Intraductal biliary and pancreatic endoscopy: An expanding scope of possibility

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Abstract

Intraductal endoscopy describes the use of an endoscope to directly visualize the biliary and pancreatic ducts. For many years, technological challenges have made performing these procedures difficult. The “mother-baby” system and other various miniscopes have been developed, but routine use has been hampered due to complex setup, scope fragility and the time consuming, technically demanding nature of the procedure. Recently, the SpyGlass peroral cholangio-pancreatocopy system has shown early success at providing diagnostic information and therapeutic options. The clinical utility of intraductal endoscopy is broad. It allows better differentiation between benign and malignant processes by allowing direct visualization and targeted sampling of tissue. Therapeutic interventions, such as electrohydraulic lithotripsy (EHL), laser lithotripsy, photodynamic therapy, and argon plasma coagulation (APC), may also be performed as part of intraductal endoscopy.

INTRODUCTION

Intraductal endoscopy describes the use of an endoscope to evaluate the biliary and pancreatic ducts. There are significant technological challenges encountered in creating a scope that allows direct visualization of these ducts. However, attempts have been made, and technology is developing that promises greater opportunity to provide improved diagnosis and therapy regarding lesions in the biliary and pancreatic ducts.

HISTORY AND TYPES OF SCOPES

Cholangioscopy was considered as early as the 1950’s[1]. However, technology at that time caused severe limitations. In the 1960’s, intraoperative cholangioscopy was first successfully utilized[2-4]. Percutaneous cholangioscopy (POCS) was initially described in the mid-1970’s. One of the first reports demonstrated that a fiberscope of 8.8 mm diameter could be directly inserted through the mouth, into the biliary system after an endoscopic papillotomy, without the need of using a second scope as a guide[5]. This scope did provide a biopsy channel to obtain tissue samples. Other investigators also successfully demonstrated the use of POCS to directly visualize the biliary system during this time[6-10].

The idea of guiding a small caliber “baby” cholangioscope through the channel of a “mother” duodenoscope into the common bile duct (CBD) gained acceptance. This “mother-baby” system is also known as duodenoscope-assisted cholangiopancreatocopy (DACP). However, use of the early cholangioscopes was difficult since...
their optical fibers were prone to break easily from pressure applied with the elevator of the duodenoscope. Regardless, Urakami demonstrated successful access to the ductal system in 25 of 30 cases in 1980 by using this technique\[31\]. The University of Chicago published their experience with a conventional “mother-baby” system utilizing a set of Olympus scopes (TJF-M20 and CHF-B20) (Olympus Inc, Tokyo, Japan), where the “baby” scope had a diameter of 4.5 mm, two-way deflection and included an instrument channel\[12\]. This system was used in patients 18 times over a 3-year study period. Initially, they demonstrated a steep learning curve, when they intubated the papilla in only 2 of 5 cases. They subsequently found it was necessary to perform a papillotomy before the “baby” scope could be passed. After this adjustment, they were successful at intubating the papilla in 13 of 13 cases. While the 1.7 mm working channel on the cholangioscope did allow for diagnostic and therapeutic intervention, the system was found to be cumbersome to use. Average time of the procedure was around 2 h. Two endoscopists were required (i.e. one for each scope). The cholangioscopes continued to be fragile and prone to breaking. Further, these cholangioscopes only had two-way deflection at the tip as opposed to the typical four-way deflection offered by other endoscopes. These limitations led this group to conclude that while this “mother and baby” system certainly offered new endoscopic potential, it would best be utilized in only select patients at highly specialized tertiary referral centers. Another study at Case Western Reserve University further validated the use of this Olympus system by successfully visualizing the biliary tree in five patients\[10\]. The steerable properties of the cholangioscope combined with the presence of the accessory channel allowed it to have significant advantages over past attempts at POCS.

The search for a less cumbersome technique to directly visualize the biliary tree led to a small pilot study with an attempt to perform direct visualization of the biliary tree with an ultra-slim upper endoscope\[14\]. This technique used endoscopic retrograde cholangiography (ERCP) to place a super-stiff 0.035-inch diameter guidewire (Boston Scientific Corp, Natick, Mass) in the CBD. Using the wire to maintain access, the duodenoscope was removed and an ultra-slim upper endoscope (GIF-XP 160, Olympus America Inc, Center Valley, PA) with an outer diameter of 5.9 mm was back loaded over the guidewire under fluoroscopic and endoscopic control into the duodenum and then across the ampulla of Vater into the CBD. Endoscopic sphincterotomy was required in order to permit passage of the endoscope into the CBD. This procedure was successful in providing direct cholangioscopy in 3 of 3 patients. Further studies will show whether this technique may have broader application. However, this technique can be performed by only one endoscopist, and the larger working channel (2.0 mm) of the endoscope allows for larger biopsies and the potential for more therapeutic applications.

Several miniscopes have been developed which allow the ability to examine the biliary and pancreatic ducts. The extreme small size of some of these scopes, ranging as small as 1 to 15 French in diameter, allowed for their delivery into even the smallest of ducts, and could allow access without the presence of papillotomy when the outer diameter of the scope is less than 2.5 mm\[15-19\]. While these very small scopes raise interesting possibilities, their use is limited by their fragility, lack of tip deflection and lack of an inner working channel. A fine-caliber flexible miniscope created by Soda\[20\], allowed access to the bile duct without necessitating sphincterotomy due to its external diameter of only 2.09 mm. However, unlike many other fine-caliber miniscopes, this scope did have a central working channel of 0.72 mm.

Slightly larger miniscopes with bi-directional angulation systems and instrument channels were developed by Olympus (CHF BP 30 with 3.4 mm diameter) and Pentax (FCP-9P with 3.1 mm diameter and FCP-8P with 2.8 mm diameter)\[21\]. Sander and Poels developed a new miniscope (2.3 mm in diameter) for POCS (PolyDiagnost, Reichertshausen, Germany), with a less fragile, steerable tip, which had two different degrees of stiffness. This scope has a working channel measuring 1.2 mm (3.6 Fr), through which a probe for electrohydraulic lithotripsy (EHL) and a stone extraction basket can be passed\[22\]. These two authors demonstrated successful pancreatoscopies with their scope in 8 of 10 cases and successful choledochoscopies in 11 of 11 cases. The presence of the instrument channel in all three of these scopes allows for therapeutic applications. Also, common to these miniscopes is their ability to be introduced through a standard therapeutic duodenoscope, hence these scopes could become part of a DACP (DACP) system. However, none of these scopes had separate air/water channels, and it is frequently necessary to continuously irrigate the bile ducts due to stone debris or sludge obscuring the view. Thus, at times, nasobiliary drainage tubes have been inserted in the bile duct along with the cholangioscope in order to allow irrigation to be effectively performed during the cholangioscopy examination.

While some of the fine-caliber miniscopes have been used to perform pancreatoscopy, one group of Japanese researchers has focused on developing a miniscope specifically designed to perform pancreatic duct visualization. Kodama and others developed a prototype peroral electronic pancreatoscope (external diameter 2.1 mm) and found its images did provide fine detail of the pancreatic duct\[23\]. They utilized an ultraminiature charge-coupled device with sequential color wheel method to generate images. This initial prototype scope was limited by its lack of a working channel. The group continued their development and in 2004 published their experience with another peroral electronic pancreatoscope prototype with a 2.6 mm external diameter and an inner working channel of 0.5 mm\[24\]. This scope was successfully inserted into the pancreatic duct without sphincterotomy in 7 of 9 cases. A duodenoscope was required to insert the scope into the pancreatic duct, and two endoscopists were required to perform the case. However, images were obtained that
provided excellent visualization of the pancreatic duct and sampling of pancreatic fluid could be performed via the working channel.

Recently, the SpyGlass peroral cholangio-pancreatoscopy system (Boston Scientific Corp, Natick, Mass) has been introduced [25]. This system makes use of a reusable optical probe, a disposable access and delivery catheter (SpyScope), and disposable biopsy forceps. The outer diameter of the SpyScope is 10 French. This system offers several advantages over previous cholangioscopes. It allows for single-operator control of both the duodenoscope and the SpyScope because the SpyScope catheter is mounted on the duodenoscope by a silastic belt. The endoscopist can sequentially manipulate the controls of both the duodenoscope and the SpyScope with one hand; thus, the need for two endoscopists is eliminated. This system also uses 4-way tip deflection, which allows for improved access of tertiary ducts. Further, the irrigation channel (0.6 mm) is separate from the working channel (1.2 mm), which allows for sustained continuous irrigation regardless of whether the working channel is in use. These advances have allowed this system to be used clinically in a number of tertiary referral centers.

Clinical data regarding the SpyGlass system continues to be collected; however, an initial feasibility study is available [26]. In this study, 35 patients underwent cholangioscopy with the SpyGlass system. Procedural success defined as attaining the diagnostic or therapeutic goal of the procedure. Procedural success was documented in 91% (32 of 35 patients). Sphincterotomy was frequently required in patients, in that 8 of 10 patients with intact sphincters required sphincterotomy at the time of the SpyGlass procedure. SpyGlass directed biopsy yielded promising results in that 19 of 20 (95%) of optically guided biopsies yielded specimens with adequate tissue for histologic evaluation. EHL was successful in 5 of 5 (100%) of patients when performed via the SpyGlass working channel. Two patients (6%) experienced procedure-related complications, namely ascending cholangitis in one patient and cholangitis with intrahepatic abscess in the other patient. Both patients recovered without sequelae. While this initial data is promising, the prospective data currently being collected from clinical use of the SpyGlass system will provide a better analysis of its potential impact on cholangiopancreatoscopy.

**DIAGNOSTIC APPLICATIONS**

Intraductal endoscopy may be used for multiple diagnostic indications (Table 1). Direct visualization of the ducts may increase the ability to differentiate and diagnose lesions accurately in comparison with standard imaging and ERCP techniques. In 1999, Siddique reported an experience of 61 choledochoscopies performed via the transpapillary route for diagnostic purposes [27]. Importantly, this study showed that direct visualization provided additional unsuspected diagnostic information in 18 of the 61 (29.5%) patients, beyond that which had been achieved by previous workup. A Korean study reviewed cholangioscopic findings from 111 patients with benign or malignant bile duct tumors [28]. By evaluating mucosal changes, presence of neovascularization, and patterns of luminal narrowing, it was determined that bile duct tumors did indeed demonstrate unique optical characteristics, that could allow optical differentiation among adenocarcinoma, adenoma, hepatocellular carcinoma, mucin-hypersecreting cholangiocarcinoma, biliary cystadenocarcinoma, and squamous cell carcinoma. Thus, it was felt that cholangioscopy can provide additional information that would be useful in differentiating benign from malignant lesions and would help characterize the type of malignant lesion. Another Korean study of 63 patients [29] with indeterminate strictures reported that cholangioscopy could potentially improve the diagnosis of cholangiocarcinoma by allowing for the optical recognition of an irregularly dilated and tortuous vessel, the so-called “tumor vessel.” They found that this “tumor vessel” was noted in 25 of 41 patients with malignancy (61%), while no patients with benign stricture had this characteristic appearance. The value of direct cholangioscopy could be seen best in this study by combining the optical observation of tumor vessel with percutaneous transhepatic cholangiography-guided biopsy resulting in a diagnosis of malignancy in 39 of 41 patients (96%). This is a significantly increased rate of preoperative diagnosis when compared with percutaneous transhepatic cholangiography-guided biopsy alone (80.4% sensitivity for diagnosis in this study). In 2005, data from 97 patients showed the additive value of combining direct POCS with standard ERCP [30]. The combination of POCS and ERCP improved the sensitivity of diagnosing malignant lesions from 58% to 93%. Additionally, POCS was especially useful in evaluating 21 filling defects of uncertain etiology which had been noted on ERCP cholangiogram. POCS was able to correctly diagnose all 8 malignant lesions and all 13 benign lesions (i.e., accuracy of diagnosis was 100%). In particular, 4 fixed and immobile bile duct stones had the appearance of:

| Table 1 Diagnostic uses of intraductal endoscopy |
|-----------------------------------------------|
| Optically guided biopsies of stricture           |
| Indeterminate stricture                          |
| Dominant stricture in primary sclerosing cholangitis |
| Evaluate fixed filling defect noted on cholangiogram or other imaging |
| Differentiate benign versus malignant intraductal mass |
| Optical examination yields visual clues           |
| Improved yield from tissue sampling under visual guidance |
| Precisely map intraductal tumor prior to resection |
| Collect significant fluid sample for cytology    |
| Visually evaluate intraductal mucinous neoplasms |
| Visually evaluate choledochal cyst               |
| Visually evaluate post-liver transplant ductal ischemia |
| Visually evaluate for intraductal spread of ampullary adenoma |
| Evaluate with visual exam and tissue sampling for infection |
| Cytomegalovirus                                  |
| Fungal infection                                 |

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tumor on ERCP, but were diagnosed correctly as benign stones at a glance with POCS.

Biliary strictures, with the exception of those clearly following surgery or trauma, are frequently concerning for malignancy. Obtaining adequate tissue from these biliary strictures, which can provide definitive diagnosis, is often challenging. Traditionally, ERCP may be of assistance in characterizing the stricture by providing tissue sampling; however, the low yield rates of ERCP-based methods for securing the pathologic diagnosis of malignancy has been demonstrated in multiple studies. The diagnostic yield is variable in the range of 35% to 70%.[31-43] Percutaneous transhepatic cholangioscopy (PTCS) and POCS have both been used to obtain visually guided biopsies. However, a risk of percutaneous cholangioscopy is the potential for tumor seeding along the tract. In 1997, Sato published results obtained from 25 bile duct carcinomas showing carcinomas and invasive carcinomas were diagnosed histologically from biopsy specimens obtained with PTCS guidance in 96% and 91% of the cases, respectively.[44] However, the sensitivity of a single biopsy for diagnosis for invasive carcinoma was only 62%, which demonstrated the need for multiple biopsies in order to obtain a higher diagnostic yield. In 2003, Somogyi reported the feasibility of using POCS with visually-guided biopsy to successfully directly biopsy an intraductal papillary mucinous tumor within the common hepatic duct.[45] Cholangioscopy additionally allowed precise mapping of the tumor in preparation for surgical resection. A 2006 report further details the usefulness of cholangioscopy in patients with indeterminate pancreaticobiliary pathology by evaluating 62 patients.[46] If a lesion was initially observed with direct POCS, biopsies were obtained under direct visualization (cholangioscopy-directed) or through the duodenoscope (cholangioscopy-assisted). Overall in this study, sensitivity to detect malignancy by utilizing POCS was 89%, and specificity was 96%, which continues to mark a significant improvement over utilization of only ERCP techniques to obtain tissue. As mentioned previously, the SpyGlass system has also been used for optically guided biopsy.[26] The sensitivity and specificity for diagnosis utilizing SpyGlass-directed biopsy was 71% and 100%, respectively, in evaluation of 20 patients’ intraductal lesions. Current multi-center trials will shed more light on the use of this new system.

Attempts have been made to utilize POCS in patients with primary sclerosing cholangitis (PSC). A study from the University of Colorado examined 41 PSC patients with POCS.[51] In order to evaluate dominant strictures, POCS-directed biopsies were obtained. In cases where the cholangioscopic biopsy forceps could not pass through the operating channel due to angulation, POCS-assisted biopsies were obtained. Impressively, tissue samples were adequate for histologic evaluation in 32 of 33 patients. The median follow-up period of 17 mo, has shown that this method of evaluation was able to successfully exclude cancer in 31 of 31 patients (100%) where biopsies were negative. The predominant difficulty in this study came due to limitations of technology with the cholangioscopes which were used (Olympus CHF BP30, Olympus CHF B160, Pentax FCP 9P), in that the stricture of interest could not be traversed in 14 cases. Another study detailing the use of POCS in PSC was published by a German group in 2006[48]. In this study, 53 PSC patients with dominant bile duct stenoses underwent transpapillary cholangioscopy and POCS-assisted tissue sampling in addition to ERCP. This study found that utilization of cholangioscopy was statistically significantly superior to ERCP for detecting malignancy in terms of its specificity (93% vs 51%) and accuracy (93% vs 55%). Thus, this group concluded that transpapillary cholangioscopy significantly increases the ability to distinguish between malignant and benign dominant bile duct stenoses in patients with PSC.

Direct pancreatoscopy can also play a diagnostic role in differentiating pancreatic duct lesions.[59] Pancreatoscopy can visualize chronic scarring and stenosis of the duct, pancreatic duct stones, and intraductal papillary-mucinous neoplasms (IPMN’s) of the pancreas. In 1997, peroral pancreatoscopy was utilized to evaluate carcinoma in situ of the pancreas.[49] The carcinoma in situ in the main duct had the optical appearance of papillary mucosa, irregular mucosa, or nodular mucosa. Pancreatic juice collected during pancreatoscopy provided a better yield than traditional catheter collection, in that fluid collected during pancreatoscopy from all 11 patients with carcinoma in situ yielded positive cytology, while only 7 of 11 patients’ cytology was positive when collected without direct pancreatoscopy. Thus, this study concluded that peroral pancreatoscopy and pancreatoscopic cytology are indeed useful for locating and diagnosing carcinoma in situ of the pancreas. In 1998, further evidence of the additive value of pancreatoscopy to supplement traditional diagnostic techniques was published[51]. In this report, pancreatoscopy was performed in 24 patients with intraductal mucinous neoplasms of the pancreas. Pancreatoscopy was able to detect 10 cases of intraductal mucinous neoplasms (IPMN’s) that were not diagnosed with endoscopic ultrasound (EUS) or ERCP. Multiple other studies have evaluated the benefits of pancreatoscopy, especially in regard to evaluating intraductal mucinous neoplasms.[52-58] However, more recently, peroral pancreatoscopy has been combined with narrow-band imaging to emphasize certain image features often seen with IPMN’s, such as mucosal structures and capillary vessels.[59] It is thought that the addition of narrow band imaging may aid in the diagnosis of the primary tumor and help in the determination of the extent of the tumor.

Other diagnostic uses of intraductal endoscopy include the evaluation of choledochal cysts.[60-62] Hemobilia of unknown etiology has been evaluated by cholangioscopy.[63] Infectious etiologies of bile duct pathology, such as cytomegalovirus (CMV) and fungal infections, have also been exposed by the use of direct cholangioscopy.[57,64] There also may be a role for evaluation of the biliary tree after liver transplant. A case report exists detailing the use of methylene blue-
Therapeutic Applications

Intraductal endoscopy is useful not only for diagnostic purposes, but it also has therapeutic applications (Table 2). Intraductal endoscopy has been frequently used to remove stones from within the ducts that cannot be removed by standard ERCP techniques in 5% to 10% of cases, due to size, location, or adherence to biliary epithelium. EHL has been used in combination with POCS in multiple reports. EHL employs the use of a bipolar electrode in an aqueous medium. The probe is placed at the surface of the stone and directly observed using the cholangioscope. The probe emits spark discharges, which create a shock wave that fragments the stone. Binmoeller reported, in 1993, that this technique was successful in removing stones where standard mechanical lithotripsy had failed in 64 of 65 patients. Arya reported, in 2004, on experience with 94 patients who received POCS combined with EHL. Of this group, 93 patients had failed previous standard stone extraction with ERCP. In this retrospective review, POCS combined with EHL was successful in performing stone fragmentation in 96% of cases, and stones were completely removed in 90% of cases. In both of these studies, there were no significant complications associated with the procedures. In elderly patients where biliary stone removal with traditional methods is unsuccessful, permanent biliary stenting has been attempted. However, Hui demonstrated in a prospective study of 36 high-risk patients with difficult CBD stones that POCS guided lithotripsy, when compared to stenting alone, allows for significantly less mortality and cholangitis. Another study using EHL with POCS reported a 100% success rate for large bile duct stone removal after failure to remove the stone with a mechanical lithotripter during ERCP. In 2002, data from 36 patients who had strictly intrahepatic stones underwent POCS guided lithotripsy. Indeed, this form of therapy was successful in these difficult cases to achieve complete stone removal in 64% of cases. Most recently, the SpyGlass-directed EHL system allowed for success in 5 of 5 patients, although after the initial procedure two patients did require repeat SpyGlass-directed EHL and one patient required repeat ERCP in order to achieve complete stone clearance.

Standard surgical management has been difficult for patients with gallstones which erode into the common hepatic duct and form a cholecystobiliary fistula (i.e. Mirizzi types 2-4). In 25 patients (23 patients with Mirizzi type 1 syndrome and two with Mirizzi type 2 syndrome), POCS combined with EHL allowed for successful treatment of the stone in all patients with type 2 Mirizzi syndrome, while it failed in both patients with type 1 Mirizzi syndrome. Thus, it was felt that POCS guided therapy may offer a safe and effective alternative to surgery in patients with type 2 Mirizzi syndrome.

There are other therapeutic interventions which have been coupled with POCS. Multiple reports describe the use of cholangioscopy along with laser lithotripsy. Laser lithotripsy may be used under fluoroscopic or direct cholangioscopy guidance. Current evidence indicates that POCS-guided laser lithotripsy is especially preferred in cases of intrahepatic stones or in patients with stones situated proximal to a bile duct stenosis. Photodynamic therapy, under peroral cholangioscopic guidance, has also been utilized for patients with biliary tumors. In 1998, Ortnner reported on the use of photodynamic therapy under cholangioscopic guidance to treat nonresectable Bismuth type III and IV cholangiocarcinoma. In this study, therapy was successful at restoring biliary drainage, improving mortality and enhancing quality of life. In 2003, Ortnner reported results of a randomized trial of cholangioscopically guided photodynamic therapy with stenting versus stenting only for nonresectable cholangiocarcinoma. The improvement of survival in the group receiving photodynamic therapy was so impressive that it was considered unethical to continue with randomization after the first 39 patients. Specifically, the photodynamic therapy group had median survival to 493 d, while the stenting only group had median survival to 98 d (P < 0.0001). Treatment with photodynamic therapy and stenting also led to improvement of cholestasis and quality of life compared with endoscopic stenting alone.

Other therapeutic applications reported in concert with cholangioscopy include Nd-YAG laser ablation of tumor stent ingrowth and biliary angiodysplastic lesions.

Complications and Safety

There are no large trials specifically addressing the safety of intraductal endoscopy. Most information regarding safety and complications comes from individual case series, often with small numbers of patients enrolled. However, intraductal endoscopy is generally believed to be a safe procedure when performed by experienced endoscopists. However, complications can occur, and patients should be aware of the potential risks before undergoing this procedure. It is important to discuss any concerns with your healthcare provider to determine if intraductal endoscopy is appropriate for your specific situation.
be a safe procedure with relatively few complications. Complications typically include minor bleeding at the time of sphincterotomy or lithotripsy. There was one report of bile duct perforation following POCs guided EHL in 1993. Obviously, the incidence of cholangitis is increased in patients with incomplete biliary drainage, from causes such as a biliary stricture or residual biliary stones; however, cholangitis has not been reported as a direct cause of POCs. Reports in the literature generally demonstrate a low threshold to give antibiotics in POCs guided procedures, but the use of antibiotics is based on the needs of an individual clinical situation. Pancreatitis has been reported in 2 of 52 (3.8%) of pancreatoscopy cases. Complication rates will be better calculated as more intraductal endoscopic procedures are performed and further prospective data is collected.

COMPARATIVE PROCEDURES

There are two other significant methods which allow optical examination of the ductal systems and deserve brief mention due to their association with POCs. PTCS, also known as percutaneous choledochoscopy, and laparoscopic choledochoscopy have both been used extensively to for diagnostic and therapeutic purposes. While PTCS is more invasive than POCs, there are times when it allows excellent visualization, even in difficult anatomic situations where a POCs technique has failed. Many of the same diagnostic and therapeutic techniques utilized with POCs are also used with PTCS, including targeted biopsy and management of stones with lithotripsy. One unique use of PTCS was documented, where a push-type sphincterotome was used via PTCS to create a papillary sphincterotomy and allow drainage of obstructing biliary stones in 3 patients who each had an endoscopically inaccessible papilla. There are no reports of percutaneous pancreatoscopy. There have been no significant randomized studies directly comparing PTCS versus POCs. Generally, POCs is preferred as the initial therapy, due to its less invasive nature. However, if POCs is not available, or if POCs techniques fail, then PTCS may be used.

Laparoscopic choledochoscopy has been utilized to explore the CBD. Frequently, this technique has been utilized at the time of laparoscopic cholecystectomy, when intraoperative cholangiogram shows concern for retained CBD stones. There are multiple surgical techniques which have been used to explore the CBD, but choledochoscopy via the cystic duct appears to be the safest and most effective approach, with success rates of 90%. A benefit of this procedure is that the papilla may be left intact without sphincterotomy. There is minimal experience with using laparoscopic techniques to perform pancreatoscopy; however, reports do exist.

CONCLUSION

Experience with intraductal endoscopy has shown its advantages over conventional ERCP in regards to the diagnosis and treatment of biliary and pancreatic disease. Direct optical examination may provide significant additional information about ductal lesions. Furthermore, the ability to guide instrumentation in the ducts under direct optical guidance provides significant advantages. As technology advances, the utilization of this endoscopic modality will only increase and new uses for this technology will likely develop.

REFERENCES

1. Roca J, Fichtenstein R, Parodi M. [Progress in the radiologic study of the biliary tract in surgery; cholangioscopy and cholangiography; utilization of apparatus; preliminary note.] Dia Med 1951; 23: 3420
2. Allegaert W. [Report concerning cholangioscopy, using closed-circuit television, during surgical operations on the biliary tract.] Acta Gastroenterol Belg 1961; 24: 599-606
3. Deister J. [Intraoperative cholangioscopy, an improvement in bile duct diagnosis.] Langenbecks Arch Klin Chir Ver Dtsch Z Chir 1963; 303: 111-122
4. Haberlin P. [Cholangioscopy] Helv Chir Acta 1966; 33: 78-80
5. Urakami Y, Seifert E, Butke H. Peroral direct cholangioscopy (PODS) using routine straight-view endoscope: first report. Endoscopy 1977; 9: 27-30
6. Nakajima M, Akasaka Y, Fukumoto K, Mitsuyoshi Y, Kawai K. Peroral cholangiopancreatoscopy (PCPS) under duodenoscopic guidance. Am J Gastroenterol 1976; 66: 241-247
7. Rosch W, Koch H, Demling L. Peroral cholangioscopy. Endoscopy 1976; 8: 172-175
8. Popiela T, Karcz D, Kulig J. Significance of intraoperative fibercholangioscopy in the diagnosis of biliary tract disorders. Endoscopy 1978; 10: 275-278
9. Nakajima M, Fukumoto K, Mitsuyoshi Y, Kato S, Aoike A. [Peroral cholangiopancreatoscopy (PCPS): its development and clinical application] Nippon Shoikyobo Gakkai Zasshi 1976; 73: 1381-1388
10. Nakajima M, Akasaka Y, Yamaguchi K, Fujimoto S, Kawai K. Direct endoscopic visualization of the bile and pancreatic duct systems by peroral cholangiopancreatoscopy (PCPS). Gastrointest Endosc 1978; 24: 141-145
11. Urakami Y. Peroral cholangiopancreatoscopy (PCPS) and peroral direct cholangioscopy (PODS). Endoscopy 1980; 12: 30-37
12. Bogardus ST, Hanan I, Ruchim M, Goldberg MJ. ‘Mother-baby’ biliary endoscopy: the University of Chicago experience. Am J Gastroenterol 1996; 91: 105-110
13. Ponsky JL, Scheeres DE, Simon I. Endoscopic retrograde cholangioscopy. An adjunct to endoscopic exploration of the common bile duct. Am Surg 1990; 56: 235-237
14. Larghi A, Waxman I. Endoscopic direct cholangioscopy by using an ultra-slim upper endoscope: a feasibility study. Gastrointest Endosc 2006; 63: 853-857
15. Kozarek RA. Direct cholangioscopy and pancreatoscopy at time of endoscopic retrograde cholangiopancreatography. Am J Gastroenterol 1988; 83: 55-57
16. Foerster EC, Schneider MU, Stommer P, Runge U, Domshke W. Miniscopes in gastroenterological endoscopy--inspection of the gallbladder and the biliary and pancreatic duct systems in autopsy specimens. Endoscopy 1988; 20: 316-320
17. Kozarek RA. Direct pancreatoscopy. Gastrointest Endosc Clin N Am 1995; 5: 259-267
18. Bourke MJ, Haber GB. Transpapillary choledochoscopy. Gastrointest Endosc Clin N Am 1996; 6: 235-252
19. Neuhaus H, Schumacher B. Miniscopes. Baillieres Best Pract Res Clin Gastroenterol 1999; 13: 33-48
20. Soda K, Shitou K, Yoshida Y, Yamanaka T, Kashii A, Miyata M. Peroral cholangioscopy using new fine-caliber flexible scope for detailed examination without papillotomy. Gastrointest Endosc 1996; 43: 223-238
Preclinical characterization of the Spyglass peroral cholangiopancreatospyscope system for the next generation: development of the peroral electronic pancreateoscope with an accessory channel. *Gastroendosc* 2004; 59: 895-900

Chen YK. Preclinical characterization of the Spyglass peroral cholangiopancreatospyscope system for direct access, visualization, and biopsy. *Gastroendosc* 2007; 65: 303-311

Chen YK, Pleskow DK. Spyglass single-operator peroral cholangiopancreatospyscope system for the diagnosis and therapy of bile-duct disorders: a clinical feasibility study (with video). *Gastroendosc* 2007; 65: 832-841

Siddique I, Galati J, Ankoma-Sey V, Wood RP, Ozaki C, Monsour H, Rajman I. The role of choledochoscopy in the diagnosis and management of biliary tract diseases. *Gastroendosc* 1999; 50: 67-73

Seo DW, Lee SK, Yoo KS, Kang GH, Kim MH, Suh DJ, Min YI. Cholangioscopic findings in bile duct tumors. *Gastroendosc* 2000; 52: 630-634

Kim HJ et al. Endoscopy; Lee SK, Yoo KS, Seo DW, Min YI. Tumor vessel: a valuable cholangioscopic clue of malignant biliary stricture. *Gastroendosc* 2000; 52: 635-638

Fukuda Y, Tsuyuguchi T, Sakai Y, Tsuchiya S, Saiyo H. Diagnostic utility of peroral cholangioscopy for various bile-duct lesions. *Gastroendosc* 2005; 62: 374-382

Desa LA, Akosa AB, Lazzara S, Domizio P, Krausz T, Benjamin IS. Cytdiagnosis in the management of extrahaepatic biliary stricture. *Gut* 1991; 32: 1188-1191

Foutch PG, Kerr DM, Harlan JR, Kummer TD. A prospective, controlled analysis of endoscopic cystectomy techniques for diagnosis of malignant biliary stricture. *Am J Gastroenterol* 1991; 86: 577-580

Glasbrenner B, Ardan M, Boeck W, Preclik G, Moller P, Adler G. Prospective evaluation of brush cytology of biliary stricture during endoscopic retrograde cholangiopancreatography. *Endoscopy* 1999; 31: 712-717

Howell DA, Parsons WG, Jones MA, Bosco JJ, Hanson BL. Complete tissue sampling of biliary strictures at ERCP using a new device. *Gastroendosc* 1996; 43: 498-502

Jailwala J, Fogel EL, Sherman S, Gottlieb K, Flueckiger J, Buckslt LG, Lehman GA. Triple-tissue sampling at ERCP in malignant biliary obstruction. *Gastroendosc* 2000; 51: 383-390

Kurzawinski TR, Deery A, Dooley JS, Dick R, Hobbs KE, Davidson BR. A prospective study of bile cytology in 100 patients with bile duct strictures. *Hepatology* 1993; 18: 1399-1403

Layfield LJ, Wax TD, Lee JG, Cotton PB. Accuracy and morphologic aspects of pancreatic and biliary duct brushings. *Acta Cytol* 1995; 39: 11-18

Lee JG, Leung JW, Baillie J, Layfield LJ, Cotton PB. Benign, dysplastic, or malignant—making sense of endoscopic bile duct brush cytology: results in 149 consecutive patients. *Am J Gastroenterol* 1995; 90: 722-726

Ponchon T, Gagnon P, Berger F, Labadie M, Liaras A, Chavaillon A, Bory R. Value of endobiliary brush cytology and biopsies for the diagnosis of malignant bile duct stenosis: results of a prospective study. *Gastroendosc* 1995; 42: 565-572

Pugliese V, Conio M, Nicolò G, Saccomanno S, Gatteschi B. Endoscopic retrograde forceps biopsy and brush cytology of biliary stricture: a prospective study. *Gastroendosc* 1995; 42: 520-526

Sugiyama M, Atomi Y, Wada N, Kuroda A, Muto T. Endoscopic transpapillary bile duct biopsy without sphincterotomy for diagnosing biliary strictures: a prospective comparative study with bile and brush cytology. *Am J Gastroenterol* 1996; 91: 465-467

Schoefl R, Haefner M, Wrba F, Pfeffel F, Stain C, Poetzl R, Gangl A. Forces biopsy and brush cytology during endoscopic retrograde cholangiopancreatography for the diagnosis of biliary stenoses. *Saud J Gastroenterol* 1997; 32: 363-368

Stewart CJ, Mills PR, Carter R, O'Donohue J, Fullarton G, Imrie CW, Murray WR. Brush cytology in the assessment of pancreatico-biliary strictures: a review of 406 cases. *J Clin Pathol* 2001; 54: 449-455

Sato M, Inoue H, Ogawa S, Ohashi S, Maetani I, Igarashi Y, Sakai Y. Limitations of percutaneous transhepatic cholangioscopy for the diagnosis of the intramural extension of bile duct carcinoma. *Endoscopy* 1998; 30: 281-288

Somogyi I, Dimashkieh H, Weber FL Jr, Buell J. Biliary intraductal papillary mucinous tumor: diagnosis and localization by endoscopic retrograde cholangioscopy. *Gastroendosc* 2003; 57: 620-622

Shah RJ, Langer DA, Antillon MR, Chen YK. Cholangioscopy and cholangioscopic forceps biopsy in patients with indeterminate pancreaticobiliary pathology. *Clin Gastroenterol Hepatol* 2006; 4: 219-225

Awadallah NS, Chen YK, Piraka C, Antillon MR, Shah RJ. Is there a role for cholangioscopy in patients with primary sclerosing cholangitis? *Am J Gastroenterol* 2006; 101: 284-291

Tischendorf JJ, Kruger M, Trautwein C, Duckstein N, Schneider A, Manns MP, Meier PN. Cholangioscopic characterization of dominant bile duct stenoses in patients with primary sclerosing cholangitis. *Endoscopy* 2006; 38: 665-669

Tajiri H, Kobayashi M, Ohtsu A, Ryu M, Yoshida S. Peroral pancreatoscopy for the diagnosis of pancreatic diseases. *Pancreas* 1998; 16: 408-412

Uehara H, Nakaiumzi A, Tatsuwa M, Iishi H, Kitamura T, Ohigashi H, Ishikawa O, Takenaka A. Diagnosis of carcinoma in situ of the pancreas by peroral pancreatoscopy and pancreaticocytology. *Cancer* 1997; 79: 454-461

Kaneko T, Nakao A, Nomoto S, Furukawa T, Hirooka Y, Nakashima N, Nagasaka T. Intraoperative pancreatoscopy with the ultrathin pancreatoscope for mucin-producing tumors of the pancreas. *Arch Surg* 1998; 133: 263-267

Kozarek RA. Direct cholangioscopy and pancreatoscopy at time of endoscopic retrograde cholangiopancreatography. *Am J Gastroenterol* 1988; 83: 55-57

Fujita N, Mochizuki F, Lee S, Kobayashi G, Kimura K, Watanabe H. Pancreatoscopy for mucus producing pancreatic tumor. *Dig Endosc* 1990; 2: 110-115

Hara T, Yamaguchi T, Ishihara T, Tsuyuguchi T, Kondo F, Kato A, Asano T, Saiho S. Diagnosis and patient management of intraductal papillary-mucinous tumor of the pancreas by using peroral pancreatoscopy and intraductal ultrasonography. *Gastroenterology* 2002; 122: 34-43

Yamao K, Ohashi K, Nakamura T, Suzuki T, Sawaki A, Hara F, Fukutomi A, Baba T, Okubo K, Tanaka K, Moriyama I, Fukuda K, Matsumoto K, Shimizu Y. Efficacy of peroral pancreatoscopy in the diagnosis of pancreatic diseases. *Gastroenterology* 2003; 125: 205-209

Koda M, Koshitani T, Sato H, Imamura Y, Kato K, Abe M, Wakabayashi N, Tatsumi Y, Horii Y, Yamane Y, Yamagishi H. Electronic pancreatoscopy for the diagnosis of pancreatic diseases. *Am J Gastroenterol* 2002; 97: 617-622

Mukai H, Kasuda K, Nakajima M. Differential diagnosis of mucin-producing tumors of the pancreas by intraductal ultrasoundsonography and peroral pancreatoscopy. *Endoscopy* 1998: 30 Suppl 1: A99-A102

Yasuda K, Sakata M, Ueda M, Uno K, Nakajima M. The use of pancreatoscopy in the diagnosis of intraductal papillary mucinous tumor lesions of the pancreas. *Clin Gastroenterol*
