

# What should be known prior to performing EUS exams? (Part II)

Christoph F. Dietrich<sup>1,2</sup>, Paolo Giorgio Arcidiacono<sup>3</sup>, Barbara Braden<sup>4</sup>, Sean Burmeister<sup>5</sup>, Silvia Carrara<sup>6</sup>, Xinwu Cui<sup>7</sup>, Milena Di Leo<sup>6</sup>, Yi Dong<sup>8</sup>, Pietro Fusaroli<sup>9</sup>, Uwe Gottschalk<sup>10</sup>, Andrew J. Healey<sup>11</sup>, Michael Hocke<sup>12</sup>, Stephan Hollerbach<sup>13</sup>, Julio Iglesias Garcia<sup>14</sup>, André Ignee<sup>1</sup>, Christian Jürgensen<sup>15</sup>, Michel Kahaleh<sup>16</sup>, Masayuki Kitano<sup>17</sup>, Rastislav Kunda<sup>18,19</sup>, Alberto Larghi<sup>20</sup>, Kathleen Möller<sup>21</sup>, Bertrand Napoleon<sup>22</sup>, Kofi W. Oppong<sup>23</sup>, Maria Chiara Petrone<sup>3</sup>, Adrian Saftoiu<sup>24</sup>, Rajesh Puri<sup>25</sup>, Anand V. Sahai<sup>26</sup>, Erwin Santo<sup>27</sup>, Malay Sharma<sup>28</sup>, Assaad Soweid<sup>29</sup>, Siyu Sun<sup>30</sup>, Anthony Yuen Bun Teoh<sup>31</sup>, Peter Vilmann<sup>32</sup>, Hans Seifert<sup>33</sup>, Christian Jenssen<sup>34</sup>

<sup>1</sup>Medical Department 2, Caritas-Krankenhaus, Uhlandstr 7, D-97980 Bad Mergentheim, <sup>10</sup>Medical Department, Dietrich Bonhoeffer Klinikum, Neubrandenburg, <sup>12</sup>Medical Department, Helios Klinikum Meiningen, Meiningen, <sup>13</sup>Department of Gastroenterology, Allgemeines Krankenhaus Celle, Celle, <sup>15</sup>Department of Hepatology and Gastroenterology, Charite CCM, <sup>21</sup>Medical Department I/Gastroenterology, SANA Hospital Lichtenberg, Berlin, <sup>33</sup>Department of Gastroenterology, Klinikum Oldenburg, Oldenburg, <sup>34</sup>Department of Internal Medicine, Krankenhaus Maerkisch-Oderland, D-15344 Strausberg and Brandenburg Institute of Clinical Ultrasound at Medical University Brandenburg, Germany; <sup>2</sup>Department of Ultrasound, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, <sup>7</sup>Department of Medical Ultrasound, Tongji Medical College, Tongji Hospital, Huazhong University of Science and Technology, Wuhan, <sup>8</sup>Department of Ultrasound, Zhongshan Hospital, Fudan University, Shanghai, <sup>30</sup>Endoscopy Center, ShengJing Hospital of China Medical University, Shenyang, Liaoning, <sup>31</sup>Department of Surgery, Division of Upper Gastrointestinal and Metabolic Surgery, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China; <sup>3</sup>Pancreatico/Biliary Endoscopy and Endosonography Division, Pancreas Translational and Clinical Research Center, San Raffaele Scientific Institute, Vita Salute San Raffaele University, <sup>6</sup>Humanitas Clinical and Research Center- IRCCS- Digestive Endoscopy Unit, Division of Gastroenterology, Rozzano, Milan, <sup>9</sup>Department of Medical and Surgical Sciences, Gastroenterology Unit, University of Bologna/Imola Hospital, Imola, <sup>20</sup>Digestive Endoscopy Unit, IRCCS Foundation University Hospital, Policlinico A. Gemelli, Rome, Italy; <sup>4</sup>Translational Gastroenterology Unit, John Radcliffe Hospital, Oxford OX3 9DU, <sup>23</sup>HPB Unit, Freeman Hospital, Newcastle Upon Tyne, England, <sup>11</sup>General and HPB Surgery, Royal Infirmary of Edinburgh, Edinburgh, UK; <sup>5</sup>Surgical Gastroenterology Unit, Groote Schuur Hospital, Cape Town, South Africa; <sup>14</sup>Department of Gastroenterology and Hepatology, Health Research Institute of Santiago de Compostela, University Hospital of Santiago de Compostela, Santiago de Compostela, Spain; <sup>16</sup>Department of Gastroenterology, The State University of New Jersey, New Jersey, USA; <sup>17</sup>Second Department of Internal Medicine, Wakayama Medical University, Wakayama, Japan; <sup>18</sup>Department of Surgical Gastroenterology, Aarhus University Hospital, Aarhus, <sup>32</sup>Department of Surgery, GastroUnit, Copenhagen University Hospital Herlev, Herlev, Denmark; <sup>19</sup>Department of Surgery and Department of Advanced Interventional Endoscopy, University Hospital Brussels, Brussels, Belgium; <sup>22</sup>Digestive Endoscopy Unit, Hopital Privé J Mermoz Ramsay Générale de Santé, Lyon, France; <sup>24</sup>Department of Gastroenterology, Research Center of Gastroenterology and Hepatology, University of Medicine and Pharmacy of Craiova, Craiova, Romania; <sup>25</sup>Interventional Gastroenterology, Institute of Digestive and Hepatobiliary Sciences, Medanta the Medicity, Gurugram, Haryana, <sup>28</sup>Department of Gastroenterology, Jaswant Rai Speciality Hospital, Meerut, Uttar Pradesh, India; <sup>26</sup>Center Hospitalier de l'Université de Montréal, Montreal, Canada; <sup>27</sup>Department of Gastroenterology and Liver Diseases, Tel Aviv, Sourasky Medical Center, Tel Aviv, Israel; <sup>29</sup>Division of Gastroenterology, Endosonography and Advanced Therapeutic Endoscopy, The American University of Beirut, Medical Center, Beirut, Lebanon

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## Address for correspondence

Dr. Christoph F. Dietrich, Medical Department, Caritas-Krankenhaus, Uhlandstr 7, D-97980 Bad Mergentheim, Germany; Department of Ultrasound, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China. E-mail: [christoph.dietrich@ckbm.de](mailto:christoph.dietrich@ckbm.de)

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## ABSTRACT

In “What should be known prior to performing EUS exams, Part I,” the authors discussed the need for clinical information and whether other imaging modalities are required before embarking EUS examinations. Herewith, we present part II which addresses some (technical) controversies how EUS is performed and discuss from different points of view providing the relevant evidence as available. (1) Does equipment design influence the complication rate? (2) Should we have a standardized screen orientation? (3) Radial EUS *versus* longitudinal (linear) EUS. (4) Should we search for incidental findings using EUS?

**Key words:** Complication rate, EUS, screen orientation

## DOES EQUIPMENT DESIGN INFLUENCE COMPLICATION RATE?

### *Introduction and review of the literature*

Detailed knowledge of the factors contributing to adverse events (AEs) that may occur during EUS and EUS-FNA is limited due to the retrospective nature of most studies. The major complication related to the echoendoscope itself is perforation, which typically occurs in the hypopharynx or the first portion of the duodenum. Perforation of the cervical esophagus is a rare but serious complication that appears to be more common among elderly female patients,<sup>[1,2]</sup> likely related to hypertrophy and/or spasm of the cricopharyngeal muscle. It is most frequently associated with procedures performed by EUS operators with limited experience.<sup>[3-5]</sup> Initial reports linked the complication rate to the use of radial instruments;<sup>[3]</sup> however, this was reported at a time when radial echoendoscopes were far more commonly used than linear scopes and had a larger caliber. There are significant differences regarding the design of instrument tips of echoendoscopes by different manufacturers; these differences include scope diameter, length of bending, and profile of the tip, and, in case of radial echoendoscopes, the shape as forward-viewing instrument or standard side-view scope. The low number of reported serious AEs, however, does not allow comparison between different echoendoscopes in view of their potential for causing esophageal perforation.

### *Arguments in favor of equipment design influencing the complication rate*

Anecdotally, it could be argued that large, rigid echoendoscopes with less tip angulation and long bending section could be prone to causing damage to the gastrointestinal (GI) wall, particularly during intubation and push movements. In contrast, it may be assumed that the use of smaller, more flexible, forward-viewing instruments may help reduce the number and severity

of these AEs. Data from a large database suggest that longitudinal echoendoscopes may carry a higher risk of duodenal perforation compared to radial scopes.<sup>[5]</sup>

### *Arguments against equipment design influencing the complication rate*

Other factors such as anatomical variations and experience of the endosonographer and his/her level of awareness of the potential risk of EUS procedures are likely to influence the rate of AE.

### *Conclusion*

The reported relatively low number of serious endoscope-related complications combined with ongoing recent advances in echoendoscope design makes it difficult and of questionable relevance to focus on the role of instrument design in the development of these complications. As the risk of esophageal and duodenal perforation directly correlates with the level of technical experience of the EUS operator, appropriate supervision of trainees and mentoring of independent operators should become the priority of teaching courses and supervisory projects in the clinical setting. We also refer to the recently published paper discussing the consent form.<sup>[6]</sup>

## SCREEN ORIENTATION

Orientation of the sonographic image obtained during longitudinal EUS is variable, with the “near point” or cranial end of the transducer in relation to the endoscope able to be located either on the left or right side of the ultrasound screen. By convention, transabdominal ultrasound is orientated in the longitudinal section, with the left side of the screen indicating the cranial position. Differences in utilization of screen orientation continue to exist among different endosonographers, with preference typically determined by an individual’s training.

### *Introduction and review of the literature*

EUS was initially developed by combining resources and techniques utilized in both endoscopic and ultrasonographic procedures. Initially, it was performed mostly by GI endoscopists who used radial echoendoscopes. Because the screen orientation was similar to that of a computed tomography (CT) scan, interpretation and comparison were relatively easy. With the aorta placed in the screen at 6 o'clock position, the left side of the screen would equate to the patient's right side, while the right side of the screen would image the patient's left, as long as the echoendoscope was in a straight position. With longitudinal echoendoscopes, the orientation and image characteristics are quite different from other radiological modalities such as CT and magnetic resonance imaging (MRI). Thus, with the advent and increase in their use, screen orientation was largely determined randomly, by personal preference or according to institutional training. Over time, a greater number of practitioners trained in transabdominal ultrasound began to perform EUS. These operators tended to choose the left cranial position because of similarities in probe positioning and image characteristics, when compared with percutaneous ultrasound.

### *Points in favor of the "cranial to the right side" orientation*

The "cranial to the right side" approach is based on the examiner's position to the right of the patient's bed from the examiner's perspective, as he/she approaches from the foot of the bed. The patient is in the left lateral position, and the tip of the echoendoscope is introduced into the mouth and upper esophagus from the right side. By pushing the scope gently forward, more distally located anatomical structures move into the screen from the left side. Needles and other instruments are introduced into the instrument channel from the right side, and the needle tip will consequently appear at the right side of the screen. Therefore, the orientation "cranial to the right side" reflects the natural course of movements by the endoscopist and the echoendoscope.

### *Points against the "cranial to the right side" orientation*

Training and experience in percutaneous ultrasound is a major advantage for operators performing EUS and is considered by many to be mandatory. Because of the overlap in standard probe positions required to illustrate specific anatomical structures/relationships (*e.g.*, aorta

with celiac trunk and mesenteric artery) and to allow meaningful comparisons between percutaneously and endoscopically obtained images, the orientation of the longitudinal picture should be cranial to the left. This has the added benefit of facilitating initial training in EUS and avoids the challenges of interpreting mirrored images.

### *Conclusion*

Screen orientation probably does not directly affect the performance of longitudinal EUS. Operators are trained differently because of institutional history in the procedure. Operators with long-standing experience in one of the two different screen orientations often experience difficulties in switching to the other. Therefore, there is no need to change the orientation in experienced operators. However, in the future, the cranial to the left position could be preferable because of the significant overlap in standard positions when compared with transcutaneous ultrasound (TUS) if we consider TUS knowledge is mandatory for EUS.<sup>[6]</sup> For training purposes, a standard orientation should be demanded.

## **RADIAL EUS VERSUS LONGITUDINAL (LINEAR) EUS**

### *Introduction and review of the literature*

Radial endosonography and longitudinal endosonography were invented at approximately the same time around 1978 and 1979. Linear echoendoscopes were first used by Eugene DiMagno in Rochester, NY, USA,<sup>[7,8]</sup> whereas Meinhard Classen and his group in Erlangen, Bavaria, Germany, and a Japanese group developed the first radial echoendoscopes.<sup>[9-11]</sup> For several reasons, early longitudinal echoendoscopes using linear arrays proved to be clinically unsuitable. The very long rigid tip of the first instruments prevented passage into the duodenum in approximately half of the patients,<sup>[8]</sup> whereas the sonographic view was limited by the narrow aperture of the linear transducer, meaning that despite the high resolution of the linear-array transducers, anatomical orientation was difficult.<sup>[12-14]</sup>

The development of mechanically rotating transducers provided radial echoendoscopes with a 360° rotating US probe, which could scan perpendicular to the long axis of the endoscope.<sup>[15-17]</sup> Images of the mediastinum obtained within the esophagus were comparable with CT scans and radial echoendoscopy initially

prevailed. For nearly 1 decade (1982–1990), only radial echoendoscopes manufactured by Olympus were commercially available and were used worldwide, particularly for staging of GI malignancies, diagnosis of subepithelial tumors, and a variety of pancreaticobiliary indications. The breakthrough for longitudinal EUS came with the prototype development of a forward-viewing gastroscope mounted with a 36-mm long 5-MHz curved-array US transducer behind the optical lens. Preliminary experience using this new type of longitudinal echoendoscope (Pentax and Hitachi) was reported in 1991 by Peter Vilmann.<sup>[18-20]</sup> The pivotal step in overcoming previous difficulties was to place the curved-array transducer in the long axis of a side-viewing endoscope with a working channel, thereby refining the direction of the ultrasound scanning planes. Now, endoscopic and sonographic views were congruent and fine-needle biopsy,<sup>[18-20]</sup> as well as transmural cholangiopancreatography<sup>[21]</sup> and one-step therapeutic interventions<sup>[22]</sup> under direct sonographic control, became feasible. To appreciate anatomical orientation with the new, unfamiliar longitudinal EUS systems, detailed descriptions of longitudinal EUS anatomy were published.<sup>[20,23-25]</sup> However, despite the obvious advantage of the curved-array transducers introducing the most advanced ultrasound technology into the field of EUS,<sup>[26-31]</sup> many traditional users of radial scanning echoendoscopes were reluctant for a long time to use the new longitudinal echoendoscopes for noninterventional diagnostic purposes. In 2000, electronic array radial echoendoscopes became available, resulting in consequent improvements in image quality over traditional mechanical radial scanning echoendoscopes.<sup>[32-35]</sup> In addition, more advanced, noninvasive technologies for tissue characterization became available in the field of radial EUS (R-EUS).<sup>[36]</sup>

Echoendoscopes with mechanical radial scanners have been available with US frequencies varying between 7.5 and 20 MHz. Despite the fact that in some institutions mechanical radial scanners and 270° electronic radial scanners may still be in use,<sup>[37]</sup> currently only electronic array 360° scanners are on the market. Two of them are forward-viewing endoscopes (Pentax-Hitachi, Fujifilm), whereas the third has a forward 55° oblique endoscopic view (Olympus). Technical differences between different types of longitudinal scanners are more remarkable. The Hitachi-Pentax longitudinal echoendoscopes are equipped with curved arrays with a 120° insonation angle. The scanning angle of the Fujifilm longitudinal

echoendoscope is 150°, and the most current Olympus longitudinal scanners have a 180° curved-array scanner. Longitudinal EBUS scopes have a smaller diameter of approximately only 6 mm and may be used as an alternative in the GI tract in patients with upper GI stenosis for EUS fine-needle sampling.<sup>[38,39]</sup> The left adrenal gland, celiac trunk area, and parts of the left lobe of the liver may be successfully approached using an EBUS scope.<sup>[38,40,41]</sup> A dedicated type of longitudinal echoendoscope is the forward-viewing echoendoscope of Olympus, which is equipped with a 90° curved array. Both the optical lens and transducer are forward-viewing and coaxially orientated to the instrumental channel. This may facilitate evaluation and sampling of lesions that are not easily accessible using conventional longitudinal echoendoscopes.<sup>[42-44]</sup>

From these descriptions, it can be concluded that a number of factors including manufacturer, generation, diameters, and transducer orientation may impact on a specific echoendoscope's characteristics, resulting in differences with respect to sonographic field of view, ease of anatomical orientation, contact to the GI wall, reach, and spatial resolution. Furthermore, quality of imaging and technological capabilities may be considerably influenced by the type of ultrasound processor used.<sup>[36,45,46]</sup>

In most traditional indications for R-EUS, studies from the early 1990s have shown comparable results using longitudinal echoendoscopes, *e.g.*, for staging of upper GI cancer,<sup>[47-51]</sup> evaluation of suspected pancreaticobiliary disease,<sup>[52,53]</sup> detection of common bile duct stones,<sup>[54-56]</sup> staging of periampullary cancer,<sup>[57]</sup> classification of mediastinal lymph nodes,<sup>[58]</sup> and evaluation of adrenal glands.<sup>[59]</sup> Nevertheless, there is a paucity of studies prospectively comparing the accuracy of diagnostic procedures using both types of echoendoscope. In 1997, a small randomized study demonstrated that both types of echoendoscope were comparably accurate in staging of pancreatic cancer and assessing vascular invasion and resectability.<sup>[60]</sup> Two randomized comparative studies showed that longitudinal and R-EUS provided similar results in terms of T-staging of upper GI cancer.<sup>[61,62]</sup> However, in one study, R-EUS detected a higher number of suspicious lymph nodes<sup>[61]</sup> while in the other longitudinal EUS took significantly longer time for staging.<sup>[62]</sup>

More recently, the imaging capabilities of modern radial and longitudinal electronic array EUS systems

have been compared for visualization of specific pancreaticobiliary anatomical structures and to determine their sensitivity for the detection of focal pancreatic lesions and features of chronic pancreatitis. In a prospective randomized study, the overall imaging capability in assessing 11 specific pancreaticobiliary areas was superior with longitudinal EUS compared with R-EUS. Visualization of the pancreatic head, body and tail, and the middle and inferior bile duct did not differ between either EUS system, whereas longitudinal EUS performed better in delineation of the pancreatic neck, the structures within the liver hilum, and the origins of the coeliac and superior mesenteric vessels. R-EUS was the superior imaging tool for the papilla of Vater and the gallbladder.<sup>[63]</sup>

In a study focusing on the diagnosis of chronic pancreatitis, R-EUS was performed comparably to longitudinal EUS with no significant differences observed in terms of interobserver variability, sensitivity, specificity, or overall discriminative ability.<sup>[64]</sup>

A retrospective study showed that both electronic radial and longitudinal EUS facilitated similar accuracy in the detection of pancreatic malignancies.<sup>[65]</sup> To discriminate between radial and linear EUS (L-EUS) in the detection of diminutive focal pancreatic lesions, Shin *et al.* conducted a prospective randomized tandem study in asymptomatic, high-risk individuals for pancreatic cancer.<sup>[37]</sup> In this study, the overall prevalence of mostly small cystic lesions was 43.2% on a peer patient analysis, with a mean size of 0.55 cm noted from a previous analysis.<sup>[37,66]</sup> Of 109 lesions, 73 (67%; miss rate 33%) were detected by R-EUS and 99 of 120 lesions (82.5%; miss rate 17.5%) by longitudinal EUS during the first examination, thus demonstrating the superiority of the curved-array echoendoscope<sup>[37]</sup> in this setting.

#### *Advantages of radial-EUS over linear-EUS*

R-EUS may be less time-consuming than L-EUS. Due to the smaller sector image of 120°–180° and orientation of the scanning plane in the long axis of the echoendoscope, longitudinal EUS may be more difficult to handle and interpret, which is mainly true for the examiner with limited experience in transabdominal ultrasound.

Due to comparability with CT and MRI and full circle delineation of the GI wall, interpretation of R-EUS

images may be easier in particular for endoscopists trained in CT and MRI. The main advantage is that the GI wall is more easily visualized using radial scanners. EUS-guided sampling is seldom indicated in patients with upper GI and rectal cancer mainly due to the success of endoscopic biopsy and histological results, but also due to a high risk of false-positive findings.<sup>[67]</sup> Moreover, differentiating between GI stromal tumors<sup>[68]</sup> and benign types of subepithelial GI lesions (*e.g.*, lipoma, leiomyoma, and ectopic pancreas) is possible in a high percentage of cases using endoscopic and endosonographic features.<sup>[69,70]</sup> This has been aided by the development of new techniques in US such as elastography and contrast enhancement, which have improved tissue characterization.<sup>[71-81]</sup> On the other hand, EUS-guided sampling in GI subepithelial tumors is only moderately accurate.<sup>[80]</sup> A recent meta-analysis showed a pooled diagnostic rate of only 59.9%.<sup>[82]</sup> However, a high diagnostic accuracy has been reported with the forward-viewing EUS scope using a 19-G needle in a sampling of subepithelial tumors.<sup>[83]</sup> Moreover, the utilization of newly commercially available FNB needles, which can also be used by nonexpert endosonographers, may overcome the limitation of EUS-tissue acquisition in this clinical setting.<sup>[84]</sup> Therefore, while radial echoendoscopes may be the preferred instrument for staging GI wall cancer and allow for examination of patients with subepithelial lesions, the diagnostic advantage of radial *vs.* linear echoendoscopes remains to be established.

The recent development of novel, dedicated biopsy needles (such as the “Acquire-,” “Trident,” or “Shark-core” needles produced by different manufacturers) has further improved the diagnostic capacity of FNA, due to these needles’ ability to produce core samples suitable for histological analysis. Tissue yield is increased and samples may be obtained in greater numbers including in patients with subepithelial tumors and autoimmune pancreatitis. However, this topic remains to be carefully elucidated by prospective, controlled clinical studies. In patients presenting with abdominal pain of unknown origin, one advantage of forward-viewing radial echoendoscopes is that in principle it can offer the opportunity to combine complete endoscopic examination of the upper GI tract with endosonographic evaluation of the GI wall and surrounding organs, especially the pancreaticobiliary system.<sup>[85,86]</sup> Therefore, R-EUS might be considered the first-line examination of patients with a suspicion of biliary origin for upper abdominal pain, in particular biliary calculi.

### *Advantages of L-EUS over R-EUS*

Longitudinal echoendoscopes are essential for performing EUS-guided tissue sampling and EUS-guided therapeutic interventions. In the German prospective EUS registry, EUS-guided sampling has been performed in approximately 13% of all EUS examinations with EUS-guided therapeutic interventions performed in a further 3% of cases. This rate may be higher in countries that utilize CT/MRI earlier in the algorithmic workup of pancreaticobiliary disease, reserving EUS for targeted morphological assessment of specific conditions: fluid or tissue acquisition and therapeutic intervention.

With the ability to perform immunohistochemistry and up-to-date molecular techniques using small specimens obtained via EUS-guided sampling<sup>[87-93]</sup> together with the adoption of multimodal, personalized, and targeted treatments in the modern management of malignant disease, the role of EUS-guided sampling and other interventions is increasing. In pancreatic pathology practice, EUS-guided sampling has been described as “an example of disruptive innovation effect.”<sup>[94]</sup> Increasingly, very small solid and cystic pancreatic lesions measuring  $\leq 15$  mm are detected by various forms of imaging, typically incidentally.<sup>[74,77,78,95]</sup> The majority of these lesions are entities distinct from pancreatic ductal adenocarcinoma (PDAC), and malignancy can be ruled out with a high degree of accuracy using advanced ultrasound technologies for tissue characterization.<sup>[74,78]</sup> Despite this, an increasing role for tissue diagnosis in small, incidentally detected lesions may be seen in coming years. This is particularly so considering evolving management strategies for both benign (small pancreatic neuroendocrine tumors, focal autoimmune pancreatitis) and malignant (neoadjuvant treatment for resectable PDAC) scenarios. However, in non-PDAC, tissue diagnosis is essential for clinical decision-making. Neoadjuvant treatment strategies might change this perspective rendering EUS-FNB mandatory also in patients with PDAC.

Therapeutically, a multitude of minimally invasive transmural EUS-guided procedures has emerged in recent years which successfully compete with conventional endoscopic and minimally invasive surgical techniques.<sup>[79,81,96]</sup> In specialized centers, EUS-guided sampling and treatment procedures are performed in more than one-third of EUS examinations.<sup>[97]</sup>

### *Conclusion*

Longitudinal echoendoscopes can be safely and successfully used for all EUS indications without significant disadvantages. They are indispensable in all kinds of EUS-guided interventions including EUS-guided tissue sampling and EUS-guided therapeutic interventions. L-EUS is also first choice for staging of lung cancer, evaluation of mediastinal lymphadenopathy, and evaluation of pancreatic disease. The examination of the gallbladder and perampullary region depends on local experience and remains controversial.

R-EUS continues to have a role in the staging of luminal cancers and the assessment subepithelial tumors. In the future, radial echoendoscopy with high-definition endoscopic imaging and increased flexibility of the scope tip may emerge as a first-line diagnostic modality in patients with upper GI complaints instead of ultrasound or cross-sectional imaging combined with esophagogastroduodenoscopy.<sup>[85,86]</sup>

## **SHOULD WE SEARCH FOR INCIDENTAL FINDINGS USING EUS?**

### *Introduction and review of the literature*

Incidental findings are defined as unexpected and clinically silent lesions unknown prior to EUS examination. Considering the potential implications, the question should be rephrased: can we interpret unexpected findings correctly based on EUS alone and how should we respond to such unexpected findings? Literature on incidental findings during EUS examination is limited to small observational studies. One Spanish study involving 239 patients noted additional diagnoses in 38.5% of cases where examination included the gut wall, pancreas, biliary tract, ampulla of the pancreas, large abdominal vessels, liver, spleen, left adrenal gland, posterior mediastinum, and the thyroid gland. Significant findings that required further investigations were found in 11.3% of patients (approximately 1 in 10).<sup>[98]</sup> A second study from Iran of 552 prospectively collected EUS examinations noted incidental findings in only 7.1% of patients, with approximately half of those requiring further investigation. This study, however, did not specifically document or discriminate examination of the spleen, left adrenal, or thyroid gland.<sup>[99]</sup> Incidentally found cystic lesions of the pancreas have been extensively discussed elsewhere.<sup>[95,100]</sup>

### *Advantages to examination of incidental lesions*

Knowledge of a patient's diagnosis prior to EUS examination may influence the scheduling and conduct of the procedure.<sup>[6]</sup> Unexpected findings during such examinations may provide new perspectives to a known disease, such as previously undetected liver metastasis in a patient with pancreatic adenocarcinoma. EUS may also reveal previously undetected metastasis in unexpected locations, for instance, a patient with proximal squamous cell carcinoma of the esophagus could be found to have suspicious retroperitoneal lymph nodes at EUS staging, with subsequent EUS-FNA providing proof of abdominal metastasis and systemic disease. Equally important consequences may arise when focal liver lesions are unexpectedly detected by EUS, as can happen with conventional transabdominal ultrasound.<sup>[101,102]</sup> The same implications are valid for splenic and adrenal incidentalomas.<sup>[59,99,103-109]</sup>

Very occasionally, purely incidental findings may lead to different or additional diagnoses in individual patients.<sup>[98-100,110]</sup> Rarely, such findings may alter clinical management of the patient, for example, a patient found to have asymptomatic common bile duct stones while undergoing EUS staging of a gastric cancer, who should first undergo endoscopic retrograde cholangiography and biliary stone removal prior to having surgery.<sup>[111,112]</sup>

### *Disadvantages to examination for incidental lesions*

Complete examination of all accessible structures in the upper GI tract may entail certain risks in some patients. For instance, in a patient with esophageal carcinoma, complete EUS examination could include exclusion of abdominal lymphadenopathy or common bile duct stones. In such circumstances, the risk of duodenal passage may outweigh the potentials benefit and may expose the patient to unnecessary and time-consuming examinations of areas with a low probability of important findings. In addition, extended EUS procedures can put pressure on experienced high-level endoscopists for whom time is a scarce commodity. Hence, prior to EUS examination, it should always be assessed whether the benefit of the procedure outweighs the potential risks in each individual clinical scenario.

### *Conclusion*

Be aware of the “beautiful flowers” or the “chirping of crickets by the wayside”. They can provide a new perspective on a known disease, influence patient

management, or even lead to a new or additional diagnosis. To find them requires time, a systematic thorough examination, and solid knowledge of normal morphological findings. Prior to each and any EUS exam, the operator should always assess whether the benefit of “seeing it all” outweighs the potential procedural risks in each patient.

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Dietrich, *et al.*: Controversies in EUS

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