

Cholangioscopy

Takao Itoi

Introduction

The first report on peroral cholangioscopy (POCS) under duodenoscope guidance, the so-called mother–baby or mother–daughter system, was by Nakajima et al. in 1976 [1]. Since then, various mother–daughter systems, such as POCS, have been developed, not only for diagnostic endoscopy but also for therapeutic endoscopy [2–6]. At approximately the same time, Urakami et al. reported a direct-insertion system POCS, the peroral direct cholangioscopy (PDCS) [7]. However, PDCS did gain widespread acceptance because of technical difficulties compared with mother–daughter system POCS. In 2006, Larghi and Waxman published the first report of PDCS using a conventional ultra-slim video endoscope [8]. Recently several endoscopists have conducted diagnostic and therapeutic PDCS using standard and/or ultra-slim endoscopes [9–15]. In this chapter, we describe the role and practical application of current various POCS systems in biliary tract diseases.

Role and Practical Applications of Cholangioscopy in Biliary Diseases

Diagnostic Cholangioscopy

White-Light Cholangioscopy

POCS can directly observe intraductal lesions and is useful for depiction of indeterminate filling defects and biliary strictures. However, the usefulness of POCS

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depends on the characteristics of the lesions—intrinsic strictures can be diagnosed with a sensitivity of 66–76 % [16, 17]. In contrast, it is extremely difficult to diagnose extrinsic strictures (sensitivity 8 %) [16]. Thus, the use of POCS is best limited to intrinsic biliary lesions. Furthermore, it is well known that cholangiocarcinoma often shows superficial mucosal spread [18]. In particular, most papillary and about half of nodular-type cholangiocarcinomas have superficial mucosal cancerous spread. Thus, intraductal evaluation of superficial mucosal cancerous spread seems to be mandatory for curative resection. In contrast, hardly any flat infiltrative type cholangiocarcinomas have mucosal cancerous spread [18].

The cholangioscope in the mother–daughter system has a 1.2-mm working channel and can accommodate a 1-mm in diameter biopsy forceps. The tissue samples acquired with this forceps are often miniscule. In contrast, PDCS allows the use of a larger standard forceps or 2-mm in diameter biopsy forceps, potentially allowing for greater tissue yield from forceps biopsy.

Image-Enhanced Cholangioscopy

In gastrointestinal (GI) tract diseases, it is well known that chromoendoscopy with various dyes enables delineation of the tumor margins and enhancement of morphological findings of the tumor. In biliary tract lesions, one study reported the usefulness of POCS using 0.1 % methylene blue for superior visualization [19]. However, images are limited because of fiberoptic POCS. Brauer et al. have reported a case using video POCS with indigo carmine in a patient with intraductal papillary mucinous neoplasm of the bile duct [20]. Chromocholangioscopy has some potential for enhancing the visualization of biliary tract lesions, unless in the presence of mucus, exudate, and bile, which tend to obscure mucosal details and interfere with the ability to achieve adequate tissue staining.

Narrow-band imaging (NBI) enhances visualization of fine surface mucosal structures and mucosal capillary microvessels in various GI tract diseases compared with white light upper and lower GI endoscopy (Fig. 1; white-light imaging (WLI) & NBI). One prospective study revealed that the ability of NBI observation to identify both the surface structure and mucosal vessels was as good as or better than conventional observation although it could not differentiate benign and malignant etiology [21].

Cholangioscopic Findings in Benign and Malignant Lesions

Several investigators have identified characteristic cholangioscopic findings in various biliary-tract diseases (Table 1). The normal bile duct shows a flat surface, with or without shallow pseudodiverticulae, which represents the orifice of the bile duct gland and a fine network of normal thin vessels. In inflammatory diseases, e.g., chronic cholangitis and primary sclerosing cholangitis, irregular surface, scarring, and pseudodiverticulae with or without intradiverticulae are often seen [22].

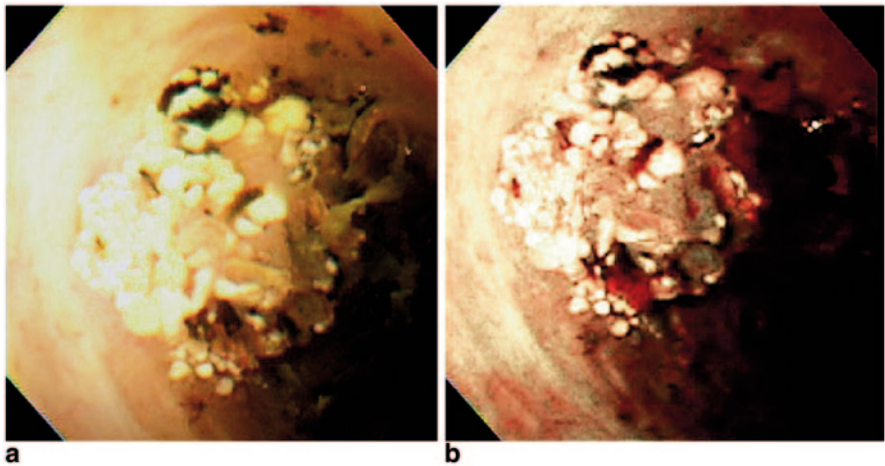


Fig. 1 Peroral video cholangioscopy. **a** white-light imaging, **b** narrow-band imaging

Table 1 Cholangioscopic findings in various biliary tract lesions

Lesions	Cholangioscopic findings
Normal	Flat surface with or without shallow pseudodiverticulae
	Fine network of normal vessels
Inflammatory lesions	Bumpy surface, pseudodiverticulae with or without intradiverticula stones
	Regular granular lesions (hyperplasia)
	Dilated or non-dilated tortuous vessels without encasement or fusion of vessels
	Scarring
Neoplasms	Irregularly papillary or granular lesions
	Nodular elevated lesions
	Friability and easily bleeding
	Dilated to non-dilated tortuous vessels
	Partially dilated vessels with or without encasement and fusion of vessels

Dilated tortuous vessels without encasement or fusion of vessels can be seen in immunoglobulin G4 (IgG4)-related sclerosing cholangitis due to vascular congestion [22]. On the other hand, irregular papillary or granular lesions, and nodular elevated lesions are typical cholangioscopic findings that raise concern for biliary neoplasia. Friability of the lesions and easy bleeding are often seen with dilated or non-dilated tortuous vessels. In terms of typical neoplastic vessels, so-called “tumor vessels,” either angiogenic or tumorigenic, are partially dilated vessels with encasement and fusion of vessels. We previously reported that the features of vessels were divided into four types: (1) sporadic fine vessels which are frequently seen in normal

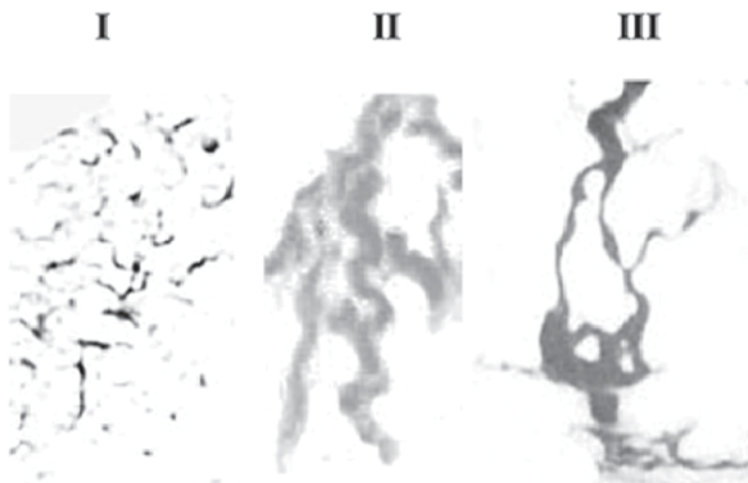


Fig. 2 Vascular patterns of bile duct mucosa

mucosa, (2) aggregated fine vessels without dilation which are frequently seen in chronic inflammation (Type I), (3) dilated and tortuous vessels without encasement or fusion of vessels (Type II), (4) partially dilated vessels without encasement and fusion of vessels (Type III; Fig. 2, Vessel patterns). Type I vessels are usually benign and Type III are typically malignant lesions. However, in the case of Type II vessels, such a differentiation between benign and malignant lesions poses a diagnostic dilemma given the cholangioscopic similarities.

Therapeutic Cholangioscopy

In a mother–daughter system, therapeutic interventions are limited by the size of the available 1.2-mm working channel. Devices which fit in this narrow-working channel include the 1.9-Fr electrohydraulic lithotripsy probe (Fig. 3) and holmium yttrium aluminum garnet (YAG) laser lithotripsy. On the other hand, in PDCS using ultra-slim endoscopes, which accommodate 5-Fr devices, various therapeutic interventions (Fig. 4) such as therapeutic drug injection, tumor resection, stone extraction, migrated stent removal, argon plasma coagulation (APC), and photodynamic therapy (PDT), are feasible.

Cholangioscopic Procedure and Outcome

Cholangioscopy procedures are performed with the patient in the prone position with intravenous anesthesia (propofol, 0.5 mg/kg) or with conscious sedation (intravenous midazolam, 0.05 mg/kg).

Fig. 3 Electric hydraulic lithotripsy for bile-duct stone (mother–daughter video cholangioscopy)

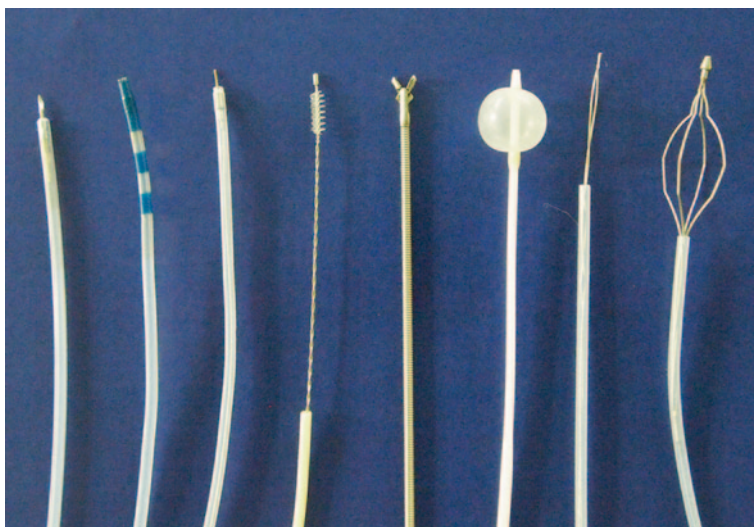
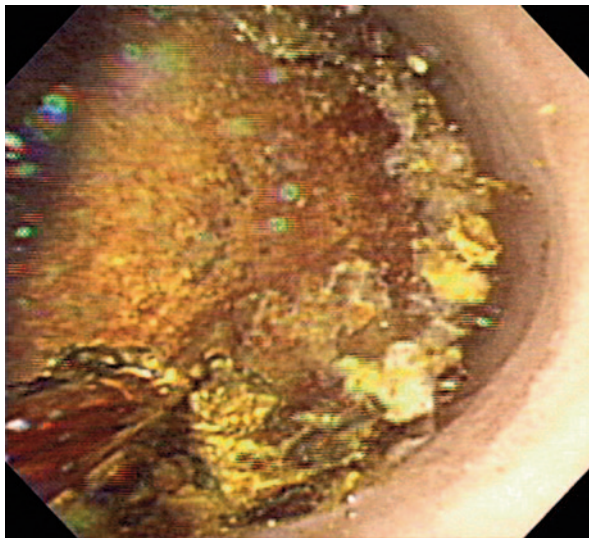


Fig. 4 5-Fr accessories for ultra-slim upper endoscopes

To improve visualization during cholangioscopy, regardless of the type of POCS used, either sterile saline solution or carbon dioxide insufflation has been used. One comparative study revealed that carbon dioxide insufflation provides better imaging and reduces procedure time compared to sterile-saline solution in almost all cases except in biliary protruding lesions [23].



Fig. 5 Mother–daughter video cholangioscopy system. **a** Actual procedure, **b** Tip of duodenal scope with daughter cholangioscope

Through-the-Duodenoscope Cholangioscopy

Mother–Daughter Type Cholangioscopy

Procedure The therapeutic duodenoscope, which is used as the mother scope has a 4.2-mm working channel, which helps to avoid kinking and damage to the cholangioscope. At present, several fiberoptic and video cholangioscopes (Fig. 5a, b) are commercially available in various countries. The specifications of the mother–daughter system video cholangioscopy are shown in Table 2. Two skilled endoscopists are required for effective control of the endoscopes and visualization.

Endoscopic sphincterotomy is a usually a prerequisite for mother–daughter system POCS to facilitate scope passage across the papilla and allow an escape route for saline and carbon dioxide used for insufflation and irrigation. The daughter

Table 2 Specification of daughter (baby) videocholangioscopy

	OLYMPUS	
	CHF-BP260	CHF-B260/B160
Angle of view, degrees	90	90
Observed depth, mm	3–20	3–20
Outer diameter, mm		
Distal end	2.6	3.4
Insertion end	2.9	3.5
Bending section, degrees		
Up/down	70/70	70/70
Right/left	NA	NA
Working length, mm	2000	2000
Working channel diameter, mm	0.5	1.2
Image-enhanced endoscopy	NBI	NBI

NA not available, NBI narrow-band imaging

cholangioscope is advanced through the 4.2-mm working channel of therapeutic duodenoscope into the bile duct either free hand or over a 0.025- or 0.035-in. guide-wire. Utilizing the daughter cholangioscopes has 2-way deflections (up and down), and the mother duodenoscopes 4-way angulation, along with the elevator mechanism on the mother scope and the ability to vary from a long to short scope position; skilled endoscopists can obtain excellent controlled visualization of the entire biliary tree. An excessive use of the elevator mechanism of the mother duodenoscope can damage the daughter cholangioscope, in particular when the V-system duodenoscope (TJF-260V, Olympus medical systems, Tokyo, Japan; TJF-160V, Olympus America, Pennsylvania (PA)) is used. The video cholangioscope (CHF-B260/B160 and CHF-BP260, B260 and BP260, Olympus medical systems, Japan; B160, Olympus America) and the NBI system (CV-260SL, CVL-260SL/CV-180, CLV-180, light source, Olympus medical systems/Olympus America) should be used to highlight the vascular topography of intraductal lesions when needed.

After inspection with peroral video cholangioscopy (PVCS), the targeted biopsies from the lesions can be performed using a 3-Fr diameter ultrathin biopsy forceps (FB-44U-1, Olympus). However, with the slimmer PVCS (the CHF-BP260), a guide-wire or biopsy forceps cannot be used because of the small-working channel (0.5-mm in diameter).

Outcome The outcomes of large case series including three retrospective studies [24–26] and 1 prospective study [27] are described in Table 3. A mother–daughter system POCS in combination with tissue sampling provided high accuracy (94–98 %), sensitivity (86–100 %), specificity (87–92 %), positive predictive value (88–99 %), and negative predictive value (96–100 %) for the diagnosis of indeterminate filling defects and biliary strictures, regardless of the use of fiberoptic or video POCS, retrospective or prospective analysis. In addition to determination of filling defects and biliary strictures, Kawakami et al. suggested that video POCS might be useful for the detection of mucosal spread of neoplasia and assists with the decision regarding extent of surgical resection in patients with cholangiocarcinoma [28].

Table 3 Summary of accuracy of mother-daughter type cholangioscopy

Authors	n	Center	Study	Scope	Methods	Ac. (%)	Sen. (%)	Spe. (%)	PPV (%)	NPV (%)
Fukuda GIE 2007	97	Single	R	Fiber	ERC/ Tissue/ POCS	94	100	87	88	100
Shah CGH 2007	62	Single	R	Fiber	W/wo Tissue/ POCS	—	86	96	89	96
Itoi CGH 2010	144	Mum	R	Video	ERC/ Tissue/ POCS	98	99	96	99	96
Nishikawa GIE 2013	33	Single	P	Video	ERC/ Tissue/ POCS	97	100	92	96	100

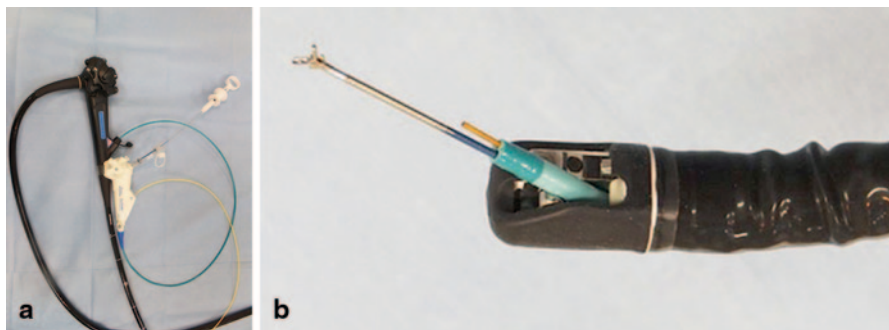


Fig. 6 Single-operator cholangioscopy system (SpyGlass). **a** Outside appearance. **b** Tip of duodenal scope with SpyScope and SpyBite

Single-Operator Fiberoptic Cholangioscopy

Procedure A single-operator system for cholangioscopy introduced recently by Bostoc Scientific has revolutionized the field of cholangioscopy. This technology incorporates a fiberoptic cholangioscopy which is to be strapped to the duodenoscope just below the working channel with a silastic belt, a pump, a light source, and a monitor, and three disposable devices: (1) a reusable 0.77-mm diameter optical probe (SpyGlass), (2) a 10F disposable 4-lumen catheter (SpyScope) consisting of a 0.9-mm channel for the SpyGlass fiber-optical probe, a 1.2-mm instrumentation channel and two dedicated 0.6-mm irrigation channels, and (3) a disposable 3F biopsy forceps (SpyBite) [29–32] (Fig. 6a, b). The modular system consists of 3 components: (1) a reusable 0.77-mm diameter optical probe (SpyGlass) for direct visual examination of the targeted duct, (2) a 10F disposable 4-lumen catheter (SpyScope) consisting of a 0.9-mm channel for the SpyGlass fiber-optical probe, a 1.2-mm instrumentation channel and two dedicated 0.6-mm irrigation channels, and (3) a disposable 3F biopsy forceps (SpyBite) for tissue acquisition in the pancreaticobiliary system [29, 30]. Since the SpyScope catheter has 4-way tip deflection, it provides good catheter maneuverability in the duct for diagnostic visualization and interventions. In contrast, the conventional mother–daughter POCS is capable of only 2-way tip deflection. Improvement of maneuverability (4-way tip deflection) may enable free-hand cholangioscope insertion without a guide-wire. Once the tip of the cholangioscope is advanced into the bile duct, irrigation of sterile saline is usually required for better visualization.

Outcome Experimental benchmark and clinical feasibility studies have already been described by Chen [29] and Chen and Pleskow [30]. To date, there are three prospective studies including one multi-center study and two single-center studies on the evaluation of SpyGlass in biliary diseases [32–34]. One single center study showed that the diagnostic accuracy of SpyGlass cholangioscopic impression was 89% although the diagnostic accuracy of SpyBite cholangioscopic biopsy was slightly lower at 82% [32]. A multi-center study revealed that the SpyGlass

cholangioscopic accuracy was 78%. In contrast, the diagnostic accuracy of Spy-Bite cholangioscopic biopsy was only 49%. These results suggest that visualization and targeted tissue acquisition are complementary during cholangioscopy. Others have reported greater success with targeted biopsy. For instance, Draganov reported that the diagnostic accuracy of POCS biopsy (85%) was superior to both cytology brushing (39%) and fluoroscopic standard forceps biopsy (54%) [34].

Peroral Direct Cholangioscopy

Urakami et al. first reported on the PDCS with a standard upper endoscope using the direct-insertion technique in 1977 [6]. However, as noted above, PDCS has not been widely adopted due to technical difficulties associated with direct peroral intubation of the bile duct with a standard upper endoscope. As a result, presently, the use of the mother–daughter system POCS has become widespread. The introduction of the single-operator cholangioscope system, has spurred efforts at direct peroral cholangioscopy. Recently, Larghi and Waxman reported a feasibility study of PDCS using a conventional ultra-slim upper video endoscope [7] (Table 4). Since then, several studies on the diagnostic and therapeutic PDCS have been published [8–15].

Procedure PDCS requires a skilled endoscopist for procedural success. Free-hand insertion of the endoscope, which is ideal for PDCS, is technically challenging and

Table 4 Direct peroral videochoangioscopy

Direct peroral videochoangioscopy					
	OLYMPUS			FUJINON EG-530NW/530N2	PENTAX EG-1690K
	GIF-XP160	GIF-XP180N	GIF-XP260N		
Angle of view, degrees	120	120	120	140	120
Observed depth, mm	3–100	3–100	3–100	4–100	4–100
Outer diameter, mm					
Distal end	5.9	5.5	5	5.9	5.4
Insertion end	5.9	5.5	5.5	5.9	5.3
Bending section, degrees					
Up/down	180/90	210/90	210/90	210/90	210/120
Right/left	100/100	100/100	100/100	100/100	120/120
Working length, mm	1030	1100	1030	1100	1100
Working channel diameter, mm	2	2	2	2	2
Image-enhanced endoscopy	NBI	NBI	NBI	FICE	i-Scan

NA not available, *NBI* narrow-band imaging, *FICE* flexible spectral imaging color enhancement

Fig. 7 Direct peroral chol-
angioscopy and anchoring
balloon catheter



has a high rate of procedural failure [3], and even when performed over a guide-wire, the success rates of ductal insertion remain disappointing. Endoscopists have described various techniques for intubation of the bile duct, including the overtube balloon technique [10, 11] and anchoring balloon technique [9, 14, 15, 35]. Of these techniques, anchoring balloon-assisted PDCS appears to be superior for bile duct intubation because of its simple technique and higher success rates.

The procedure of PDCS using an intraductal balloon catheter requires initial sphincterotomy of the major papilla followed by balloon sphincteroplasty with a 12–15 mm dilating balloon. PDCS is then performed using the over-the-wire technique, assisted by an intraductal balloon catheter (5-Fr, B5-2Q; Olympus; Fig. 7). First, the endoscope is removed, leaving a 0.018–0.025-in. stiff guide-wire (Pathfinder®, Boston Scientific Japan, Tokyo, Japan, or VisiGlide®, Olympus) with the proximal end positioned in the intrahepatic bile duct. The ultra-slim endoscope (Table 4) is then advanced into the bile duct over the guide-wire to the papilla. Next, an intraductal balloon catheter is advanced up to the intrahepatic bile duct and inflated as an anchor. If the guide-wire access is lost during insertion of the ultra-slim endoscope, direct biliary cannulation and guide-wire insertion to the intrahepatic bile duct using a 5-Fr tapered catheter (PR-110Q, Olympus) is performed as previously described [36].

During the initial insertion of the cholangioscope into the lower bile duct, the floppy ultra-slim endoscopes usually acquires an “α” shape (extended scope position; Fig. 8a) or “reverse-J” shape (retracted position; Fig. 8b). For distal bile duct lesions, this limited access may prove adequate for diagnostic visualization or

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