

# SPYGLASS<sup>®</sup> DIRECT VISUALIZATION SYSTEM

INTERIM RESULTS FROM INTERNATIONAL PATIENT REGISTRY  
PRESENTED AT DIGESTIVE DISEASE WEEK<sup>®</sup> 2008



*Lead Authors:*

Yang K. Chen, MD

Mansour A. Parsi, MD

Douglas Pleskow, MD



# BACKGROUND AND INVESTIGATORS

*“The SpyGlass registry provides important information to physicians in assessing the safety and clinical effectiveness of the system.”*

## **Yang K. Chen, MD**

Lead Investigator  
University of Colorado Hospital  
Denver, Colorado

## *Background*

For over 30 years, peroral cholangioscopy (PO) has been used to detect biliary pathology, guide stone therapy and obtain biopsies, but widespread use has been hampered by fragility, limited steerability, poor irrigation capabilities and the need for a second operator. The SpyGlass® Direct Visualization System addresses many of these limitations by being the first single-use direct visualization system that requires only a single physician operator, features dedicated irrigation and therapeutic channels and provides four-way steerability in a four lumen single-use catheter.

A 15-center international registry has documented the performance and utility of PO using the SpyGlass System in 297 patients requiring PO for stone therapy or investigation of suspected pathology with or without biopsy. Twelve-month follow-up data will be collected on the registry patients through March 2009. Interim results from this registry were presented at Digestive Disease Week® (DDW®) in San Diego on May 20<sup>th</sup>, 2008.

## *Investigators and Institutions*

### **Yang K. Chen, MD**

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University of Colorado Hospital  
Denver, Colorado

### **Mansour A. Parsi, MD**

Dept. of Gastroenterology & Hepatology  
Cleveland Clinic Foundation  
Cleveland, Ohio

### **Douglas Pleskow, MD**

Div. of Gastroenterology  
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### **Kenneth Binmoeller, MD**

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New York, New York

# REGISTRY OVERVIEW

## *Lead Investigators and DDW® Presenters*

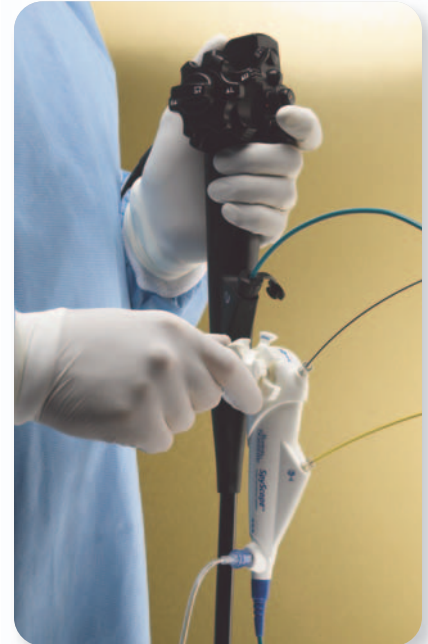
**Yang K. Chen, MD**, University of Colorado Hospital, and lead investigator of the multi-center international study presented overall registry results. Two additional subset analyses from the patient registry data were also presented by: **Mansour A. Parsi, MD**, Cleveland Clinic Foundation, evaluating the efficacy and safety of the SpyGlass® System for treatment of difficult-to-remove biliary stones; and **Kenneth F. Binmoeller, MD**, California Pacific Medical Center, San Francisco, evaluating the sensitivity data for diagnosing malignancies of targeted biopsies obtained under direct visualization using the SpyGlass System.\*

## *Selection Criterion and Endpoints*

Primary selection criterion for the study was indication for ERCP/cholangioscopy with or without biopsy. The primary endpoint was procedural success - defined as the ability to visualize stricture and obtain biopsy adequate for histological examination for stricture and suspected malignancy cases, or the ability to visualize stone(s) and successfully initiate stone fragmentation and removal for stone cases. Secondary endpoints included impact of cholangioscopy on diagnosis and patient management, and sensitivity and specificity of biopsy.

## *Overall Results*

Overall results from the study indicated that peroral cholangioscopy (PO) using the SpyGlass System may be safely performed by a single operator and provides reliable access to target sites for visual inspection and stone therapy using Electro Hydraulic Lithotripsy (EHL) or Holmium Laser Lithotripsy to fragment large or impacted stones.\*\* In addition, the SpyBite® Biopsy Forceps were found to obtain adequate histologic tissue specimens.



*SpyScope® Access & Delivery Catheter*



*SpyBite® Biopsy Forceps*



*SpyGlass System Capital Components*

\* Kenneth F. Binmoeller, MD, presented on behalf of Douglas Pleskow, MD, Beth Israel Deaconess Medical Center, Boston, a principal investigator in the study.

\*\* The SpyGlass® System has been shown to be compatible with the following therapeutic devices:  
- Northgate® 1.9Fr Biliary Probe (9-195-25) and the Northgate Autolith® Intracorporeal Electrohydraulic Lithotripsy iEHL Generator (9-201-00).  
- Lumenis® SlimLine™ 365 micron Laser probe (M0068408420) and the Lumenis® VersaPulse PowerSuite® 20 Watt Holmium Laser Generator (M0068408220).

# CLINICAL SUMMARY

## Peroral Cholangioscopy (PO) Using a Disposable Steerable Single Operator Catheter for Biliary Stone Therapy and Assessment of Indeterminate Strictures – a Multi-center Experience Using the SpyGlass® System

### Lead Author & Presenter:

#### Yang K. Chen, MD

Div. of Gastroenterology & Hepatology  
University of Colorado Hospital  
Denver, Colorado



Stones in the CBD



Optically-guided biopsy with SpyBite® Forceps

### Conclusions

- Interim analysis demonstrates that cholangioscopy using the SpyGlass System is safe and achieves a **high rate of procedural success**
- Direct visualization **improves the accuracy** of cholangiographic findings when used in conjunction with ERCP
- Direct visualization has **good diagnostic predictive value** in patients with biliary obstructive symptoms of indeterminate origin
- Cholangioscopy-guided bile duct biopsy **provides specimens adequate for histological examination** in the great majority of cases
- Cholangioscopy has **clinical utility** for lithotripsy of difficult biliary stones

**Enrollment:** 297 patients

**Background:** An interim analysis was conducted on 296 patients (out of the 297 enrolled) from a 15-center international study. 49% of the patients were male and 51% female. The mean age was 63 (with a standard deviation of +/- 16). 36% of the patients were inpatient and 64% outpatient. In 56 cases, a SpyGlass System was used for visualization only, 137 cases had a SpyBite® Biopsy attempt, 98 cases were for stone treatment and 5 had failed access.

### Primary Indications

#### Primary indications for ERCP were:

Indeterminate strictures	<b>38.5%</b>
Bile duct stones	<b>30.1%</b>
Jaundice	<b>6.8%</b>
Mass on other imaging study	<b>5.1%</b>
Cholangitis	<b>3%</b>
Pancreatitis	<b>0.3%</b>
Other	<b>16.2%</b>

#### Primary indications for the SpyGlass System were:

Indeterminate strictures non-PSC	<b>35.9%</b>
Stone management only	<b>31.9%</b>
Exclusion of malignancy in PSC	<b>10.5%</b>
Indeterminate filling defect	<b>6.4%</b>
Other non-diagnostic prior ERCP findings with or without tissue sampling	<b>5.4%</b>
Other	<b>9.8%</b>

#### Sites of interest were:

Common bile duct (CBD)	<b>55%</b>
Common hepatic ducts (CHD) and hilum	<b>53%</b>
Main hepatic ducts	<b>23%</b>
Intrahepatic	<b>7%</b>
Ampulla	<b>4%</b>

### Results

Procedural success was **88%** overall – **92%** in stones with EHL/Laser Lithotripsy\*\* group (mean stone size **19mm**); **93%** in stones with conventional (mechanical) Lithotripsy/ extraction group (mean stone size **10mm**); **96%** in stricture/suspected malignancy without biopsy group (visual assessment only); **89%** in stricture/suspected malignancy with biopsy group; and access to target site was unsuccessful in 5; and missing data in 8.

All cases were performed by a single operator. Visual diagnosis (DX) was discordant from ERCP diagnosis in **19%**. SpyGlass System visual impression vs. malignancy at complete follow-up (12 mos.) was available on 43 patients with an accuracy of **86%** (37/43) and sensitivity of **90%** (35/39).

#### There were 23 serious adverse events related to device and/or procedures:

Cholangitis	<b>7 (2.4%)</b>
Bacteremia	<b>2 (0.7%)</b>
Abdominal pain	<b>2 (0.7%)</b>
Pancreatitis	<b>2 (0.7%)</b>
Hypotension	<b>2 (0.7%)</b>
Nausea	<b>1 (0.3%)</b>
Liver Abscess	<b>1 (0.3%)</b>
Radiculopathy	<b>1 (0.3%)</b>
Perforation of bile duct (guidewire)	<b>1 (0.3%)</b>
Probable infection	<b>1 (0.3%)</b>
Inflammatory syndrome	<b>1 (0.3%)</b>
Transient oxygen desaturation	<b>1 (0.3%)</b>
Elevated amylase & lipase without clinical pancreatitis	<b>1 (0.3%)</b>

\*\* The SpyGlass® System has been shown to be compatible with the following therapeutic devices:  
- Northgate® 1.9Fr Biliary Probe (9-195-25) and the Northgate Autolith® Intracorporeal Electrohydraulic Lithotripsy iEHL Generator (9-201-00).  
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## CLINICAL SUMMARY

## Biopsy of Indeterminate Biliary Strictures – Does Direct Visualization Help? – a Multicenter Experience

**Enrollment:** 137 patients

**Background:** Of the 297 patients enrolled in the study, 137 had biopsies using the SpyBite® Biopsy Forceps during the procedure. Of these, 124 patients had complete baseline data, including histology. Those patients with a benign biopsy were followed until a definitive malignant diagnosis was made or up to 12 months. In 4 patients the data was incomplete and they were counted as failures in this intent to treat analysis. The mean number of biopsies per patient attempted was 4.3 and the mean number of successful bites obtained was 3.6.

## Results

Procedural success was attained in **86% (118/137)**.

### The ease of passing the SpyBite Biopsy Forceps through the SpyScope® Catheter:

Easy	<b>31%</b>
Moderate	<b>65%</b>
Impossible	<b>4%</b>

### Analysis of the data set of *intrinsic* indeterminate strictures (76 patients):

Accuracy of biopsies with SpyBite Forceps vs. final diagnosis at complete follow-up	<b>74% (28/38)</b>
Sensitivity	<b>78% (21/27)</b>
Specificity	<b>64% (7/11)</b>
Extrinsic malignant lesions	<b>14% (1/7)</b>
Benign lesions	<b>75% (3/4)</b>

### There were 13 serious adverse events related to ERCP and SpyGlass® System cholangioscopy:

Cholangitis	<b>6 (4.4%)</b>
Hypotension	<b>2 (1.5%)</b>
Bacteremia	<b>1 (0.7%)</b>
Radiculopathy	<b>1 (0.7%)</b>
Probable infection	<b>1 (0.7%)</b>
Inflammatory syndrome	<b>1 (0.7%)</b>
Nausea	<b>1 (0.7%)</b>

### The ability to obtain biopsies:

Excellent	<b>25%</b>
Good	<b>50%</b>
Fair	<b>22%</b>
Poor	<b>3%</b>

### Analysis of the total data set of *extrinsic* and *intrinsic* indeterminate strictures combined (124 patients):

Accuracy of biopsies with SpyBite Biopsy Forceps vs. malignancy at complete follow-up	<b>60% (26/43)</b>
Sensitivity	<b>59% (23/39)</b>
Specificity	<b>75% (3/4)</b>
PPV	<b>100% (23/23)</b>
NPV	<b>20% (3/15)</b>

### Lead Author:

#### Douglas Pleskow, MD

Division of Gastroenterology  
Beth Israel Deaconess Medical Center  
Boston, Massachusetts

### Presented by:

#### Kenneth F. Binmoeller, MD

Interventional Endoscopy Services  
California Pacific Medical Center  
San Francisco, California



Optically-guided biopsy with SpyBite Forceps

## Conclusions

From interim results of the multi-center international registry:

- Targeted biopsies using the SpyGlass System with SpyBite Forceps **provides specimens adequate for histology in 89% of cases**
- The **sensitivity of biopsies** using the SpyBite Biopsy Forceps for diagnosing ***intrinsic* malignant strictures is higher** than that reported for transpapillary tissue sampling methods
- New SpyGlass System directed tissue sampling devices are needed to improve the yield for diagnosing malignant tumors ***extrinsic*** to the bile duct

# CLINICAL SUMMARY

## Peroral Cholangioscopy-Guided Stone Therapy – Report of an International Multi-center Registry

*Lead Author & Presenter:*

**Mansour A. Parsi, MD**

Dept. of Gastroenterology & Hepatology  
Cleveland Clinic Foundation  
Cleveland, Ohio



*Large stone in biliary duct*

**Conclusions**

From interim results of the multi-center international registry:

- Peroral cholangioscopy using the SpyGlass System is **safe and effective** for treatment of difficult-to-remove biliary stones
- The rate of **missed stones by ERCP** may be higher than previously reported

**Enrollment:** 98 patients

**Background:** To evaluate the efficacy and safety of the SpyGlass® System for the management of difficult-to-remove biliary stones and to assess the utility for detection of missed stones by ERCP.

**Methods:** Per protocol, each patient underwent ERCP immediately followed by cholangioscopy-guided stone therapy using the SpyGlass Direct Visualization System. Procedural indications were bile duct stones not amenable to removal by conventional methods or missed by ERCP. Procedural success was defined as the ability to adequately visualize and initiate stone therapy. All patients had 1 month of follow-up after cholangioscopy.

**Results**

- In **29%** of cases, stones were missed during the ERCP immediately preceding cholangioscopy
- **66%** of cases were treated with Electro Hydraulic Lithotripsy (EHL) or Holmium Laser Lithotripsy\*\* - mean size of stones **19mm**
- Procedural success of stones treated with the SpyGlass System and EHL or Laser\*\* was **92%**.
- The remaining cases were treated with conventional/mechanical methods (without SpyGlass System) - mean size of stones **10mm**
- Procedural success of stones treated with conventional methods (without the SpyGlass System) was **93%**.

**Location of stones (66% impacted) treated with EHL or Laser\*\*:**

- 57% in the common bile duct
- 24.5% in the common hepatic duct
- 11% in the cystic duct
- 6% in the intrahepatic duct
- 1.5% in the gallbladder

**There were 6 serious adverse events related to ERCP and the SpyGlass System (all resolved without sequela):**

- Cholangitis
- Bacteremia
- Liver abscess
- Bile duct perforation
- Transient oxygen desaturation
- Abdominal pain

\*\* The SpyGlass® System has been shown to be compatible with the following therapeutic devices:  
 - Northgate® 1.9Fr Biliary Probe (9-195-25) and the Northgate Autolith® Intracorporeal Electrohydraulic Lithotripsy (EHL) Generator (9-201-00).  
 - Lumenis® SlimLine™ 365 micron Laser probe (M0068408420) and the Lumenis® VersaPulse PowerSuite® 20 Watt Holmium Laser Generator (M0068408220).

# SELECTED CLINICAL DATA

## *Presented Data*

### **Digestive Disease Week® (DDW®) 2008**

*Oral presentations from 15-center international study - interim results:*

- **Peroral Cholangioscopy (PO) Using a Disposable Steerable Single Operator Catheter for Biliary Stone Therapy and Assessment of Indeterminate Strictures – a Multi-center Experience Using SpyGlass;** Yang K. Chen, MD, et al.
- **Biopsy of Indeterminate Biliary Strictures – Does Direct Visualization Help? – a Multi-center Experience;** Douglas Pleskow, MD, et al. (Presented at DDW by Kenneth F. Binmoeller, MD)
- **Peroral Cholangioscopy Guided Stone Therapy – Report of an International Multi-center Registry;** Mansour A. Parsi, MD, et al.

*Poster Presentations:*

- **Single Operator Cholangioscopy Enhances Diagnostic and Therapeutic Applications of Endoscopic Retrograde Cholangiopancreatography;** Udayakumar Navaneethan, MD, Joseph B. Palascak, MD, Mayar Al Mohajer, MD, Shailendra S. Chauhan, MD, Andres Gelrud, MD; University of Cincinnati, Cincinnati, Ohio, USA.
- **SpyGlass Cholangioscopy – Impact on Patients with Bile Duct Filling Defect(s) of Uncertain Etiology;** Ayman M. Abdel Aziz, MD, Stuart Sherman, MD, Kenneth F. Binmoeller, MD, Jacques M. Deviere, MD, Robert H. Hawes, MD, Oleh Haluszka, MD, Horst Neuhaus, MD, Douglas Pleskow, MD, Isaac Rajman, MD – Multi-center study - 8 US and European sites.

### **SAGES 2008**

- **Safety and Feasibility of SpyGlass: A New Peroral Single Operator Choledochoscopy System,** Jose M. Martinez, MD, Charles Y. Ro, MD, Alberto Iglesias, MD, Emanuele Lo Menzo, MD, Atul K. Madan, MD, Brian J. Dunkin, MD, Div. of Laparoendoscopic and Bariatric Surgery, University of Miami, Miami, Florida (USA); Dept. of Surgery, The Methodist Hospital, Houston, Texas (USA).

### **UEGW 2007, Paris, France**

*Oral presentation from 15-center international study - interim results:*

- **Peroral Cholangioscopy in Indeterminate Biliary Strictures and Difficult Bile Duct Stones – an International Registry Using SpyGlass;** Horst Neuhaus, MD, et al, Medizinischen Klinik, EVK Dusseldorf, Dusseldorf, Germany.

### **Digestive Disease Week (DDW) 2007:**

- **SpyGlass Cholangioscopy (SGC): Preliminary Clinical Experience in 3 Tertiary Care Centers;** S. Lo, MD; R. A. Kozarek, MD; A. Slivka, MD.
- **Biliary Stone Extraction (BSE) Guided by Direct Visualization Using the New SpyGlass Direct Visualization System;** P. D. Stevens, MD; Y. K. Chen, MD; D. K. Pleskow, MD; O. Haluszka, MD; B. Petersen, MD.
- **Biliary T-tube Remnant as the Cause of Microlithiasis and Recurrent Acute Pancreatitis, Detected by a New Peroral Cholangioscopy System (Spyglass);** M. A. Parsi, MD, M. R. Sanaka, MD, J. A. Dumot, MD.

## *Published Data*

### **Gastroenterology & Hepatology, July 2008**

- **Advances in Endoscopy: The SpyGlass Direct Visualization System for Cholangioscopy;** Peter Draganov, MD, Associate Professor of Medicine, Division of Gastroenterology, Hepatology, and Nutrition, University of Florida, Gainesville, Florida, USA.

### **GIE, Vol. 67, No. 7: 2008**

- **Management of Biliary Stricture Guided by the SpyGlass Direct Visualization System in a Liver Transplant Recipient: an Innovative Approach;** Harlan Wright, MD, Sharad Sharma, MD, MRCS, Ahmet Gurakar, MD, FACC, Anthony Sebastien, MD, Vivek Kohli, MD, Nicolas Jabbour, MD, FACS, Oklahoma City, Oklahoma, USA.

### **Pancreatology, 2007;7: 539**

- **Iatrogenic Recurrent Pancreatitis;** Mansour A. Parsi, MD, Madhusudhan R. Sanaka, MD, John A. Dumot, MD; Center for Endoscopy and Pancreatobiliary Disorders, Dept. of Gastroenterology and Hepatology, Cleveland Clinic, Cleveland, Ohio, USA.

### **GIE, Vol. 65, No. 6: May 2007**

- **SpyGlass Single-Operator Peroral Cholangiopancreatography System for the Diagnosis and Therapy of Bile-Duct Disorders: a Clinical Feasibility Study,** Yang K. Chen, MD, Douglas Pleskow, MD.

### **GIE, Vol. 65, No. 2: February 2007**

- **Preclinical Characterization of the Spyglass Peroral Cholangiopancreatography System for Direct Access, Visualization and Biopsy,** Yang K. Chen, MD.

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