MOUEN KHASHAB: Today, we will be talking about optimizing the diagnosis and treatment of pancreaticobiliary diseases, digital cholangioscopy using the SpyGlass DS system.

This lecture will be based on the Gastroenterology and Endoscropy News special report that was printed and distributed in April. There was an analysis of more than 40 published studies on the SpyGlass DS system. This report is currently published online, and everybody has access to it.

Let's start with the background on cholangioscopy. This was first introduced in the 1970s for intraoperative localization of stones during open bile duct exploration. Since then, it has emerged into a technology that can be routinely applied as an adjunct to ERCP or PTC for a variety of indications.

This is the SpyGlass DS system. It illuminated the probe that was used with the legacy. There is enhanced control, with consistent tip deflection and consistent accessory exit point. The scope redesign facilitated easier procedure, with a tapered SpyScope tip.

The major advancement is in imaging. As you know, now SpyGlass involves digital imaging. The image is 60% wider. There's automatic light control via two independent LEDs. It's a single use, so there's no degradation from reprocessing, and there's auto white balance and autofocus.

It's really like plug and play, very easy to setup. There's a processor. You plug it in. You attach the suction. You attach the water irrigation, and you're ready for use.

Our lecture today will be focused on two main aspects for the use of SpyGlass DS. One is management of biliary stones, and second is management of biliary strictures. So let's start with biliary stones.

Just as a backup, when do we perform ERCP for biliary stones, or suspected biliary stones? If the patient has very strong predictors for presence of choledocolithiasis, such as imaging evidence of common bile duct stones, or there's clinical evidence of cholangitis, or there is a significant obstructive pattern, with bilirubin above 4, then we go straight to ERCP, because there is a high likelihood for the presence of choledocolithiasis.

If there are some strong predictors, such as a dilated bile duct with a high bilirubin, but moderate elevation bilirubin, in these cases, what we do is perform endoscopic ultrasound, or MRCP. And if a patient has evidence of stones in the bileduct, then we move for same session ERCP.

Similarly, for patients who develop gallstone pancreatitis. A lot of endoscopists think that ERCP is warranted in a lot of these patients. Actually, only one in five patients who develop biliary pancreatitis will have a retained stone. Therefore, it would depend on EUS and/or MRCP for pre-ERCP workup.

So now, how do we define difficult stones? You know, small stones we can all manage easily with a sphincterotomy and balloon sweep or baskets retrieval. But then we have to move to some enhanced methods of stone management in patients with suspected or known difficult stones.

So if you look here, so the stones that are large, usually 50 millimeter or larger, periampullary position, or patients with stones, cystic duct stones, impacted stones, or multiple stones, these are all expected to have difficult to retrieve or remove stones. Also, bile duct morphology is important. So if there's angulation of the bile duct, or if there's a stricture, even if there's a 10-millimeter proximal stone and there is a distal structure, this is a relatively difficult stone to remove.

Also, as you know, patients with Mirizzi syndrome, these are difficult-to-manage patients.

These are some examples of difficult stones. This is a stone that's 2 centimeters in diameter. These are stones above a distal stricture. This is multiple intrahepatic stones. And these are multiple common bile duct stones. So these all sets five criteria for difficult-to-manage biliary stones.

If you look at the *Gastroenterology and Endoscopy News Report,* there are treatment results from 10 studies on management of difficult biliary stones. And these results are summarized in the table. If you take all these results together, the published rate for successful stone removal using the Spy DS system was impressively at 95.6%.

And of course, these patients had complex impacted stones. Many of them had previously unsuccessful ERCP. And more than 2/3 of patients who are managed in a single session.

I'll highlight some studies that were summarized in that table. This is one of the initial studies published a few years back, and included 17 patients. This is a prospective study on use of SpyGlass DS with laser lithotripsy for management of complicated stones.

The results from the study are notable for including patients with a median age of 76 years. The stone clearance was achieved in 94% of patients. And these were, of course, difficult stones. The median size was 2 centimeters, impacted stones in 47%, and prior mechanical lithotripsy failure in more than half of the patients.

This is another study published in *Gastrointestinal Endoscopy* in 2016. It included 36 patients with difficult-to-remove stones, including about half of the patients having three or more stones. The median size of stones was 15 millimeter. And complete duct clearance for these difficult-to-remove stones was achieved in 97%.

This is an old slide just to show you that in the older literature here, that the success rate was 60%, 70%, 80%. These days with SpyGlass DS, we're moving to a 90% to 100% consistently among studies.

This is a study we published in *Clinical Gastro and Hepatology* in 2018. This is the largest study published to date on management of difficult stones. It's a multi-center study from 22 tertiary centers, including 407 patients. Using Spy DS for management of difficult bile duct stones.

As we already talked or discussed, these stones were defined as large, multiple, impacted. Location intrahepatic or cystic in the cystic duct, or associated with the structure or difficult anatomic access or Mirizzi Syndrome. So as you see, these are difficult to manage stones.

And we either used electrohydraulic lithotripsy or laser lithotripsy. And look at this impressive technical success with stone clearance that was achieved in 95% of patients, vast majority in a single session, and fewer than 5% of patients requiring additional treatment. In this study, EHL laser lithotripsy were equally effective in the management of these difficult-to-treat bile duct stones.

Give you an example of some of these patients. This is a patient with 15 to 20-millimeter stone, but with a narrow distal duct. You can see here beautiful image using SpyGlass DS. We can use irrigation to keep our perfect vision during the procedure. We irrigate with saline to improve outcomes. We keep the tip of the EHL probe 1 to 2 millimeter from the stone. And our goal is to create a shock wave that will fragment the stone.

We start at low power and increase it as needed. And we notice quickly nice fragmentation of these stones followed by a retrieval with a basket or a balloon. This is a very efficient process. And our goal or intention is always to complete the procedure in one session. And this is repeat occlusion cholangiogram. And you see a complete clearance of the stone. Also another thing we can do is reinsert the SpyGlass at the end of the procedure to have cholangioscopic evidence of complete duct clearance.

This is another impressive stone that basically involves the entire bile duct up into the left intrahepatic system. This is a stone that was 5 to 6 centimeters in size. Although it is this large, our goal was still to use SpyGlass DS for management and completion of the procedure within one session.

Here we see the adequate visualization that allows efficient and specific and accurate delivery of electrohydraulic lithotripsy for management of this very difficult stone. This procedure can be lengthy when you deal with these large stones. But it continues to be efficient, and you're able to send the patient home in most of the cases without the need for any repeated procedures, which is very, very important, of course.

We do administer periprocedural of antibiotics to minimize the risk of cholangitis. And I will shortly show you some data on that.

So this is clearance of the duct with occlusion cholangiogram impressively showing complete clearance of the duct in one session.

This is a study with the senior author Doug Pleskow from Boston comparing outcomes of first generation SpyGlass legacy to the second generation older SpyGlass DS. And what it shows it has a higher rate of stone clearance in the first procedure-- 83% versus 58%.

We see better, we can deliver the energy better and more accurately, and we are more successful in one procedure. Procedure time is shorter-- 49 minutes versus 57 minutes. And of course, very importantly, we are using less fluoroscopy.

So this is the section on biliary stones. Let's now move to diagnosing and mapping biliary strictures.

Indeterminate biliary strictures. Biliary strictures, as you know, remain a diagnostic dilemma because a significant proportion of them remain inconclusive for malignancy despite a thorough evaluation. Strictures are considered indeterminate when basic workup that include transabdominal imaging and ERCP with routine brushing and biopsy are non-diagnostic. So we call these strictures indeterminate.

Intraductal brushing during ERCP is the first-line approach. But the results are really sub-optimal, with a sensitivity of about 27% to 56%.

Use of cholangioscopy has helped overcome these limitations by enhancing direct visualization to obtain more accurate diagnostic sampling.

The diagnostic applications for SpyGlass DS is for indeterminate structures, indeterminate filling defects. We see a filling defect on imaging or cholongiography. Is that a tumor or a stone?

Cholangioscopy is important in differentiating between both. We can sample tissue with targeted biopsies, features, and extent of cholangiocarcinoma and intraductal papillary mucous neoplasia. I'll show you some studies and recent data on this important and developing indication.

This is one of the larger studies published in surgical endoscopy on diagnostic and therapeutic single-operated cholangioscopy with SpyGlass DS, results from a multi-center retrospective cohort. This study included 250 patients.

Look at the impressive cholangioscopy results with a sensitivity and specificity of about 95%. The sensitivity of biopsies was 57%, but the specificity was 100%.

Here I want to shed light on the risk of this procedure. This procedure is pretty safe. Most common adverse event afterwards, as you can imagine with management of these difficult biliary pathologies, include pancreatitis and cholangitis.

Risk of cholangitis was only 1% if you administered periprocedural antibiotics. It was 8%-- sorry-- it was 12.8% if you don't. So that's why now it's routine that we administer periprocedural antibiotics and to minimize the risk of cholangitis.

The investigators from this study concluded that cholangioscopy using SpyGlass DS should be a new standard for the diagnosis of indefinite biliary lesions.

I want to shed light on this example of a biliary stricture. This is a tight stricture that looks ugly, let's say that. And it looks severe. And the first impression is that this is malignant stricture.

You know, not all tight structures are malignant. And this is why Spy DS is very important. This is actually a symmetric stricture. We don't see any lesions. We don't see any dilated tortuous vessels. This is a benign stricture.

And this patient, when we gave them steroids, you can see it open up. And this patient had evidence of IGG 4 related disease, or autoimmune cholangiopathy.

This is one of the first studies from a multi-center group on the use of SpyGlass DS system for diagnostic purposes. It included 108 patients. And the first author was Raj Shah and the senior author was Doug Pleskow.

What this shows is that SpyGlass DS system visual impression had an impressive sensitivity and specificity in the high 90s. What this means is with experts if you get this high definition cholangioscopic image, you're able to tell if this is benign or malignant with the sensitivity and specificity of more than 90%.

Let's say you get a biopsy from these lesions. The sensitivity was 86% and the specificity was 100%. We did not see these numbers with the Spy Legacy. SpyBite biopsy results sensitivity was around 50% to 60%. Now we're having improved numbers. Similarly, the visual impression is getting better.

These are some examples of images we see with SpyGlass DS. This is a high def image of a biliary stricture. We can see the dilated tortuous vessels here and here and here. These are all malignant structures.

These are benign strictures. If we look at this lesion and this lesion, we might say this is an ugly looking stricture that is tight and severe. So we may have the impression that this is malignant. But these are bland severe structures that are almost avascular with no mass lesions. These are benign strictures.

Visual impression is very important. And a SpyGlass DS allows us to have a good impression if these strictures are benign or malignant.

Show you some videos. This is a high definition image of a distal bile duct stricture. This is a patient with cholangiocarcinoma. Look at this impressive high def picture where this lesion with clear nodules and mass within the bile duct and very dilated and torturous vessels. Using the SpyBite, this allows targeted biopsies of these lesions. So now we target the lesions where the nodules are, where the dilated vessels are, and get better biopsy results.

This is another high definition SpyGlass video of a patient with cholangiocarcinoma. And look at this transition zone. Normal bile duct mucosa. And if we back up, we can see nodules, mass, dilated tortuous vessel, which allows us to obtain targeted biopsies.

Similarly here, this is the SpyBite that comes consistently at 6:00. What we want to do is push against these masses, get a biopsy. And we routinely get four to six biopsies per lesion.

This is a study on digital SpyGlass DS on 44 patients with indeterminate strictures. So again, ERCP is brushing and biopsies were done and these strictures remain indeterminate.

So if you just look at it-- and these are, of course, results by experts-- we can see impressive sensitivity of 90% specificity of 95.8%. As I mentioned before, the results from the biopsies are better than we used to have with the Legacy. With a sensitivity of 85% and a specificity of 100%.

Let's move a little bit to mapping. So this study is on digital pancreatical cholangioscopy for mapping of pancreatical biliary neuroplasia. Can we alter the surgical resection margin?

So these are patients with cholangiocarcinomas with main duct IPMNs. If we perform cholangioscopy or pancreatoscopy on these patients, can we change treatment? And this study is starting to shed light on that, yes, we may be able to change treatment in these patients.

Pancreatical cholangioscopy changed the surgical plan in 34% of patients. In the bile duct, 5% of patients have less extensive surgery and 25% avoided surgery.

So this is impressive, right? A quarter of patients avoided surgery. This can be two ways. One is, patients with indeterminate strictures were thought to be malignant and were sent for surgery for no good reasons. So now we're able to avoid surgery in these patients.

And another part of these patients-- another subset of these patients-- patients were sent for surgery because the malignancy was thought to be resectable. But now the stage is higher it was thought to be Bismuth II or IIIA. Now it's a Bismuth IV on cholangioscopy, and these patients are not surgical candidates.

Similarly, in the pancreatic duct, four patients had more extensive surgery, and four patients had less extensive surgery. The conclusion from this study was that digital pancreatical cholangioscopy can be effectively used as a mapping tool to delineate the degree of involvement of biliary lesions before surgical resection, in some cases altering the surgical plan.

Studies use of SpyGlass DS to evaluate the longitudinal tumor extent in patients with cholangiocarcinoma. So this is another study, again, on mapping. And this is what the concept of mapping is. What these authors showed was that if you have a distal malignant stricture, you are able to cross the stricture, go to the proximal biliary lesion-- biliary system-- and assess for another focal or another disease more proximal.

Cholangiocarcinoma can be multi-focal. I will say this is more common in Asia, but occasionally we see it here. What these authors do is obtain biopsies from the malignancy itself, from the confluence of the right and left hepatic ducts, from the B4 confluence in the left system, and of course, as I mentioned, from the main lesion.

This is what mapping entails. This is an important developing concept. So we have to cross the lesion and look at the proximal biliary system to assess for multi-focal disease.

We can see from this study this was feasible in 88% of patients. And this is what these authors did. You can see here the distal malignant biliary stricture. You go to the confluence of the right and left before confluence and from the lesion. And send these results for actual pathology and assess for multi-focal disease.

So this is what mapping of the biliary system entails. And it's an evolving concept.

Let's move to another use of cholangioscopy. This is another evolving concept of cholangioscopy-guided RFA ablation. Now as many of you know, Boston Scientific owns this part RFA probe. It is meant for ablation of biliary malignancies.

This is a typical patient with a high [INAUDIBLE] cholangiocarcinoma. You can see here that this is a Bismuth IV. And on cholangioscopy we see it a tight stricture with nodules and dilated tortuous vessels.

This is the RFA probe that was advanced through the [INAUDIBLE] scope over a standard wire that's passed through the stricture in the right main duct. And then this is ablated. Then it's passed to the left system, and it's ablated.

And we can see right afterwards, after ablation, we can see improved cholangiography with patency of the ducts. And here repeat cholangioscopy we can also see impressive improvement in the diameter of the bile.

Why do we need to do this? Of course, this is an evolving field. But what we can do is map these strictures. We don't want to ablate normal ducts. Especially here in the right system. We're very close to vessels, including the hepatic artery.

So you want to ablate tumors. We understand the presence of tumor and the extent of the tumor, and this guides us with RFA ablation. Post-ablation that allows us to know that we ablated the entire tumor.

So in the last part of this talk, I will shed some light on couple of studies that show some economic advantages of a SpyGlass DS. This is a group that implemented SpyGlass DS in their system, in their ERCP practice. And this resulted in total net positive cost savings of $2,900 per patient over 90-day followup after the procedure.

Of course, to look at cost saving you have to look forward. Because if you have a diagnosis of a indeterminate biliary stricture, you don't have to keep bringing the patient back for more procedures, more stenting, more sampling procedures, more imaging. You're not sending these patients for unnecessary surgeries. You're shortening hospital stay. So all of these aspects can be associated with some cost savings.

This is a study from Europe by Pierre Deprez. And this is a modeling study that compared the treatment pathway without cholangioscopy to a treatment pathway after implementing cholangioscopy. We can see that after implementing cholangioscopy the number of procedures that are needed was less, mainly the surgeries was more less.

31% decrease in procedures. So look at dollars. Of course, to acquire equipment it costs some dollars. Implementation of the system requires some dollars. But avoiding surgery and decreasing hospital stay resulted eventually in 12,000 or 15,000 euros cost savings per patient.

Potential for money savings is the efficient setup and operation. We showed you how this is plug and play. It's disposable. So no cleaning or reprocessing is needed.

Reduce use of fluoroscopy. Avoid need for repeated procedures, as we discussed. Avoid need for unnecessary surgeries, as we showed. And avoid need for repeat and surveillance imaging, which is very important.

Some future directions where this field is heading. I think now we're moving to studies for evaluation of strictures resulting in improving outcomes and reduced costs. So we need some prospective multi-center data to make sure that this is what's happening in the real world.

Enhanced visualization capabilities may initiate a shift to radiation-free interventions for biliary procedures. We actually already see that in our practice. Standardized biopsy protocol, improving diagnostic yield by using touch and print cytology.

We didn't talk much about that. But basically what that is is similar to what we do with EUS guided fine needle aspiration, having rapid on-site evaluation of these biopsy specimens inside the endoscopy suite with direct feedback whether we have adequate specimens or not. We're starting to see more accessories, including a snare and a retrieval basket to broaden the utility of therapeutic cholangioscopy.

To conclude, SpyGlass DS system has rendered cholangioscopy easier and more widespread. Cholangioscopy using the SpyGlass DS system offers a valuable adjunct to ERCP for the visualization, diagnostic sampling, and treatment of biliary and pancreatic diseases. Use of cholangioscopy is safe and cost-effective. SpyGlass DS system should be considered for the first-line management of strictures and difficult stone disease, and for use in pre-surgical planning.