INTRODUCTION

This profile summarizes the technical aspects and the preliminary literature related to the use of the SpyGlass Direct Visualization System. This novel technology provides the endoscopist with a direct intraluminal view of the biliary duct system. Consequently, lesions within the biliary tract can be biopsied under direct vision. It also allows for the application of therapeutic devices such as electrohydraulic lithotripsy (EHL) and holmium laser to fragment stones. This technology has utility when imaging limitations of conventional endoscopic retrograde cholangiopancreatography (ERCP) are encountered. It also appears to have overcome many of the limitations of earlier generation choledochoscopes.

HISTORICAL PERSPECTIVE

For the better part of forty years, biliary duct evaluation via cholangioscopy, in one form or another, has been in use by gastroenterologists. The techniques and technology through which this has been possible have been under significant scrutiny and constant refinement from its onset. The evolution of peroral cholangioscopy (POCS) is impressive, and has been well documented.

The earliest attempts at visualizing biliary anatomy with fiberscopes were only a glimpse of what was to come. Roughly thirty years after the first intraoperative cholangioscopy, the “mother-baby” scope was introduced. Initially a lengthy procedure requiring two specially trained endoscopists, POCS cases often lasted upwards of two hours. In addition, the early scopes were large, cumbersome and fragile. Often their specially designed optical fibers would break from the movement of the duodenoscope alone. Also, the first steering apparatuses were bidirectional as opposed to the four-quadrant steering of standard endoscopes. The initial working channels were sometimes less than adequate for biopsy forceps.
The evolution of miniscopes came next. These smaller scopes were more apt to access the common bile duct (CBD) without papillotomy, and, as technology allowed the scopes to get smaller, the working channels became more useful in therapeutic situations. While not yet perfect (e.g., no separate working channels), the option to move away from the “mother-baby” scope was present, and it was now possible to pass the miniscopes through the duodenoscope (duodenoscope assisted cholangiopancreatoscopy—DACP). As more technology went into the miniscopes, their size became smaller, their resolution sharper, and their therapeutic applications broader. Great strides have been made from the first miniscope to the advent of the SpyGlass peroral cholangiopancreatoscopy system, not the least of which are separate working and irrigation channels as well as four-way maneuvering (1–3).

ERCP has been a proven means of evaluating and treating a myriad of biliary pathologies. It remains the gold standard for CBD stone removal, therapeutic sphincterotomy and biliary stent placement (for benign or malignant strictures), but often the pathology in question during ERCP needs further imaging beyond fluoroscopy. Direct evaluation of the biliary tree now allows optically guided biopsies, real-time video of questionable lesions and a view of previously seen strictures with the chance of determining whether they are benign or malignant.

**SpyGlass Direct Visualization System**

In May of 2007, Boston Scientific introduced the SpyGlass Direct Visualization System. The goal of the system was to overcome the limitations of prior cholangioscopes and simplify peroral cholangioscopy.

Theoretically, at least, direct optical visualization of biliary ducts has advantages. As discussed above, standard ERCP allows a radiographic view of the ducts; however, interpretation and extrapolation are required. Radiologic imaging during ERCP may be insufficient to make a correct diagnosis. As gastroenterologists, we are trained to recognize, diagnose and treat diseases with direct real-time visualization of pathology; SpyGlass now allows those trained in the procedure to do just that. Further, the ability to biopsy

(continued on page 19)
within the biliary system, with direct view of a lesion, is now afforded with the SpyGlass System.

Major components of the system (Figure 1) include the SpyGlass® fiber optic probe, SpyScope® access and delivery catheter and the SpyBite® biopsy forceps. A “single-use, single-operator” device, the SpyScope® catheter consists of four lumens; a) a 1.2 mm accessory channel, through which the SpyBite® forceps can pass, b) two irrigation channels and c) an optic channel. This 10 Fr catheter allows four-quadrant biliary viewing due to a tip that has four-way steering capabilities. The total length of the Access and Delivery Catheter is 230 cm and is stabilized by the endoscopist with its placement just below the operating channel of the duodenoscope. The SpyGlass fiber optic probe, a “multiple-use” device, is a fragile 231 cm long catheter with an outer diameter of 0.77 mm which easily passes through the SpyScope Catheter. As both a transmitter of light (6,000 pixels) and intra-ductal images, its angle of viewing is 70×. The SpyBite® forceps are “single-use,” similar to the catheter, and have a central spike that minimizes the loss of small biopsies. Used in conjunction with the fiber optic probe, direct visualization of the biopsy site is now possible.

The SpyGlass system is compatible with EHL and holmium laser, for stone fragmentation. EHL uses the principle of high pressure shock waves generated by high voltage discharge and laser treatment offers another therapeutic alternative to EHL (4,5). This allows direct visualization of two proven methods of ablation for stones that may not be amenable to removal by conventional therapies (i.e. stones too large to pass after sphincterotomy).

CLINICAL ASSESSMENT PRIOR TO SPYGLASS PROCEDURE

While no standard patient protocol or evaluation has been advocated prior to performing SpyGlass, general guidelines are useful and are outlined here. The current trend has been toward performing ERCP and SpyGlass under general anesthesia and therefore each patient should have a routine laboratory evaluation. This includes at minimum a complete blood count (CBC), a chemistry panel (electrolytes, BUN, creatinine) and a coagulation panel (PT, PTT), no more than 14 days preceding the surgery. On arrival to the endoscopy suite or operating room (OR), the patient should have a full history and physical (H&P) performed, or at least an “H&P update” if a full H&P has been performed within the past 30 days. Vital signs, which should be continuously monitored by anesthesia for the duration of the procedure, should include a pulse-oximetry reading, blood pressure, pulse, respiratory rate, as well as temperature.

Table 1

Diagnostic and Therapeutic applications of SpyGlass Single-Operator Peroral Cholangiopancreatography System

Diagnostic
- Biopsy stricture under direct visualization (indeterminate stricture, dominant stricture in primary sclerosing cholangitis)
- Evaluate fixed filling defect noted on prior radiologic study
- Differentiation of intraductal mass (benign vs. malignant)
- Precision mapping of intraductal tumor prior to resection
- Collection of significant fluid sample for cytology
- Evaluate intraductal mucinous neoplasms under direct vision
- Evaluate choledochal cyst under direct vision
- Evaluate post liver-transplant ductal ischemia under direct vision
- Evaluate intraductal spread of ampullary adenoma under direct vision
- Evaluate for infection (CMV, fungal infection) using direct vision and tissue sampling

Therapeutic
- Choledocholithiasis (EHL, laser lithotripsy, argon plasma coagulation)
- Photodynamic therapy
- Nd-YAG laser ablation
- Cystic duct stent placement
- Foreign body removal
- Extraluminal applications
- Placement of stent through post liver transplant tight stricture
Confirmation of the indication(s) for performing the procedure is also warranted. Routinely, transaminases (AST, ALT), alkaline phosphatase (Alk P), bilirubin and other markers of hepatic function (dysfunction) are obtained and reviewed prior to initiation of the procedure. Imaging, usually via one or more separate modalities, should also be reviewed as often they indicate when SpyGlass direct visualization is warranted. A right upper-quadrant ultrasound is usually the first means of biliary evaluation in patients who have a liver-function test (LFT) derangement. Focus should be on the common bile duct (CBD) size and course as well as abnormalities noted within the visible biliary tree. The next form of radiographic evaluation may be computed tomography (CT); however, this not always the optimal test for biliary tree visualization. A magnetic resonance imaging (MRI) of the abdomen and pancreas (MRCP), if not included with the MRI abdomen, provides a better evaluation of the biliary anatomy, tumors and surrounding structures (6,7). MRI is not mandatory pre-procedure; in fact, in our experience, less than a quarter (22.2%) of our SpyGlass cases had an MRI prior, but all of our patient’s did have radiographic imaging of one form or another [CT, MRI/MRCP, ERCP, right upper quadrant ultrasound (US)]. It is also likely that many patients will have undergone ERCP pre-SpyGlass. In fact, the use of SpyGlass often hinges on the inability of ERCP to clinically distinguish the difference between benign and malignant biliary strictures or lesions on fluoroscopy.

**INDICATIONS AND CONTRAINDICATIONS FOR USE OF SPYGLASS**

A number of indications are standard for patients undergoing ERCP. Commonly, this procedure is done for evaluation and therapy of a number of conditions including, but not limited to: obstructive jaundice, biliary strictures, cholelithiasis, recurrent pancreatitis (of unknown origin), suspected bile leaks and ampullary neoplasms, intrahepatic biliary tract and pancreatic duct disease and trauma (both biliary and pancreatic), and unexplained and persistent LFT abnormalities (8).

SpyGlass is intended to provide direct visualization of the biliary tree for diagnostic and therapeutic applications. Judah and Draganov have compiled a nearly all-inclusive list of diagnostic uses for intraductal endoscopy that range from the evaluation of fixed filling defects (on ERCP, cholangiogram or MRCP) to determining benign from malignant tumors and subsequent mapping of intraductal tumors (prior to surgery) to evaluating cysts and for ischemia (1). Therapeutic and sampling options are also highlighted; these include optically guided biopsies of indeterminate strictures and strictures seen in primary sclerosing cholangitis (PSC), fluid sampling for cytology and further tissue sampling for infection and cancer. Further abstracts and studies, as described below, have pushed the limits of SpyGlass and what is now possible is ever-expanding. Table 1 reviews these numerous indications.

As for contraindications, if a patient is not medically suited to undergo an ERCP, they should not have the SpyGlass procedure performed. Utilization of anesthesia is recommended as the above procedures may last an hour or more. Patients with prior adverse reactions to anesthesia, a prior history of underlying or active heart disease, a propensity for arrhythmias and a history of lung disease will be considered at higher risk for the procedure, and these risks may outweigh the benefits of endoscopic evaluation. As with every procedure performed within the OR or endoscopy suite, informed consent must be obtained prior to initiation. Potential procedure risks including abdominal pain, bleeding, perforation, infection, pancreatitis, cardiopulmonary arrest, and death should be listed on the consent form and discussed with the patient before deciding whether or not to proceed.

**SPYGLASS TECHNIQUE**

Boston Scientific supplies standard “manufacturer recommendations” for the use of the SpyGlass system. The cholangioscopy procedure with the SpyGlass system is performed by a single operator with the SpyScope® access and delivery catheter positioned just below the operating channel of the duodenoscope. This positioning allows the endoscopist to control both the tip deflection wheels of the duodenoscope and the knobs of the SpyScope Catheter visualization system with the same hand. Stabilization of the both systems
is performed with the physician’s other hand. The SpyGlass system is introduced into the therapeutic duodenoscope. The bile duct is cannulated (Figure 2), after a sphincterotomy as needed, and the SpyScope® catheter guides the SpyGlass direct visualization probe into the biliary tree. The SpyScope® catheter and SpyGlass probe are maneuvered up to the desired area of interest within the duct for direct visualization. Selected ducts and branches of interest (Figure 3A) can be examined during repeated advancement and withdrawal of the scope. If strictures (Figure 3B) or other biliary pathology is encountered, the SpyBite® biopsy forceps guided by the SpyScope® catheter can be introduced and an endoscopic guided biopsy taken (Figure 3C). Furthermore, as mentioned earlier, biliary tract stones can be seen under direct vision (Figure 3D) and EHL can be easily applied (Figures 3E, F).

Our experience has been similar to that described by the manufacturer. Minimizing the use of contrast prevents clouding of the video with SpyGlass. Routine irrigation using the foot assisted washing system also improved picture clarity. Generally four to six biopsies are useful in increasing yield as is post biopsy aspiration of bile duct fluid for cytology.

**POST SPYGLASS CARE**

Routine pre- and post- procedure care applies to all patients having an ERCP and/or SpyGlass direct visualization. While SpyGlass itself lengthens the time required to perform a complete optically guided biliary evaluation, data does not exist whether the procedure has greater risk than ERCP alone. Despite efforts to minimize the risks of these procedures, mortality and morbidity risks remain high with ERCP. More than 7% of patients undergoing ERCP have experienced a myriad of complications; this is up more than 1% from prior decades (9,10). Ranging from mild to severe, everything from pancreatitis, infection, reaction to anesthesia, bleeding, perforation, cardiopulmonary arrest, and death may occur. The risk of bleeding, for example from sphincterotomy, is greater for the patient on an anticoagulant or with thrombocytopenia, and the risk of infection increases with biliary manipulation. Thus, the importance of post-SpyGlass care/monitoring must be stressed.

**CLINICAL TRIALS REPORTING ON SPYGLASS OUTCOMES**

Chen, in a preclinical characterization of the SpyGlass system, used a bench simulator to directly compare SpyGlass to a control fiberoptic transendoscopic...
choledodochoscope with two-way deflection (10). The bench simulator consisted of acetal guide blocks and supports, glass tubing (mimicking the esophagus), and silicone tubing (configured with a curvature as to simulate in vivo bile ducts). The following capabilities of the two systems were assessed: accessing quadrants within the simulated bile duct with and without SpyBite forceps, opening and closing the forceps, accessing simulated biopsy targets (monofilament suture knots with a spherical diameter of 1.2 mm placed in each quadrant approximately 18 cm proximal to the simulated papilla), and performing simulated biopsies, and ease of insertion and removal of forceps through the working channel. Main outcome measurements were rate ratios (RR) and 95% confidence intervals (CI). SpyGlass demonstrated higher success rates for accessing all quadrants, both with (RR 2.00, 95% CI 1.56–2.78) and without (RR 1.71, 95% CI 1.39–2.29) biopsy forceps. It also had higher success rates for accessing biopsy targets (RR 2.09, 95% CI 1.60–2.91) and performing simulated biopsies (RR 2.94, 95% CI 2.05–4.52). This study also looked at high level disinfection (HLD) of the reusable optic probe and achieved microbial species log reductions of 6.0 to 7.0 (criterion of effective HLD was a ≥6 log reduction). Lastly, this study looked at the feasibility of in vivo biopsy in a porcine model. The SpyGlass system was advanced into the biliary and hepatic ducts of five anesthetized pigs and biopsies were attempted at above and below the hepatic bifurcation. During pathologic examination the adequacy of each specimen was assessed on a gross (adequate, inadequate, no sample)
and histologic (excellent, adequate, inadequate, and no sample) basis. A total of 34 biopsies were taken (14 above and 20 below the hepatic bifurcation). Ninety-one percent (31 of 34 bites) of the gross specimens were deemed adequate. Ninety percent (28 of 31 specimens were rated adequate or excellent).

Chen and Pleskow, in a prospective observational clinical feasibility study, evaluated the clinical utility and safety of the SpyGlass system in 35 patients (11). Study inclusion criteria were failure of prior ERCP to either answer a biliary diagnostic question or perform a therapeutic intervention. Specific indication for SpyGlass included indeterminate stricture {22}, indeterminate filling defect {5}, stone therapy {5}, cystic lesion {2} and gallbladder stent placement {1}. The main outcome measurement was a procedural success rate defined as proportion of SpyGlass procedures in which the diagnostic or therapeutic objectives were attained. This was achieved in 32 out of 35 patients (91%) [95% CI 77–98]. In the five patients with previously failed stone therapy, SpyGlass-directed EHL succeeded in five of five patients (100%). Nineteen of twenty patients (95%) who underwent SpyGlass directed biopsy had specimens deemed adequate for histological examination. Sensitivity and specificity of SpyGlass directed biopsy to diagnose malignancy was 71% and 100%, respectively.

Several recent clinical trials/clinical studies have been reported in preliminary form in 2007 and 2008. Canlas, et al retrospectively evaluated the clinical utility, safety, and ease of use of SpyGlass during their institution’s initial experience with the device (12). In six patients, they assessed the following outcomes: success of introducing the device into the bile duct, successful identification of filling defects, use and success of electrohydraulic lithotripsy (if performed), and use and success of directly visualized forceps. Five of six patients had successful cannulation of the common bile duct. The one failed cannulation was secondary to difficult anatomy from a suspected malignant biliary stricture in the common bile duct. Identification of filling defects occurred in four of the five cases where successful cannulation was achieved (three stones and one suspected malignancy). Biopsies were performed once (in the case where suspected malignancy occurred) and was successful in diagnosing a ductal carcinoma. EHL via the SpyGlass device was attempted in two patients (one with a CBD stone and one with a cystic duct stone) and partial stone clearance was achieved in each case. Failure of complete lithotripsy was attributed to the size of the CBD stone and inability to maintain adequate probe to stone contact in the cystic duct. The authors concluded that the SpyGlass system achieved adequate visualization of the biliary tree to facilitate both the diagnosis of biliary strictures and lithotripsy of stones during ERCP.

Parsi, et al presented a case report of a 62-year-old female patient status post-cholecystectomy with recurrent pancreatitis, mildly elevated LFTS, and a dilated biliary tree (13). Subsequent work-up with ERCP times two, CT scan, and MRCP failed to provide a diagnosis. SpyGlass revealed a foreign body that was found to be a remnant of a T-tube used during the patient’s cholecystectomy. The hollow (filled with contrast during ERCP and bile during MRCP) and radiolucent (not seen on CT scan) nature of the T-tube evaded detection with prior diagnostic modalities. Thus, direct cholangioscopy facilitated diagnosis and subsequent removal of the foreign body.

Stevens, et al examined the performance of SpyGlass in treating biliary stones with EHL in 15 patients who had previously failed biliary stone extraction using conventional ERCP techniques (14). Stone clearance was achieved in 85% of cases where EHL was attempted. Sixty-one percent of cases cleared with one EHL treatment and 23% of cases cleared with two EHL treatments. The mean number of EHL probes needed to complete stone extraction was one (range one-to-two). There were no reported complications.

Kuperschmit, et al reviewed their initial experience with SpyGlass and assessed its usefulness as both a diagnostic and therapeutic tool (15). In retrospective examination of 26 cases, success in each of the following areas was assessed: imaging the desired ductal structures, performing EHL, and in guiding biopsy. The authors concluded that excellent visualization was achieved in all cases. In spite of good stone visualization and EHL probe placement, stone clearance was only achieved in one out of four cases. They authors concluded that EHL was technically facilitated by SpyGlass but two cases of very hard stones proved recalcitrant. Tissue was obtained in all patients and
was diagnostic of malignancy in 4/13 patients. The authors concluded that SpyGlass added to their ability to diagnose malignancy, though at a lower than expected yield. In the majority of cases, the authors found SpyGlass to be clinically useful.

Lo, et al reported on preliminary technical experience with the device among three endoscopists in 22 patients (16). SpyGlass indications included direct biopsy {6}, confirm ductal abnormalities {6}, examine stricture {5}, facilitate EHL {4}, and visualize filling defects {1}. A five-point scale was used to report their observations, with five being most favorable. Visualization upon bile duct entry was rated as poor (mean 2.3). However, flushing with either saline or water eventually resulted in an acceptable examination (3.1). Satisfaction with quality of examination by location was as following: common hepatic duct/CBD > right hepatic duct > left hepatic duct/intrahepatic ducts. Global score for technical satisfaction was three. When compared to their prior experience with cholecdochoscopy, the three operators regarded SpyGlass as easier to operate by one person {3.6}, having better tip deflection {4}, easier to pass wire/optical probes (3.6), but inferior in brightness (2.4) and visualization of target tissue (2.6). Overall SpyGlass was useful in 16 cases (ruled out pathology in 10, directed biopsy in four, and facilitated EHL in two) and in six cases added no value. The authors concluded that the SpyGlass device was relatively easy to use by a single operator, able to reach above the hepatic bifurcations, and had excellent performance with respect to tip deflection, optical fiber protection, and tip-locking mechanism. With regard to illumination and visualization, they concluded it was slightly suboptimal. They admitted further experience was needed before definitive conclusions could be drawn.

Chen, et al reported their SpyGlass experience with direct access and visualization of the pancreatic ducts [peroralpancreatoscopy (PP)] for pancreatic stone therapy and investigation of suspected pancreatic lesions (17). Their aim was to document the performance, safety, and utility of the SpyGlass system in 48 consecutive patients requiring PP for the following indications: pancreatic stones {17}, indeterminate strictures {11}, dilated ducts {5}, indeterminate filling defects {11} and mass {4}. EHL led to successful stone clearance in eight out of 10 patients. Using disposable SpyBite forceps, PP-guided biopsies were attempted in 10 patients and a mean 4.4 biopsy specimens per patient provided adequate specimens for histological analysis. No serious adverse events occurred. They concluded that for PP Spyglass is technically feasible, allows access to target sights in the main pancreatic duct for visual inspection, stone therapy, and tissue sampling in most patients. They also concluded that the procedure could be safely performed in patients with pancreatic stones, intraductal papillary mucinous neoplasm (IPMN), and indeterminate strictures. However, they commented that its safety and clinical utility has yet to be proven in patients with small ducts and or non-obstructed ducts. They also made the statement that a smaller catheter diameter is preferred for pancreatic application.

Raijman, et al assessed Spyglass performance, feasibility, and safety in 128 patients, 72 (56%) with therapeutic indications [CBD stones, pancreatic duct (PD) stones, and biliary strictures] and 56 (44%) with diagnostic indications (abnormal LFT’s, abnormal imaging, and cholangiocarcinoma staging) (18). Percutaneous endoscopy was utilized in 121 and percutaneous in seven. Spyglass was successful in all cases. Per-oral use was easier than percutaneous, due to the ability of the duodenoscope to control SpyGlass. Visualization was deemed good in 108, fair in 10, and poor in 10. Removal of the guide wire from its working channel improved SpyGlass maneuverability. The use of EHL and biopsy forceps was possible in 65/70 patients. In five patients the EHL probe could not be advanced due to scope angulation. There was no associated morbidity. The authors concluded that the device is effective in the evaluation and treatment of various biliary and pancreatic tract diseases, modifying a pre-procedure diagnosis in a significant number of patients. Per-oral use was found to be easier compared to the percutaneous approach. They felt further use and technical improvements were needed.

Navaneethan, et al evaluated the efficacy and practicality of SpyGlass for diagnosis and therapy of biliary disorders as compared to conventional ERCP (19). After conventional ERCP was performed in 17 patients, a total of 19 SpyGlass examinations were per-
formed. Indications for the SpyGlass procedure included previously failed treatment for large biliary stones (N = 9) and indeterminate biliary stricture (N = 10). Of note one patient had both stone and stricture and one patient underwent removal of a migrated intraductal metal coil (previously placed to embolize a hepatic artery aneurysm). Overall procedure success rate was 94.7% and cholangioscopic stone removal with EHL was successful in 88.9%. SpyGlass altered patient management compared to the initial ERCP in 42.1% of procedures. One procedural complication (aspiration) occurred with uneventful recovery. The authors concluded that SpyGlass provided a safe means of expanding diagnostic and therapeutic applications as compared to conventional ERCP.

Raijman and Fishman directly compared SpyGlass to an established choledochoscope (FCP-9P, Pentax, USA) in five patients (20). Indications included the following: large choledocholithiasis {3}, bile duct stricture {1}, and biliary stricture {1}. The following parameters were evaluated: ease in setting up, ease of advancement through the scope, time to complete the choledochoscopic procedure, visual clarity, intraductal cannulation and maneuverability, irrigation, and ability to provide therapy. Results showed that there was no difference in ease of set up, ease of advancement through the scope, in ductal cannulation, or in time to perform and complete the procedure. EHL advancement was possible in all FCP-9P cases while it was not possible in one SpyGlass case. When performed without a guide wire, intraductal maneuverability was equal. Visual clarity was superior with FCP-9P. Intended outcome occurred in 100% of FCP-9P cases and 80% of SpyGlass cases. Authors concluded that SpyGlass was effective in the evaluation and treatment of various biliary tract diseases. They felt its major advantage compared to FCP-9P is that it is single operator and has an independent irrigation channel. They opined that future refinement of the SpyGlass scope is needed.

Chen, et al, in a 15 center 12 month follow-up registry, documented performance and utility of peroral cholangioscopy (PO) using SpyGlass in 146 patients requiring PO for stone therapy or investigation of suspected pathology with and without biopsy (21). Procedural success was defined as the ability to visualize/biopsy target lesion or initiate stone therapy. SpyGlass indications were non-PSC indeterminate strictures (39%), stone management (34%), exclude cancer in PSC (10%), other non-diagnostic ERCP findings (8%), indeterminate filling defect (6%), other (4%). Biopsies were taken in 40% of patients. Overall procedural success was 89%. Preliminary sensitivity and specificity at 30 days relative to clinical diagnosis of malignancy are 90% and 89%, respectively. Fourteen serious adverse events related to device/procedure occurred: cholangitis, bacteremia, abdominal pain, pancreatitis, liver abscess, abdominal distension, nausea, transient hypotension, and radiculopathy. The authors concluded that SpyGlass can be safely performed by a single operator, provides reliable access to target sites for visual inspection, stone therapy, and tissue sampling, and obtains adequate histological samples. They also concluded that the combination of visual diagnosis and directed tissue sampling using SpyGlass may improve diagnostic accuracy in patients with indeterminate bile duct lesions.

Pleskow, et al looked at whether targeted biopsies obtained under direct visualization might improve diagnostic sensitivity of intraductal biopsies, as ERCP-guided brushings and biopsies of indeterminate biliary strictures have low sensitivity for the detection of malignancy (22) Sixty international multicenter registry patients with indeterminate biliary strictures or filling defects underwent ERCP followed by SpyGlass cholangioscopy with biopsy. The amount of tissue obtained at biopsy was deemed adequate in 87% of cases. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of biopsies for detection of malignancy in 29 patients who had at least six months of follow-up were 78%, 100%, 100%, and 60%. The authors concluded targeted biopsies using SpyGlass are feasible, safe, and well-tolerated. They also concluded that SpyGlass had a high sensitivity for diagnosing pancreatobiliary malignancies via biliary biopsies obtained under direct visualization.

Loren, et al reported the clinical applications and technical performance of SpyGlass cholangioscopy/pancreatoscopy at three tertiary referral centers (23). Thirty-five patients underwent a total of 39 SpyGlass procedures. Indications included: indeterminate biliary stricture (62%), choledocholithiasis (21%), pancreatic
duct stones, evaluation of IPMN, suspected biliary mass, and cholangiocarcinoma surveillance. In 24% of the indeterminate biliary stricture cases, the clinical diagnosis was altered from suspected malignant stricture to benign stricture. Stone clearance with EHL or laser was successful in 100% of the nine cases, requiring only one session in all but one case. Visualization alone facilitated diagnosis in 7% of cholangioscopic cases and two-thirds of pancreatoscopic cases. Biopsy was performed in 24 cases and 88% yielded tissue deemed adequate for histologic evaluation. Procedure-related complications occurred in five patients and were all within the spectrum of those reported with other interventional pancreatobiliary procedures.

Raijman and Slivka evaluated the feasibility of the SpyGlass system for percutaneous use (24). Percutaneous access to the pancreatobiliary system via percutaneous transhepatic cholangiography (PTC) is indicated when ERCP has failed to access the biliary tree or when the papilla is inaccessible. Once percutaneous access was achieved using standard interventional radiology techniques, the SpyGlass scope loaded with the SpyGlass optical probe was introduced into the bile duct using a standard 10 Fr sheath. In one patient, introduction of the optical probe and a standard 7 Fr sheath alone were sufficient. In all cases, direct visualization was achieved. Thus, diagnostic and therapeutic capabilities of PTC are expanded when used in conjunction with SpyGlass. With the exception of minimal oozing from EHL probe in one patient, there were no complications.

Keswani, et al (25) described their preliminary experience in 26 patients who underwent SpyGlass at a single center. The most common SpyGlass procedure indications were evaluation of biliary (14) and pancreatic (2) strictures. Other indications included evaluation of small filling defects, suspected malignancy without stricture and placement of a bifurcation tumor stent. SpyBite directed biopsy was obtained in 13 patients with a diagnosis of malignancy obtained in four patients. One of the nine patients with a negative SpyBite biopsy was found to have cancer in follow-up. In two additional patients a malignant mass was biopsied with conventional intraductal forceps after being visualized with SpyGlass. EHL was successfully performed in three cases, with one patient requiring further lithotripsy. Mean procedure time was 80.5 minutes, with a trend towards decreased procedure time as SpyGlass experience increased. Two patients developed post-procedural interstitial pancreatitis. SpyGlass altered clinical management in 14 patients (53.8%). The authors concluded that in the majority of patients SpyGlass provides additional information. They felt that it may be most useful in evaluating indeterminate strictures and in performing EHL. Increased operator experience leads to decreased procedure time.

Aziz, et al evaluated the impact of SpyGlass on patient care in cases where ERCP had previously identified bile duct filling defects of uncertain origin (26). These defects included questioned stones (11), suspected benign lesions (3), suspected malignant lesions (4), and indeterminate mass (2). In ERCP cases of questioned stones SpyGlass confirmed stones in nine of 11 cases, directly visualizing a benign lesion in one instance and air bubbles in the other. In the three ERCP suspected benign lesions, SpyGlass demonstrated one benign lesion and two malignant lesions. In the four ERCP suspected malignant lesions, SpyGlass showed two stones, one malignant lesion, and one benign lesion. In the two ERCP suspected indeterminate masses, SpyGlass revealed stones in one and air bubbles in the other. Recommended follow-up based on SpyGlass findings included SpyGlass directed EHL for large stones (40%) and surgery (20%). The authors concluded that SpyGlass with and without biopsy is highly accurate in identifying the etiology of bile duct filling defects of uncertain etiology and had a favorable impact on patient care. They also concluded that SpyGlass was effective in identifying stones missed during ERCP and in directing stone therapy in patients who had failed conventional stone therapy.

Raijman, et al evaluated the performance, feasibility, and safety of using SpyGlass and lithotripsy using electrohydraulic and holmium laser methods in the management of 41 patients with difficult bile duct stones (27). Six of the 41 patients underwent SpyGlass using a percutaneous approach as they had previously undergone Roux-en-Y surgery with stones above anastomotic stricture. Indications for choledochoscopy included large choledocholithiasis (26), intrahepatic lithiasis (10), lithiasis associated with bile duct strictures (11) [seven with intrahepatic lesions], and
Mirizzi syndrome [1]. Stone clearance was achieved in 37 patients after one procedure and in four patients after two procedures. There was no morbidity associated with the use of SpyGlass. Authors concluded that the SpyGlass is effective in the evaluation and treatment of difficult extra-hepatic and intra-hepatic bile duct stones. In the majority of patients ductal clearance can be achieved after one session. PO SpyGlass use was technically easier compared to the percutaneous route.

Wright, et al reported a case where SpyGlass facilitated cholangioscopic placement of a guide wire across a tight anastomotic stricture after an orthotropic liver transplantation [28]. Previous attempts to cannulate the stricture with a guide wire during ERCP had failed. ERCP management of tight strictures is a blind approach and usually requires multiple attempts by the endoscopist in a hit or miss fashion. Following cannulation, the stricture was subsequently dilated and stented. The success of the SpyGlass procedure prevented the need for repeat ERCP, percutaneous approach, or revision surgery.

**TRANSLUMINAL SPYGLASS APPLICATIONS**

Recently, the first report of SpyGlass being used outside the biliary tree or main pancreatic duct was reported [29]. A patient was referred for endoscopic ultrasound (EUS) to further evaluate an 8-cm cystic lesion in the pancreas on CT considered suspicious but not diagnostic for a pseudocyst. During EUS a suspicious pancreatic-cyst-wall abnormality was noted. Using a conventional needle-knife, a small cyst-gastrostomy opening was created. The track was dilated with a 6-mm biliary balloon dilator. The SpyGlass access and a 10F delivery catheter and a 0.9-mm-diameter optical probe were introduced through the 3.7-mm accessory channel of the echoendoscope and then into the cyst. Under direct visualization, the wall of the cyst was carefully inspected the focal wall abnormality was biopsied with SpyBite biopsy forceps. The pathological findings were consistent with pseudocyst. The authors suggested several potential EUS-assisted SpyGlass transluminal applications. One potential application is examining, taking biopsy, and guiding therapy of abdominal lymph nodes. Another is EUS-guided SpyGlass mediastinoscopy. In more general terms they posit that it might have application in natural orifice transluminal endoscopic surgery (NOTES).

**SUMMARY**

While much of the data is preliminary, SpyGlass appears to have overcome many of the limitations of earlier choledochoscopes. Some of its major advantages include the fact that it is a single operator system, allows directed biopsy and, as standard for routine endoscopy, four-way steering capabilities. This system allows direct visualization of previously noted lesions as seen on endoscopic retrograde cholangiopancreatography or other radiologic means. Indications and contraindications for the procedure are straightforward, and the therapeutic opportunities afforded with SpyGlass are growing. While admittedly only a first generation device, a few disadvantages are apparent: at times image clarity is slightly sub-optimal and the scope and components are fragile. In spite of some of these limitations it is currently a key component in evaluating biliary anatomy. Future prospective studies will provide further insight into the therapeutic role of endoscopy with SpyGlass.

**Financial and Competing Interest Disclosure**

Dr. Roorda has no conflict to declare. Dr. Kupec has no conflict to declare. Dr. Sundaram serves on NIH and VA Study Section and advisory boards for Abbott Laboratories and UCB, Inc.

**References**


