameter of 3.3 mm and an accessory channel of 1.2 mm [10]. Two output irrigation channels in the catheter tip for irrigation pipes that clears debris in the bile ducts and provides better visual images throughout the procedure. The four-way tip deflection SpyScope® catheter aids in better visualization of the bile ducts, and can help in negotiating difficult strictures.

The SpyScope® access and delivery catheter is connected to the duodenoscope by a silastic band below its working channel. The procedure is always performed in conjunction with ERCP and sphincterotomy is usually carried out to better access to the biliary tree [8, 11], with selective and deep cannulation. A guide wire is then inserted and positioned in the bile duct (or pancreatic duct) under fluoroscopy. The SpyScope® catheter together with the optical probe are introduced through the duodenoscope together as a unit and advanced into the bile duct for direct viewing. Once inside the common bile duct, the SpyScope® catheter is slowly advanced under fluoroscopy guidance. Once the SpyScope® catheter is positioned in the common bile duct, the guidewire is removed. The optical

probe is then advanced beyond the tip of the catheter, and direct visualization of the bile ducts is accomplished through the repeated advancing and withdrawing of it. Captured images definition is lower than those captured by video cholangioscopes. However, recently, an improved SpyGlass® system, the SpyGlass® DS Direct Visualization System (SpyGlass® DS) became available [12]. It is now equipped with a better image quality and an easier set-up compared to the previous SpyGlass® system, which is a big improvement and may be a promising tool for the pancreatobiliary field.

The SpyBite® biopsy forceps is a single-use device that has a working length of 286 cm. The forceps is inserted through the 1.2 mm SpyScope® catheter working channel. The forceps jaws are designed with a center point, and have an outer diameter of 1 mm to obtain a small targeted biopsy under direct visualization.

The accessory channel of the SpyGlass® system allows the use of lithotripsy devices, namely electrohydraulic lithotripsy (EHL) and laser lithotripsy (LL). EHL works on the principle that sparks discharged under water generate high frequency hydraulic pressure waves. Through the continuous supply of saline solution and under cholangioscopic orientation, an electric shock is administered directly on the stone to break it. Its high energy pulse for disintegrating stones can damage the bile duct, so cholangioscopic display of the target stone can help minimize the risks of bile duct damage associated with EHL therapy [13]. Laser equipment is more expensive than EHL, and the quartz fiber that transmits the laser beam is fragile and difficult to move forward in tortuous small bile ducts. However, pulsed dye LL is a promising method for achieving a rapid and safe clearance of the bile duct [13]. In order to avoid injury to the bile duct due to laser energy transmission, cholangioscopic laser fiber orientation is generally recommended.

BILIARY DISEASES

Diagnostic applications

The direct visualization and biopsy of indeterminate biliary lesions is one of the main indications for SpyGlass® choledochoscopy. When a patient with a biliary stricture is approached, ERCP is used initially. However, the diagnosis based on ERCP through the use of brush cytology and/or intraductal biopsies is limited by its low sensitivity [14]. Early and accurate diagnosis is essential, and impacts not only patients' outcome but also possible surgical treatments and targeted chemotherapies. From 13% to 24% of patients with presumed hilar cholangiocarcinoma are found to have benign disease at surgery [15, 16], and precise diagnosis is essential to avoid unnecessary surgery for patients with benign strictures.

Certain visual indicators, such as masses or intraductal dilated and tortuous vessels (called tumor vessels) have been described in the literature to be highly specific to malignant tumors of the bile duct [17, 18]. One study involving 63 patients with indeterminate strictures who underwent cholangioscopy reported that „tumor vessels” were observed in 25 of 41 patients with malignant tumors (61%), while no patients with a benign stricture had this characteristic appearance. By combining the optical observation with percutaneous transhepatic cholangiography-guided biopsy, it

resulted in a diagnostic accuracy of 96% for malignancy (39 of 41 patients). Unfortunately, the specificity is compromised by the use of direct visualization alone. Not only extrinsic compression can be due to benign etiology, but also in certain intraductal diseases such as PSC, biliary mucosa may have irregular patterns without harboring malignancy [7]. This can lead to false-positive results, so definitive diagnosis requires histological evaluation.

It is now accepted that the SpyBite® forceps has the ability to gather material for histological analysis in most situations, ranging from 82% to 97% [3, 19]. The lower specificity in the earlier study (82%) was driven by biopsy results that were inadequate for a histologic interpretation on an intention to treat (ITT) analysis. In a prospective study conducted by Navaneethan et al., the authors compared SpyBite® forceps biopsies with standard cytology brushings and standard forceps biopsies [19]. Sample quality was considered adequate in 96% of brushing forceps biopsies. The common limitation of traditional sampling methods (brushing cytology and biopsy guided by fluoroscopy) has been the low sensitivity and negative predictive value, both due to the relatively high rate of false-negative results. Cholangioscopy using the SpyGlass® with a SpyBite® forceps can potentially overcome this deficiency, allowing the evaluation of the mucosa and biopsies be obtained under direct visualization. Sensitivity of SpyBite® biopsy forceps is much greater for intrinsic (66%) than for extrinsic (8%) malignant lesions [19]. On the other hand, the sensitivity of SpyGlass® visual impression alone was less severely compromised by extrinsic (62%) than intrinsic (84%) lesions.

In a recent systematic review including 10 studies involving 456 patients, the combined sensitivity and specificity of cholangioscopy-guided biopsies in the diagnosis of malignant biliary strictures was 60.1% and 98.0%, respectively [20]. The combined diagnostic odds ratio to detect malignant biliary strictures was 66.4. In the few studies including patients who had no previous image and brushing and/or intraductal biopsies, the combined sensitivity and specificity for the diagnosis of malignant biliary stricture was 74.7% and 93.3%, respectively. The combined sensitivity and specificity to detect cholangiocarcinoma was 66.2% and 97.0%, respectively. The combined diagnostic odds ratio to detect cholangiocarcinoma was 79.7. Thus, the authors concluded that SpyGlass® cholangioscopy with SpyBite® biopsies has moderate sensitivity for the diagnosis of malignant biliary strictures.

In summary, SpyGlass® cholangioscopy significantly facilitates the diagnosis of malignant intrinsic biliary strictures, particularly cholangiocarcinoma, providing means for direct visualization and tissue diagnosis in patients with previous negative or inconclusive histologic analysis. The yield in patients with bile duct strictures due to extrinsic malignancy is slightly smaller.

In small case series and case reports, there has been an expansion of the use of the SpyGlass® system in other difficult to diagnose conditions of the biliary tree, including cholangiocarcinoma staging, evaluation of the bile duct ischemia after liver transplantation, cystic lesions in the tract bile, assessment of bile duct involvement in the presence of an ampulloma and hemobilia of unknown sources [21]. The

successful use of the SpyGlass® system has also been reported in patients with post-surgical Roux-en-Y and post-gastrectomy Billroth II anatomy [22].

Therapeutic applications

In most cases extraction of biliary stones with conventional ERCP techniques is successful; however, in 5% to 10% of the cases the stones are large, located above strictures, or adherent to the biliary wall and difficult to remove [23]. Intraductal endoscopy can assist in removing these difficult stones, by allowing direct visualization and guiding lithotripsy. Furthermore, standard fluoroscopy based cholangiograms routinely loosen remaining stones or stone fragments after lithotripsy [24]. Parsi et al. [25] were able to diagnose at least 29% of ERCP-lost gallstones by later cholangioscopy, leading them to conclude that the lost stones rates in ERCP may be higher than previously thought. In patients with difficult to treat stones, Arya et al. [26] described peroral cholangioscopy with EHL in 94 patients reporting a fragmentation rate of 96% and stone removal rate of 90% at the end.

In particular, SpyGlass® cholangioscopy has been shown to be beneficial for the initial diagnosis of gallstones, for documentation of residual stones after what was believed to be complete clearance of the bile duct, and more importantly, therapy of difficult-to-remove gallstones. An observational prospective study of feasibility in two tertiary medical centers showed that the SpyGlass® system can successfully guide stone therapy [7, 27]. Electrohydraulic lithotripsy carried out under SpyGlass® orientation cleared bile duct stones in all patients after previous extraction failure with conventional ERCP. In the largest prospective study to date on the use of SpyGlass® system in the treatment of gallstones made by Neuhaus et al. [28], 99 of 297 patients underwent SpyGlass®-directed stone therapy. The most common stone location was the common bile duct. The median number of stones per patient was 2, and the average size of the largest stone was 17 mm. Impacted stone(s) were present in 65% of the patients. Methods for fragmenting difficult stones were mechanical lithotripsy or SpyGlass® guided lithotripsy EHL/laser, depending on the individual case and preferences of the participating center. Impacted stones were treated by SpyGlass®-guided EHL or SpyGlass®-guided LL in 66 patients (66.7%). The study showed an overall success rate of 92%, defined as suitable stone visualization and initiation of stone fragmentation and removal. More recently, a Brazilian group reported their initial experience with 20 patients undergoing cholangioscopy with SpyGlass®. The most common indication was for the treatment of complex biliary tract lithiasis (60%) [29]. Electrohydraulic lithotripsy was applied in eight patients (66%), and was successful in seven (87.5%). Partial stone fragmentation occurred in a patient with a large stone causing stone-common bile duct disproportion, which was solved by placing a biliary plastic stent and a second endoscopic approach scheduled in three months.

Other reported therapeutic applications of the SpyGlass® system include treatment of post-liver transplantation anastomotic biliary stricture, transpapillary gallbladder drainage in acute cholecystitis, removal of bile duct foreign body and assistance in the placement of the guide wire [8, 30-32]. SpyGlass® guided EHL via a therapeutic colonoscopy has

also been used successfully in a patient with choledocholithiasis and Roux-en-Y anatomy [33]. Another relevant therapeutic application for SpyGlass® has been the management of choledocholithiasis during pregnancy in the first trimester [34], due to the elimination of radiation exposure during stone removal.

PANCREATIC DISEASES

Diagnostic applications

Direct visualization of any duct abnormalities and consequent biopsy can be valuable when the diagnosis of pancreatic strictures remains uncertain after multi-detector computed conventional tomography (MDCT), magnetic resonance imaging (MRI), ERCP and/or endoscopic ultrasound (EUS) evaluation. Pancreatography can view chronic scarring and stricture of the pancreatic duct, pancreatic duct stones, and intraductal papillary mucinous neoplasms (IPMNs) of the pancreas. Given the caliber of this device, generous sphincterotomy is universally required and SpyGlass® pancreatography is often not possible unless there is a marked dilatation of the pancreatic duct [35].

In 1997, peroral pancreatography was used to evaluate carcinoma in situ of the pancreas [36]. Carcinoma in situ in the main duct had the optical appearance of papillary mucosa, irregular mucosa, or nodular mucosa. Pancreatic juice collected during pancreatography provided a better yield than the traditional catheter collection, so this study concluded that peroral pancreatography and pancreatographic cytology are really helpful to locate and diagnose carcinoma in situ of the pancreas.

A study by Yamaguchi et al. [37] reported an improved ability to diagnose IPMNs by pancreatic cytology using “mother-baby” systems. Importantly, this study also found that there is no diagnostic value for pancreatic juice cytology in the diagnosis of pancreatic carcinoma. Since then, several case reports and case series have been published describing the role of cholangioscopy with the SpyGlass® system in diagnosing IPMNs in which dilatation of main pancreatic duct was sufficient, strengthening its high diagnostic accuracy [38-40]. In a recent Japanese prospective multicenter study with the use of SpyGlass® cholangiopancreatography, 24 out of 148 were submitted to pancreatography, out of which 16 had a suspicion of IPMN. The accuracy of the visual impression was 87.5% (14/16) [41].

Therapeutic applications

Pancreatic lithiasis in chronic pancreatitis, especially in the main pancreatic duct (MPD), can cause pain due to pancreatic stasis or increased MPD pressure. Elimination of the pancreatic stone is an appropriate treatment for pain and prevents the exacerbation of pancreatitis. Extracorporeal lithotripsy by shock waves (ESWL) is usually the first treatment option because it is minimally invasive and has fewer early complications than other treatments [42]. Management in cases of large stones requires lithotripsy, for which combined endoscopic therapy (ET)/ESWL is more effective than ESWL therapy alone. Data on the use of SpyGlass® in the treatment of complex pancreatic lithiasis is scarce. In a report by Ito et al., where lithotomy endoscopic / ESWL combination failed,

EHL was performed as a second attempt [43]. In most cases recent X-ray guided EHL using a 7 Fr biliary tract dilator as an external coating was performed when a 10 Fr SpyGlass® catheter delivery system was hard to insert into the main pancreatic duct stricture. Clinical success was defined as an improvement in abdominal symptoms after sphincterotomy/pre-cut and/or treatment of pancreatic lithiasis, while technical success was defined as clearance of the target pancreatic stone after treatment. Although not describing separately the results of using SpyGlass®, the overall success of endoscopy/EHL was 66% (4/6 patients), whereas the two cases of failure referred to two of the three patients with stones of the body portion of the main duct and it appeared to be differences according to the size of the stones [44].

COMPLICATIONS AND SAFETY PROFILE

Again, the available data on the SpyGlass® safety profile is limited. The same happens with older cholangioscopy systems. However, intraductal endoscopy is generally believed to be a safe procedure with relatively few complications that are comparable to those reported for ERCP [45]. These potential complications associated with cholangioscopy are numerous and range from relatively mild life-threatening sequelae conditions, including the following: cholangitis (most common complication), bacteremia, abdominal pain, pancreatitis, hypotension, nausea, liver abscess, radiculopathy, bile duct drilling (from the guide-wire), amylase and lipase elevation without clinical pancreatitis, and systemic inflammatory syndrome [45]. In a retrospective study including 402 ERCPs with cholangioscopy (a minority with SpyGlass® system) of a total of 3475 ERCPs, there was a higher rate of adverse events in the combination group (7% vs. 2.9%) [46]. There was a similar rate for drilling and pancreatitis between groups, but a significantly higher rate of cholangitis in the group undergoing ERCP combined with cholangiopancreatography (1% vs. 0.2%). The authors proposed that intermittent saline irrigation during cholangiopancreatography to get a proper view can be the pathophysiological process behind the increased risk of cholangitis. In one trial that utilized diagnostic SpyGlass® choledochoscopy to evaluate 36 patients who had indeterminate biliary strictures and/or filling defects, cholangitis that resolved with antibiotic therapy occurred in 2 patients (5.6%), and mild pancreatitis developed in 1 (2.8%), during a follow-up of at least 1 month [47]. Duodenal perforation seemed to be extremely rare and was treated conservatively [48, 49].

FUTURE DIRECTIONS

The availability of the SpyGlass® DS system with better image definition can significantly improve diagnostic capacity of the first generation system. Much of the knowledge acquired to date will surely be improved, and can really be a landmark in the near future.

Conflicts of interest: No conflicts of interest to report.

Authors' contribution: P.P. and A.P. wrote the manuscript. P.A. and G.M. critically reviewed the manuscript.

REFERENCES

- Rosch W, Koch H, Demling L. Peroral cholangioscopy. *Endoscopy* 1976;8:172–175. doi:[10.1055/s-0028-1098405](https://doi.org/10.1055/s-0028-1098405)
- Urakami Y, Seifert E, Butke H. Peroral direct cholangioscopy (PDCS) using routine straight-view endoscope: first report. *Endoscopy* 1977;9:27–30. doi:[10.1055/s-0028-1098481](https://doi.org/10.1055/s-0028-1098481)
- Chen YK, Parsi MA, et al. Peroral cholangioscopy (PO) using a disposable steerable single operator catheter for biliary stone therapy and assessment of indeterminate strictures - A multicenter experience using SpyGlass®. In: Abstracts of Digestive Disease Week, May 17–22, 2008 and the ASGE (American Society for Gastrointestinal Endoscopy) Postgraduate Course, May 21–22, 2008. San Diego, California, USA. *Gastrointest Endosc* 2008; 67:AB103.
- Woo YS, Lee JK, Oh SH, et al. Role of SpyGlass peroral cholangioscopy in the evaluation of indeterminate biliary lesions. *Dig Dis Sci* 2014;59:2565–2570. doi:[10.1007/s10620-014-3171-x](https://doi.org/10.1007/s10620-014-3171-x)
- Parsi MA. Peroral cholangioscopy in the new millennium. *World J Gastroenterol* 2011;17:1–6. doi:[10.3748/wjg.v17.i1.1](https://doi.org/10.3748/wjg.v17.i1.1)
- Moon JH, Terheggen G, Choi HJ, Neuhaus H. Peroral cholangioscopy: diagnostic and therapeutic applications. *Gastroenterology* 2013;144:276–282. doi:[10.1053/j.gastro.2012.10.045](https://doi.org/10.1053/j.gastro.2012.10.045)
- Chen YK, Pleskow DK. SpyGlass single-operator peroral cholangiopancreatography system for the diagnosis and therapy of bile-duct disorders: a clinical feasibility study (with video). *Gastrointest Endosc* 2007;65:832–841. doi:[10.1016/j.gie.2007.01.025](https://doi.org/10.1016/j.gie.2007.01.025)
- Chen YK. Preclinical characterization of the SpyGlass peroral cholangiopancreatography system for direct access, visualization, and biopsy. *Gastrointest Endosc* 2007;65:303–311. doi:[10.1016/j.gie.2006.07.048](https://doi.org/10.1016/j.gie.2006.07.048)
- SpyGlass® Direct Visualization Probe [brochure]. Natick (MA): Boston Scientific Corporation 2007. DVG1820 500 5/07.
- Chathadi KV, Chen YK. New kid on the block: development of a partially disposable system for cholangioscopy. *Gastrointest Endosc Clin N Am* 2009;19:545–555. doi:[10.1016/j.giec.2009.06.001](https://doi.org/10.1016/j.giec.2009.06.001)
- Judah JR, Draganov PV. The use of SpyGlass direct visualization system in the management of Pancreato-Biliary diseases. In: Wu GY, Sridhar S. (Eds.). *Diagnostic and therapeutic procedures in Gastroenterology*. Springer Science; New York 2011:195–210. doi:[10.1007/978-1-59745-044-7](https://doi.org/10.1007/978-1-59745-044-7)
- Ishida Y, Itoi T, Okabe Y. Types of peroral cholangioscopy: how to choose the most suitable type of cholangioscopy. *Curr Treat Options Gastroenterol* 2016;14:210–219. doi:[10.1007/s11938-016-0090-2](https://doi.org/10.1007/s11938-016-0090-2)
- Seelhoff A, Schumacher B, Neuhaus H. Single operator peroral cholangioscopic guided therapy of bile duct stones. *Hepatobiliary Pancreat Sci* 2011;18:346–349. doi:[10.1007/s00534-010-0360-7](https://doi.org/10.1007/s00534-010-0360-7)
- Navaneethan U, Njei B, Lourdasamy V, Konjeti R, Vargo JJ, Parsi MA. Comparative effectiveness of biliary brush cytology and intraductal biopsy for detection of malignant biliary strictures: a systematic review and meta-analysis. *Gastrointest Endosc* 2015;81:168–176. doi:[10.1016/j.gie.2014.09.017](https://doi.org/10.1016/j.gie.2014.09.017)
- Clayton RA, Clarke DL, Currie EJ, Madhavan KK, Parks RW, Garden OJ. Incidence of benign pathology in patients undergoing hepatic resection for suspected malignancy. *Surgeon* 2003;1:32–38.
- Gerhards MF, Vos P, van Gulik TM, Rauws EA, Bosma A, Gouma DJ. Incidence of benign lesions in patients resected for suspicious hilar obstruction. *Br J Surg* 2001;88:48–51. doi:[10.1046/j.1365-2168.2001.01607.x](https://doi.org/10.1046/j.1365-2168.2001.01607.x)
- Seo DW, Lee SK, Yoo KS, et al. Cholangioscopic findings in bile duct tumors. *Gastrointest Endosc* 2000;52:630–634. doi:[10.1067/mge.2000.108667](https://doi.org/10.1067/mge.2000.108667)
- Kim HJ, Kim MH, Lee SK, Yoo KS, Seo DW, Min YL. Tumor vessel: a valuable cholangioscopic clue of malignant biliary stricture. *Gastrointest Endosc* 2000;52:635–638. doi:[10.1067/mge.2000.108969](https://doi.org/10.1067/mge.2000.108969)
- Draganov PV, Chauhan S, Wagh MS, et al. Diagnostic accuracy of conventional and cholangioscopy-guided sampling of indeterminate biliary lesions at the time of ERCP: a prospective, longterm follow-up study. *Gastrointest Endosc* 2012;75:347–353. doi:[10.1016/j.gie.2011.09.020](https://doi.org/10.1016/j.gie.2011.09.020)
- Navaneethan U, Hasan MK, Lourdasamy V, Njei B, Varadarajulu S, Hawes RH. Single-operator cholangioscopy and targeted biopsies in the diagnosis of indeterminate biliary strictures: a systematic review. *Gastrointest Endosc* 2015;82:608–614. doi:[10.1016/j.gie.2015.04.030](https://doi.org/10.1016/j.gie.2015.04.030)
- Chen YK, Pleskow DK. SpyGlass single-operator POCPS system for the diagnosis and therapy of bileduct disorders: a clinical feasibility study (with video). *Gastrointest Endosc* 2007;65:832–841. doi:[10.1016/j.gie.2007.01.025](https://doi.org/10.1016/j.gie.2007.01.025)
- Mou S, Waxman I, Chennat J. Peroral cholangioscopy in Roux-en-Y hepaticojejunostomy anatomy by using the Spy-Glass Direct Visualization System (with video). *Gastrointest Endosc* 2010;72:458–460. doi:[10.1016/j.gie.2009.11.017](https://doi.org/10.1016/j.gie.2009.11.017)
- Classen M, Hagenmuller F, Knyrim K, Frimberger E. Giant bile duct stones--non-surgical treatment. *Endoscopy* 1988;20:21–26. doi:[10.1055/s-2007-1018119](https://doi.org/10.1055/s-2007-1018119)
- Williamson JB, Draganov PV. The usefulness of SpyGlass™ choledochoscopy in the diagnosis and treatment of biliary disorders. *Curr Gastroenterol Rep* 2012;14:534–541. doi:[10.1007/s11894-012-0287-z](https://doi.org/10.1007/s11894-012-0287-z)
- Parsi MA, Neuhaus H, et al. Peroral Cholangioscopy Guided Stone Therapy -Report of an International Multicenter Registry. In: Abstracts of Digestive Disease Week, May 17–22, 2008 and the ASGE (American Society for Gastrointestinal Endoscopy) Postgraduate Course, May 21–22, 2008. San Diego, California, USA. *Gastrointest Endosc* 2008;67:AB102.
- Arya N, Nelles SE, Haber GB, Kim YI, Kortan PK. Electrohydraulic lithotripsy in 111 patients: a safe and effective therapy for difficult bile duct stones. *Am J Gastroenterol* 2004;99:2330–2334. doi:[10.1111/j.1572-0241.2004.40251.x](https://doi.org/10.1111/j.1572-0241.2004.40251.x)
- Fishman DS, Tarnasky PR, Patel SN, Rajiman I. Management of pancreaticobiliary disease using a new intra-ductal endoscope: the Texas experience. *World J Gastroenterol* 2009;15:1353–1358.
- Neuhaus H, Parsi MA, Binmoeller K, et al. Peroral cholangioscopy for biliary strictures and bile duct stones—an international registry using SpyGlass®. Abstract UEGW 2009.
- Moura EG, Franzini T, Moura RN, Carneiro FO, Artifon EL, Sakai P. Cholangioscopy in bile duct disease: a case series. *Arq Gastroenterol* 2014;51:250–254. doi:[10.1590/S0004-28032014000300015](https://doi.org/10.1590/S0004-28032014000300015)
- Wright H, Sharma S, Gurakar A, Sebastian A, Kohli V, Jabbour N. Management of biliary stricture guided by the SpyGlass Direct Visualization System in a liver transplant recipient: an innovative approach. *Gastrointest Endosc* 2008;67:1201–1203. doi:[10.1016/j.gie.2007.10.055](https://doi.org/10.1016/j.gie.2007.10.055)
- Barkay O, Bucksot L, Sherman S. Endoscopic transpapillary gallbladder drainage with the SpyGlass cholangiopancreatography system. *Gastrointest Endosc* 2009;70:1039–1040. doi:[10.1016/j.gie.2009.03.033](https://doi.org/10.1016/j.gie.2009.03.033)

32. Ransibrahmanakul K, Hasyagar C, Prindiville T. Removal of bile duct foreign body by using spyglass and spybite. *Clin Gastroenterol Hepatol* 2010;8:e9. doi:[10.1016/j.cgh.2009.08.033](https://doi.org/10.1016/j.cgh.2009.08.033)
33. Baron TH, Saleem A. Intraductal electrohydraulic lithotripsy by using SpyGlass cholangioscopy through a colonoscope in a patient with Roux-en-Y hepaticojejunostomy. *Gastrointest Endosc* 2010;71:650–651. doi:[10.1016/j.gie.2009.08.016](https://doi.org/10.1016/j.gie.2009.08.016)
34. Uradomo L, Pandolfe F, Aragon G, Borum ML. SpyGlass cholangioscopy for management of choledocholithiasis during pregnancy. *Hepatobiliary Pancreat Dis Int* 2011;10:107–108.
35. Nguyen NQ. Getting most out of SpyGlass cholangio-pancreatography: how and when? *J Gastroenterol Hepatol* 2012;27:1263–1265. doi:[10.1111/j.1440-1746.2012.07178.x](https://doi.org/10.1111/j.1440-1746.2012.07178.x)
36. Uehara H, Nakaizumi A, Tatsuta M, et al. Diagnosis of carcinoma in situ of the pancreas by peroral pancreatoscopy and pancreatoscopic cytology. *Cancer* 1997;79:454–461. doi:[10.1002/\(SICI\)1097-0142\(19970201\)79:3<454::AID-CNCR5>3.0.CO;2-I](https://doi.org/10.1002/(SICI)1097-0142(19970201)79:3<454::AID-CNCR5>3.0.CO;2-I)
37. Yamaguchi T, Shirai Y, Ishihara T, et al. Pancreatic juice cytology in the diagnosis of intraductal papillary mucinous neoplasm of the pancreas: significance of sampling by peroral pancreatoscopy. *Cancer* 2005;104:2830–2836. doi:[10.1002/cncr.21565](https://doi.org/10.1002/cncr.21565)
38. Nagayoshi Y, Aso T, Ohtsuka T, et al. Peroral pancreatoscopy using the SpyGlass system for the assessment of intraductal papillary mucinous neoplasm of the pancreas. *J Hepatobiliary Pancreat Sci* 2014;21:410–417.
39. Arnelo U, Siiki A, Swahn F, et al. Single-operator pancreatoscopy is helpful in the evaluation of suspected intraductal papillary mucinous neoplasms (IPMN). *Pancreatology* 2014;14:510–514. doi:[10.1016/j.pan.2014.08.007](https://doi.org/10.1016/j.pan.2014.08.007)
40. Tanaka SA, McKee JD, Conway WC. Intracystic Biopsy and Diagnosis of Intraductal Papillary Mucinous Neoplasm via SpyGlass Pancreatography. *Ochsner J* 2015;15:452–454.
41. Kurihara T, Yasuda I, Isayama H, et al. Diagnostic and therapeutic single-operator cholangiopancreatography in biliopancreatic diseases: Prospective multicenter study in Japan. *World J Gastroenterol* 2016;22:1891–1901. doi:[10.3748/wjg.v22.i5.1891](https://doi.org/10.3748/wjg.v22.i5.1891)
42. Sauerbruch T, Holl J, Sackmann M, Werner R, Wotzka R, Paumgartner G. Disintegration of a pancreatic duct stone with extracorporeal shock waves in a patient with chronic pancreatitis. *Endoscopy* 1987;19:207–208. doi:[10.1055/s-2007-1018284](https://doi.org/10.1055/s-2007-1018284)
43. Dumonceau JM, Costamagna G, Tringali A, et al. Treatment for painful calcified chronic pancreatitis: extracorporeal shock wave lithotripsy versus endoscopic treatment: a randomised controlled trial. *Gut* 2007;56:545–552. doi:[10.1136/gut.2006.096883](https://doi.org/10.1136/gut.2006.096883)
44. Ito K, Igarashi Y, Okano N, et al. Efficacy of combined endoscopic lithotomy and extracorporeal shock wave lithotripsy, and additional EHL using the SpyGlass direct visualization system or X-ray guided EHL as needed, for pancreatic lithiasis. *Biomed Res Int* 2014;2014:732781.
45. Williamson JB, Draganov PV. The usefulness of SpyGlass™ choledochoscopy in the diagnosis and treatment of biliary disorders. *Curr Gastroenterol Rep* 2012;14:534–541. doi:[10.1007/s11894-012-0287-z](https://doi.org/10.1007/s11894-012-0287-z)
46. Sethi A, Chen YK, Austin GL, et al. ERCP with cholangiopancreatography may be associated with higher rates of complications than ERCP alone: a single-center experience. *Gastrointest Endosc* 2011;73:251–256. doi:[10.1016/j.gie.2010.08.058](https://doi.org/10.1016/j.gie.2010.08.058)
47. Ramchandani M, Reddy DN, Gupta R, et al. Role of single-operator peroral cholangioscopy in the diagnosis of indeterminate biliary lesions: a single-center, prospective study. *Gastrointest Endosc* 2011;74:511–519. doi:[10.1016/j.gie.2011.04.034](https://doi.org/10.1016/j.gie.2011.04.034)
48. Kawakubo K, Isayama H, Tsujino T, et al. Peroral cholangioscopy in a patient with a Billroth II gastrectomy using the SpyGlass Direct Visualization System. *Endoscopy* 2011;43:E241–E242. doi:[10.1055/s-0030-1256606](https://doi.org/10.1055/s-0030-1256606)
49. Draganov PV, Lin T, Chauhan S, Wagh MS, Hou W, Forsmark CE. Prospective evaluation of the clinical utility of ERCP-guided cholangiopancreatography with a new direct visualization system. *Gastrointest Endosc* 2011;73:971–979. doi:[10.1016/j.gie.2011.01.003](https://doi.org/10.1016/j.gie.2011.01.003)