Recent Advances of Peroral Cholangioscopy

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Cholangioscopy

- Direct visualization of the biliary tree
- Improve ability to diagnose biliary lesions
- Permits endoscopic guidance for therapeutic procedures
Peroral Cholangioscopy (POC) Using Mother-Baby Endoscopic System

- Nakajima M, Kawai K, et al. 1976, in Japan
- Rösch W, et al. 1976, in Europe
- The babyscope (Olympus CHF B20/BP30) introduced a working channel into the motherscope (Olympus TJFM 20/TJF)

- POC standard for over 30 years

CHF-B260 (Olympus)

- Slim cholangioscope
  - Outer diameter: 3.4 mm
- Performed with conventional therapeutic duodenoscope (TJF, 4.2 mm accessory channel)
- Electronic, video cholangioscope
  - Excellent quality images
  - Available narrow band imaging
Disadvantages of Current POC Using “Mother-Baby” Endoscopic System

- Requires two skilled endoscopists
- Requires two endoscopic systems
- Fragile
- Difficult to use
- Small working channel (1.2 mm)
- Expensive
- Available at few referral centers
New Types of Cholangioscopy System

- Single-operator cholangioscopic system
  - SpyGlass direct visualization system
  - Direct peroral cholangioscopy using an ultra-slim upper endoscope
Single Operator Cholangioscopic System I

- SpyGlass direct visualization system
  - SpyGlass single-operator peroral cholangiopancreatoscopy system for the diagnosis and therapy of bile-duct disorders: a clinical feasibility study (with video)
    *Chen YK, et al. Gastrointest Endosc 2007*
  - Single-operator cholangioscopy in patients requiring evaluation of bile duct disease or therapy of biliary stones (with videos)
    *Chen YK, et al. Gastrointest Endosc 2011*
  - Prospective evaluation of the clinical utility of ERCP-guided cholangiopancreatoscopy with a new direct visualization system
    *Draganov PV, et al. Gastrointest Endosc 2011*
  - Single operator peroral cholangioscopic guided therapy of bile duct stones
    *Seelhoff A et al. J Hepatobiliary Pancreat Sci 2011*
  - Role of single-operator peroral cholangioscopy in the diagnosis of indeterminate biliary lesions: a single-center, prospective study
    *Ramchandani M, et al. Gastrointest Endosc 2011*
Single Operator Cholangioscopic System I

- Direct peroral cholangioscopy using ultra-slim endoscope
  - Endoscopic direct cholangioscopy by using an ultra-slim upper endoscope: a feasibility study
  - Overtube-balloon-assisted direct peroral cholangioscopy by using an ultra-slim upper endoscope (with videos)
  - Intraductal balloon-guided direct peroral cholangioscopy with an ultraslim upper endoscope (with videos)
  - Direct peroral cholangioscopy using an ultra-slim upper endoscope for the treatment of retained bile duct stones
  - Direct peroral cholangioscopy using an ultraslim endoscope and overtube balloon-assisted technique: a case series
    Tsou YK, et al. Endoscopy 2010
  - Feasibility of a novel system for intraductal balloon-anchored direct peroral cholangioscopy and endotherapy with an ultraslim endoscope (with videos)
    Waxman I, et al. Gastrointest Endosc 2010
  - Peroral cholangioscopy for diagnosis and therapy of biliary tract disease using an ultra-slim gastroscope
  - Clinical feasibility of direct peroral cholangioscopy-guided photodynamic therapy for inoperable cholangiocarcinoma performed by using an ultra-slim upper endoscope (with videos)
  - Direct transnasal cholangioscopy with ultraslim endoscopes: a one-step intraductal balloon-guided approach
SpyGlass Direct Visualization System

- Boston Scientific, USA
- Direct visualization of the biliary tree
- Component
  - Capital equipment
  - SpyGlass direct visualization probe
  - SpyScope access and delivery catheter

International, Multicenter Study of SpyGlass Cholangioscopy

Chen YK, et al. Gastrointest Endosc 2011;74:805

297 total cases

226 diagnostic

66 stone lithotripsy (EHL/Laser)

5 failed access

86 without biopsy 93.0 Success (%)

140 with biopsy 87.1 Success (%)

88.6 Total Success (%)
# Diagnostic Accuracy of Forceps Biopsy Using SpyGlass Cholangioscopy for Indeterminate Biliary Strictures

<table>
<thead>
<tr>
<th>Biopsy Method</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology brush</td>
<td>5.8</td>
<td>100</td>
<td>38.5</td>
</tr>
<tr>
<td>Standard forceps biopsy</td>
<td>29.4</td>
<td>100</td>
<td>53.9</td>
</tr>
<tr>
<td>Mini-forceps biopsy using SpyGlass system</td>
<td>76.5</td>
<td>100</td>
<td>84.6</td>
</tr>
</tbody>
</table>

*Draganov PV, et al. Gastrointest Endosc 2012;75:347*
Disadvantages of the SpyGlass Cholangioscopy System

- Unsatisfactory image quality
- Expensive equipment and accessories
- Small working channel (1.2 mm)
- Lack of suction capability
- Requires two endoscopic systems with completely different endoscopic set-up
- Durability?
SpyGlass Cholangioscopy Imaging Reading
Interobserver Agreement (n = 27)

<table>
<thead>
<tr>
<th>Final Diagnosis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant</td>
<td>11</td>
</tr>
<tr>
<td>Benign</td>
<td>11</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interobserver agreement (IOA)</th>
<th>Kappa</th>
<th>Overall IOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface</td>
<td>0.12</td>
<td>slight</td>
</tr>
<tr>
<td>Vessels</td>
<td>0.14</td>
<td>slight</td>
</tr>
<tr>
<td>Lesions</td>
<td>0.11</td>
<td>slight</td>
</tr>
<tr>
<td>Findings</td>
<td>0.08</td>
<td>poor</td>
</tr>
<tr>
<td>Final diagnosis</td>
<td>0.08</td>
<td>poor</td>
</tr>
</tbody>
</table>

Mean diagnostic accuracy of observers 45% (range, 22-55)

Digital SpyGlass Direct Visualization System

- Much better imaging quality (X6)
- Integrated visual probe in access catheter
- Single use endoscope
- Easy handling
- Good price (?)
- 2015 (?)
- Etc.............
Direct POC Using Ultra-Slim Endoscope

- Direct insertion of ultra-slim upper endoscope into the biliary tree through the papilla
- Visualization of the biliary tract using conventional endoscope
- Controlled by single operator
Advantages of Direct POC

- POC using conventional endoscope with standard endoscopic set-up
  - *Most economic solution for POC*
Advantages of Direct POC for the Diagnosis of Biliary Lesions

• High quality endoscopic imaging
• Easy performance of enhanced endoscopy
• Effective tissue sampling
Advantages of Direct POC for the Treatment of Biliary Lesions

- Large working channel (2.0 mm)
  - Effective therapeutic intervention
  - Acceptable of 5 F instruments
Conditions for Successful Direct POC

- Opened orifice of ampulla of Vater
  - Sphincterotomy, or balloon dilation
- Dilated bile duct (≥8 mm)
- Ultra-slim endoscope with good performance
- Using proper accessories
# Accessories to Assist Direct POC with the Ultra-Slim Endoscope

<table>
<thead>
<tr>
<th>Accessory</th>
<th>Author(s)</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal balloon</td>
<td>Mori A, et al.</td>
<td>2008</td>
</tr>
</tbody>
</table>

*Larghi A, Waxman I. Gastrointest Endosc 2006;63:853
Moon JH, et al. Gastrointest Endosc 2009; 2009;70:297*
Intraductal Balloon Through the Scope

- Permits access to proximal biliary tree
- Provides stability and positioning of the slim endoscope within the biliary system
- Can be a useful accessory for direct POC
New Accessory or Scope for Direct POC

- Access balloon catheter for cholangioscopy
- Peroral direct cholangioscope
Access Balloon Catheter for Cholangioscopy

- MTW (Germany)
- Cutting handle without deflating balloon
- Easy exchange of duodenoscope with a slim endoscope after ballooning
- Provides stability and positioning of the slim endoscope in the bile duct
Prototype Peroral Direct Cholangioscope

- Olympus (Japan) new cholangioscope
- Outer diameter: 5.6 mm
- Working length: 133 Cm (30 Cm longer)
- 2 accessory channels; diameters of 2.0/1.2 mm
- Short distal bending section
- 4 way deflection

Itoi T, et al. GIE 2011;73:841
2nd G Prototype Multibending Peroral Direct Cholangioscope

- Olympus (Japan) new cholangioscope
- Outer diameter; 5.2 mm
- Working length; 133 Cm (30 Cm longer)
- 2 accessory channels; diameters of 2.2/0.85 mm
- Multi-bending sections
  - Proximal; 90° up/down
  - Distal; 160° up/100° down
- 2 way deflection

Itoi T, et al. GIE 2012;46:454
Diagnostic Indications for Direct POC

- Evaluation of indeterminate biliary strictures
- Differentiation of indeterminate filling defects
- Evaluation of equivocal cholangiogram findings
- Diagnosis and extent of BD cancer, intraductal papillary mucinous neoplasia, biliary papillomatosis
- Hemobilia of unknown etiology
- Detection of remnant stones after lithotripsy
Diagnostic Procedures with Direct POC

- Endoscopic visual observation
- Tissue sampling with biopsy forceps
- Enhanced endoscopy (NBI, etc)
  - Target biopsy with NBI
Tissue Sampling with Biopsy Forceps

• Major advantage of Direct POC
• Only means for providing a definitive diagnosis
• Critical role in identifying patients unsuitable for surgical therapy
Narrow-Band Imaging (NBI)

- Easy of performance with ultra-slim endoscope
- Detailed images of surface structure and mucosal microvessels
- Emphasize mucosal structures
- Improves the utility of endoscopic images

- Can be used to distinguish neoplastic from normal tissue
Probe-Based Confocal Laser Endomicroscopy (pCLE)

• Cellvizio (Mauna Kea Technologies, Paris, France)
• Virtual histopathological diagnosis using fluorescence
• Combination of confocal microscopy & endoscopy
  – Microscopic examination during ongoing endoscopy
• Features
  – Magnification up to cellular imaging
  – Surface and subsurface imaging
  – Optical sectioning
## pCLE Miami Criteria for Prediction of Neoplasia in the Biliopancreatic System

<table>
<thead>
<tr>
<th>Criteria suggestive for malignant strictures</th>
<th>Criteria suggestive for benign strictures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thick, dark bands (&gt;40 μm)</td>
<td>Thin, dark (branching) bands</td>
</tr>
<tr>
<td>Thick, white bands (&gt;20 μm)</td>
<td>Thin, white bands</td>
</tr>
<tr>
<td>Dark clumps</td>
<td></td>
</tr>
<tr>
<td>Epithelium visualized (villi, glands)</td>
<td></td>
</tr>
<tr>
<td>Fluorescein leakage</td>
<td></td>
</tr>
</tbody>
</table>

*pCLE; probe-based confocal laser endomicroscopy*

Direct Visualization of Indeterminate Biliary Strictures with pCLE

<table>
<thead>
<tr>
<th>Versus final endpoint</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCLE</td>
<td>98</td>
<td>67</td>
<td>81</td>
</tr>
<tr>
<td>Index tissue sampling</td>
<td>45</td>
<td>100</td>
<td>75</td>
</tr>
<tr>
<td>ERCP</td>
<td>88</td>
<td>88</td>
<td>88</td>
</tr>
</tbody>
</table>

*pCLE; probe-based confocal laser endomicroscopy*

Possible Therapeutic Interventions with Direct POC

- Endoscopic lithotripsy
- Endoscopic extraction
- Endoscopic biliary drainage
- Endoscopic resection
- Endoscopic tumor ablation therapy
Endoscopic Lithotripsy by Direct POC

• Electrohydraulic lithotripsy (EHL)
• Laser lithotripsy (LL)
• Indications
  – Impacted stones
  – Overly large stones
  – Combined anatomical difficulties
    • Stone located proximal to ductal stricture
    • Disproportionately narrowed distal bile duct

### Overall Success Rates of Lithotripsy by Direct POC

<table>
<thead>
<tr>
<th>Method</th>
<th>Number</th>
<th>Success Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overtube-Assisted POC</td>
<td>3</td>
<td>100% (3/3)</td>
</tr>
<tr>
<td>ID Balloon-Guided POC</td>
<td>18</td>
<td>88.9% (16/18)*</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>21</strong></td>
<td><strong>90.5% (19/21)</strong></td>
</tr>
</tbody>
</table>

*; Reason for failure in 2 patients – lost of scope position after removal of ID balloon catheter in 1, inadequate probe position in 1

Endoscopic Drainage by Direct POC

- Selective guide-wire access
- Endoscopic nasobiliary drainage with 5F catheter
- Endoscopic biliary drainage with 5F plastic stent

Endoscopic Ablation Therapy under DPOC

- Intraluminal radiotherapy
- Drug injection therapy (ethanol, etc)
- Argon plasma coagulation (APC)
- Photodynamic therapy (PDT)
Argon Plasma Coagulation (APC)

- Coagulation necrosis by non-contact electrocoagulation
- Effective and safe ablation
- Treatment of large surface with superficial depth

Brauer BC et al. Gastrointest Endosc 2008;67:574
Photodynamic therapy (PDT)

✓ Local ablative method
  - Selective accumulation of photosensitizer in tumor tissue followed by light activation
  - Disturbance of the microvasculature and degradation of membranes and lysosomes by cytotoxic radicals (singlet oxygen)

✓ Photosensitizer
  - Hematoporphyrin derivatives (Photosan-3®, Photofrin II®)

✓ Access route
  - Percutaneous access (PTC)
  - Transpapillary access: ERCP, peroral cholangioscopy

Choi HJ, Moon JH, et al. GIE 2011;73:808
Cholangioscopy - Future Development

- Easy manipulation
- High-quality endoscopic imaging
- Enhanced endoscopy capability
- Larger working channel
- Good economic solution
Conclusion

• Peroral cholangioscopy
  – Safe and useful endoscopy
    • to diagnose biliary lesions
    • for therapeutic intervention for selected biliary diseases

• The future of biliary endoscopy
  – Direct visualization to enable diagnostic and therapeutic procedures