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# Implementation of endoscopic submucosal dissection in Europe: survey after 10 ESD Expert Training Workshops, 2009 to 2018

Tsuneo Oyama, MD, PhD,<sup>1</sup> Naohisa Yahagi, MD, PhD,<sup>2</sup> Thierry Ponchon, MD, PhD,<sup>3</sup> Tobias Kiesslich, PhD,<sup>4,5</sup> Andrej Wagner, MD, PhD,<sup>4</sup> Takashi Toyonaga, MD, PhD,<sup>6</sup> Toshio Uraoka, MD, PhD,<sup>7</sup> Akiko Takahashi, MD,<sup>1</sup> Alexander Ziachehabi, MD,<sup>8</sup> Daniel Neureiter, MD, PhD,<sup>9</sup> Maria Fuschlberger,<sup>4</sup> Franz Schachinger, Mag,<sup>10</sup> Hans Seifert, MD, PhD,<sup>11</sup> Georg Kaehler, MD, PhD,<sup>12</sup> Alexandr Mitrov, MD,<sup>13</sup> Sergey V. Kantsevov, MD, PhD,<sup>14</sup> Helmut Messmann, MD, PhD,<sup>15</sup> Juergen Hochberger, MD, PhD,<sup>16</sup> Frieder Berr, MD, PhD,<sup>4,5</sup> the ESD Workshop Training Group\*

Saku, Tokyo, Kobe, Maebashi, Japan; Lyon, France; Salzburg, Linz, Altheim, Austria; Oldenburg, Heidelberg, Augsburg, Berlin, Germany; Nizhny Novgorod, Russian Federation; Baltimore, Maryland, USA

**Background and Aims:** Adoption of the endoscopic submucosal dissection (ESD) technique for early GI cancer from Japan requires expert-supervised experimental training before unsupervised implementation of clinical ESD. The aim of this study was to evaluate unsupervised implementation of ESD intention-to-treat (ie, any resection planned and started as en bloc ESD).

**Methods:** ESD workshops (in vivo porcine model) lasted 3.3 days, including a 1-day theory seminar, for 177 participants from 135 Western referral centers. A questionnaire was sent to the senior participant of all 135 centers. This cross-sectional questionnaire survey included main outcome measurements such as performance, organ distribution, and severe adverse events of ESD intention-to-treat.

**Results:** Feedback was received from 113 centers (84%): 73 (54%) ESD centers and 40 centers (30%) with zero ESDs. Ten (7%) had published ESDs; no feedback was received from 12 (9%) centers with unknown status. Altogether, 83 centers (61.5%) performed ESDs: 21 (16%) had >150 ESDs (professional category), 33 (24%) had 31 to 150 ESDs (competent category), and 29 (21.5%) had ≤30 ESDs (initial learning category). Most implemented ESD centers (91% [72 of 79]) were analyzed: centers on initial learning (420 ESD) compared with centers with >30 ESDs (5676 ESDs) performed en bloc ESDs in 64% versus 84%, hybrid ESD in 26% versus 11%, and piecemeal EMR in 10% versus 5.2%. The majority of ESDs (66%-68%) performed were in the colorectum, with a low risk overall (30-day mortality, 0.03%; surgical repair, 3.5% vs 1.7%) and satisfactory outcome (oncosurgery, 7.4% vs 5.2%; local recurrence, 1.5% vs 0.3%).

**Conclusions:** Beyond guideline recommendations, unsupervised implementation of ESD was successful in the colorectum with a step-up approach. Western ESD centers must now aim for professional (ie, >80%) curative ESD. (iGIE 2023;2:472-80.)

The adoption of endoscopic submucosal dissection (ESD) for early GI cancer from Japan to Europe requires expert-supervised experimental training of experienced endoscopists before they can implement human ESD in Europe. In 2008, a structured approach had been proposed by Japanese experts, including observation of expert ESD procedures and performance of 5 ESD procedures under the supervision of leading Japanese experts in an in vivo experimental model before starting to perform unsupervised ESD procedures on patients.<sup>1,2</sup> From 2009 to 2018, Paracelsus Medical University (Salzburg, Austria) had set up 10 such annual ESD Expert Training Workshops (2.3 days' hands-on training plus 1-day theory seminar) to allow for an average of 4 to 5 supervised ESD procedures per

participant in a porcine model,<sup>3</sup> complemented with a third day (UPDATE seminar) of clinical case studies and theory presented by the Japanese and Western experts. The strategy of this ESD training program, how to implement and advance ESD centers in Western countries, has been detailed in a topic article.<sup>2</sup>

The objective of the study's questionnaire survey was to evaluate in the participating centers the extent of unsupervised implementation of clinical ESD intention-to-treat (ESD-ITT; ie, any resection planned and started as en bloc ESD) and any related severe adverse events (SAEs).

En bloc ESD allows precise histopathologic staging of tumor category, grading, and resection margin status and provides cure of early GI cancer.<sup>4-9</sup> The Japan Gastrointestinal

Endoscopy Society (JGES) has validated classical criteria of histopathologic curative ESD (zero risk of metastasis) in the entire GI tract and expanded criteria (risk <4% of regional metastasis) in the stomach and esophagus.<sup>7,10,11</sup> Endoscopic classifications (macroscopic, microsurface, and microvessel types) predict with high accuracy (>85%-90%) premalignant and malignant lesions in the early stage and define indications for ESD versus piecemeal EMR versus surgery with lymphadenectomy.<sup>12-16</sup> Professional ESD centers in Japan achieve >80% curative resection (CR) with ESD.<sup>4,10,11</sup>

Implementation of ESD thus requires 2 learning curves for (1) accurate endoscopic prediction of pT tumor category using image-enhanced endoscopy, which is the basis for correct differential indication of ESD versus surgery with lymphadenectomy; and (2) highly skilled endoscopic electrosurgical resection. In Japan, ESD has rapidly been adopted through carefully designed clinical training systems based on direct day-to-day individual supervision of the learners by the top Japanese experts. Such expertise was not yet available in Europe in 2009.<sup>1</sup> European interventional endoscopists had to master the learning curve for ESD in an unsupervised fashion.<sup>1,2</sup>

## METHODS

### Ethics committee

For the questionnaire survey, ethics committee approval was not required because feedback from the 135 participating centers regarding implementation of clinical ESD has been used for anonymized descriptive analyses, and all 73 centers providing quantitative data have approved the manuscript and listing of the senior participant by name and affiliation. Each annual ESD workshop has been a priori approved by the governmental Ethics Committee and Animal Ethics Committee (BMWF 66.012/0006-II/10b/2009 through 66.019/0029-WF/V/3b/2018), was led by veterinarian teams, and was monitored for compliance with European regulations for protection of animals in experimental research. All ESD workshop and Update events have been endorsed by the European Society of Gastrointestinal Endoscopy (ESGE), including the ESD Live events,<sup>17</sup> and since 2016 for educational credits by the European Union of Medical Specialists (<https://eaccme.uems.eu>).

### Description of the annual ESD Training Workshop and Update

The basic format of the hands-on training course on piglets (20-25 kg body weight) in general anesthesia has been described in detail<sup>3</sup>; additional details regarding the annual ESD course program are provided in [Supplementary Appendix 1](#) (available online at [www.igiejournal.org](http://www.igiejournal.org)). All 10 experimental hands-on workshops were held at the anatomic training facilities of the Paracelsus Medical University and included an introductory seminar (2.5 hours of instruction regarding course structure and techniques) on

the day of arrival, 2 full days of hands-on training (two 4.5-hour sessions per day), and the clinical Update seminar on the third day (open to the general audience) with case studies and interactive presentations by the experts (including 4 ESD Live events every year since 2012). From 2009 to 2013, there were 6 working stations: 2 each for Hook-knife,<sup>6</sup> Dual-knife,<sup>18</sup> (Olympus Europe, Hamburg, Germany), and Hybrid-knife (ERBE Elektromedizin GmbH, Tübingen, Germany).<sup>19,20</sup> From 2014 to 2018, there were 8 working stations: 2 stations each for Hook-knife, J, Dual-knife, J, hybrid-knife, and Flush knife BT<sup>21</sup> (FUJIFILM Europe GmbH, Ratingen, Germany).

Supervision and individualized instruction on the ESD technique was given by 3, respectively 4 top experts from Japan and the same number of Western experts at the parallel training stations. In brief, participants performed hands-on training in teams of 3, taking turns every 20 minutes and rotating to another working station after every 60 minutes. Hence, each participant passed through all 8 training stations and tutors per day. Reference material was an annually updated syllabus on the endoscopic analysis of early GI neoplasias, differential indications (EMR vs ESD vs resective surgery), and details on ESD techniques, electrosurgical settings, supply material, training steps, risks for and management of AEs (under [www.early-cancer.eu](http://www.early-cancer.eu) [password on request from the corresponding author]), and, since 2014, an atlas on endoscopic analysis and differential indication (according to JGES) for early GI neoplasias.<sup>13</sup>

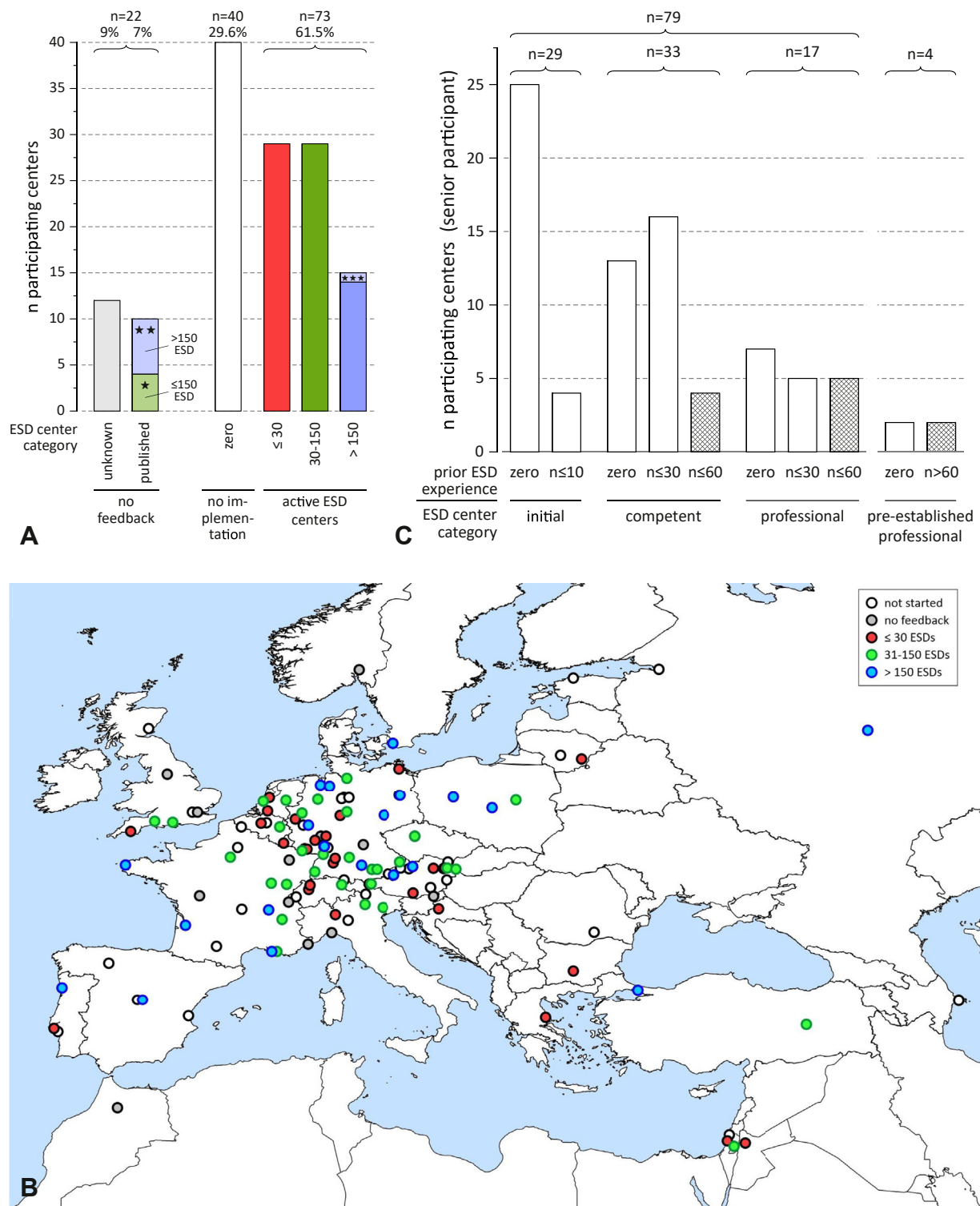
### Participants

All candidates were senior endoscopists highly experienced with EMR from major referral centers and who had to state prior experience with human ESD (if any) to match the training teams of each 3 participants with comparable experience. In accordance with an ESGE board member (T.P.), participating candidates were chosen based on best interventional experience as well as geographical distribution and suitability of their centers.

The ESD Expert Training Workshops 2009 to 2018 provided 210 trainee slots ( $5 \times 18$  [2009-2013] +  $5 \times 24$  [2014-2018]) for 208 trainee participants (and 2 cancellations). A total of 177 trainees have participated; 27 trainees participated 2 times, and 2 participated 3 times. The 177 participants came from 144 centers (29 centers had 2 participants and 2 centers had 3 participants). Nine centers (6%) were excluded from analysis because of loss to follow-up of the participant: 3 in the United States and 1 each in England, Argentine, Reunion (France), New Zealand, Singapore, and Morocco. Altogether, 135 centers were surveyed: 133 from Europe and Mediterranean Near East, and 2 from the United States.

### Course feedback of participants

In all 10 workshops and Updates, participants have rated the teaching excellent by the leading ESD experts



**Figure 1.** Supply network of endoscopic submucosal dissection (ESD) centers started/implemented by senior workshop participants. **A**, Categories of ESD implementation for the 135 participating centers. Feedback from 73 active centers (29 in the initial category, 29 in the competent category, and 15 in the professional category (\*\*\*) pre-established ESD center was excluded from statistical analysis) and from 40 centers without implementation (zero ESD). No feedback was received from 22 centers: 12 with unknown performance status and 10 with ESD publications and assigned performance category (\*competent; \*\*professional) yielding 83 active ESD centers. **B**, Distribution of participating ESD centers (as categorized in panel A) across Europe and the Mediterranean Near East. Circles represent centers, and the insert color represents the ESD category: gray = unknown, white = zero, red = initial (≤30 ESDs), green = competent (31-150 ESDs), and blue = professional (>150 ESDs). **C**, Categorial analysis: ESD prior experience of the senior trainee of the 83 active ESD centers: distinguished in 79 started or implemented centers and 4 pre-established professional centers at the time of participation. ESD center categories are as in panel A.

from Japan and by Western experts and the course very helpful in implementing the novel ESD procedure in their hospitals (Supplementary Fig. 1, available online at [www.igiejournal.org](http://www.igiejournal.org)).

## Questionnaire

A structured questionnaire including the recommended ESD center structure<sup>2</sup> (Supplementary Table 2, available online at [www.igiejournal.org](http://www.igiejournal.org)) was e-mailed to the senior participant of all 144 centers in March 2018 (and in May 2019 for Workshop 2018) to obtain information on implementation of ESD-ITT. The senior participant received a reminder after 1 month and by telephone after 2 months.

## Statistical analysis

A total of 73 centers responded with completed questionnaire data; 1 (Institute Paoli Calmettes, pre-established ESD center<sup>22</sup>) was excluded, and 72 were included in the statistical analysis. Overall mortality was calculated on total number of cases per total number of ESDs reported by the 72 centers. All other parameters are given as percentage of total ESD number per center, analyzed for mean  $\pm$  standard error and for statistical differences by using one-way analysis of variance with Bonferroni's adjustment.

For categorical analysis of the supply network of ESD centers, all active ESD centers were categorized as proposed by Oyama et al<sup>2</sup>: initial learning category for the first 30 unsupervised ESD-ITT, competent performance category for 31 to 150 ESD-ITT, and professional category after 150 ESD-ITT. In addition, any human ESD experience of the senior participant before this course was accordingly categorized.

## RESULTS

### Survey of centers

Of all 135 centers, feedback had been obtained by the senior participant for 113 (84%): 73 responding active ESD centers (54%) and 40 centers (30%) with zero ESD performed. No feedback had been received from 22 centers (16%): 12 without ESD reputation or publication and 10 centers with published ESDs (6 in the professional category in Augsburg, Berlin, Istanbul-Kocaeli, Lyon, Marseille, and Porto<sup>22-27</sup> and 4 in the competent category in Besançon, Grenoble, Liège, and Leiden<sup>28-30</sup>) (Fig. 1A). A total of 83 centers (61%) had been performing ESDs: 29 in the initial category, 33 in the competent category, and 21 in the professional category. The centers of ESD workshop trainees have implemented an ESD supply network (Fig. 1B); other ESD centers in Europe that had not participated are not shown<sup>31-41</sup> (current affiliation of Dr Agapov [31] is St. Petersburg).

### Centers with implementation of ESD

Categorical analysis revealed 79 implemented ESD centers and 4 pre-established ESD centers (Fig. 1C). From

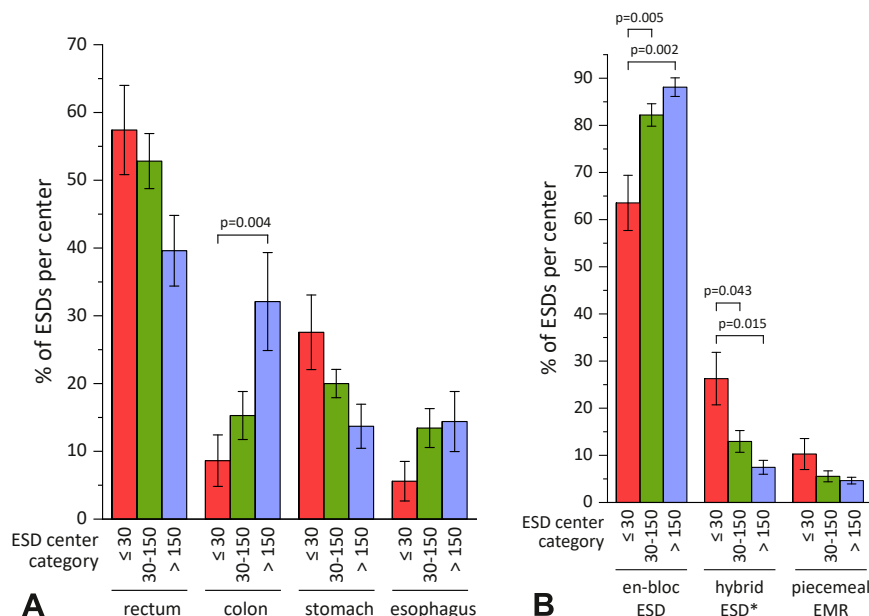
2017 to 2018, the 4 pre-established professional centers had delegated 2 participants on zero experience (Berlin and Istanbul-Kocaeli)<sup>24,25</sup> or had participated with 2 advanced experts.<sup>22,27</sup> The 29 centers on initial learning ( $\leq 30$  ESDs) were started by trainees without prior ESD experience ( $< 10$  ESDs). The 33 centers in the competent category (31-150 ESDs) were implemented by senior participants on zero or initial ( $\leq 30$  ESD) prior experience ( $n = 29$ ) or competent ( $n = 4$ ) prior experience. Trainees on zero or initial prior experience have set up 12 of 17 professional category centers, and trainees on competent ESD prior experience ( $n = 5$ ) contributed to the other 5 (Augsburg, Lodz, Mannheim, Nizhniy Novgorod, and Poznan). Thus, 70 (89%) of the 79 started or implemented ESD centers had zero or only initial ESD prior experience.

### Performance of ESD during implementation

The survey data include 72 responding centers only and none of the pre-established or nonresponding published centers. The survey of years 2018 to 2019 provides a cross-sectional overview on unsupervised implementation of ESD by former participants of this expert training course. All questionnaires stated the data are based on ESD indications according to JGES (Tab 1 in [2]); histologic assessment for grading, extension and invasion of early cancer; and a prospective data register for ESD indication, performance, outcome, and follow-up. The annual ESD volume during the past year was  $30 \pm 5$  ESDs for competent category centers and  $77 \pm 18$  ESDs for professional category centers. Performance of ESD is compared between 29 centers on initial learning ( $n = 420$  ESDs; follow-up  $18 \pm 3$  months), 29 competent ( $n = 2104$  ESDs; follow-up  $49 \pm 6$  months), and 14 professional ( $n = 3572$  ESDs; follow-up  $82 \pm 5$  months) category centers by subgroup analysis; significance levels are shown in Figure 2.

The majority (mean, 66%-72%) of all ESD-ITT were performed on colorectal neoplasias ( $46 \pm 3\%$  malignant), irrespective of the performance category. Nevertheless, some step-up approach is apparent from the data (Fig. 2A): beginners performed, on average, 57.5% of the rectal ESDs, 28% of the gastric, 9% of the colonic, and 5.5% of the esophageal ESDs. Competent and professional category centers show stepwise fewer rectal (mean, 53% and 39%) and gastric (20% and 14%) ESDs and up to 3-fold more colonic (15% and 32%,  $P < .005$ ) and esophageal (13% and 15%) ESDs. Some of these centers implemented ESD mainly or exclusively with a colorectal step-up approach.<sup>42-45</sup>

Mean rate of en bloc ESD was low (64%) for centers on initial learning but significantly higher in the competent category (82%) and the professional category (88%) (Fig. 2B). Beginners frequently (26%) used hybrid ESD compared with competent (13%,  $P < .05$ ) and professional (7.5%,  $P < .02$ ) categories, and conversion to piecemeal EMR occurred in 10% versus 6% and 4.5%.



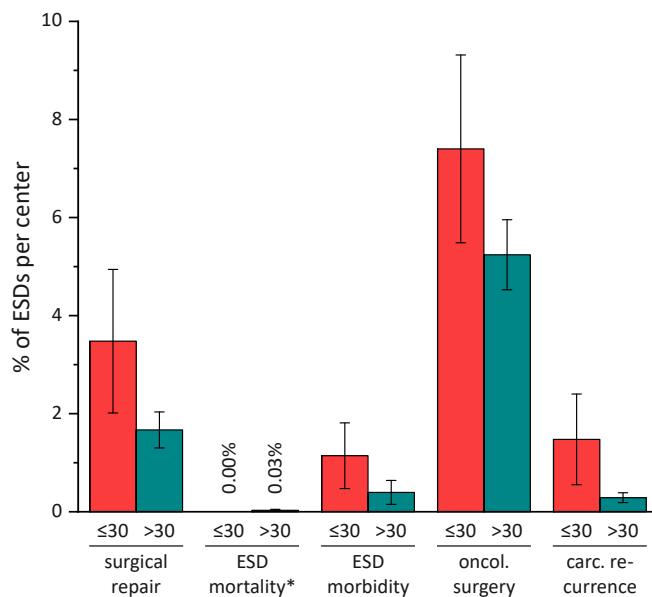
**Figure 2.** Performance of endoscopic submucosal dissection (ESD) during implementation period. Organ distribution (A) and technical performance (B) of ESD intention-to-treat (mean  $\pm$  standard error) of the 72 responding centers is shown for the center categories initial (red), competent (green), and professional (blue). Total subgroup analyses yields only 5 significant differences as shown. \*Hybrid ESD in 1 to 3 pieces.<sup>60</sup>

### Adverse outcome of ESD-ITT

Even without supervision during the initial learning curve, clinical ESD has been implemented by course participants with low risk and satisfactory oncologic outcome. Overall, 30-day mortality is .03% (2 cases in professional centers during initial and competent phases) and long-term morbidity is .7%  $\pm$  .2% (strictures after esophageal or anorectal ESD) in the 72 ESD centers (6497 ESDs; follow-up 41  $\pm$  3 months). The survey results as split into beginners ( $\leq 30$  ESDs) and competent to professional ( $>30$  ESDs) category centers show low rates of procedural and oncologic SAEs of ESD-ITT (Fig. 3): (1) surgical repair for ESD AEs was needed in 3.5%  $\pm$  1.5% versus 1.7%  $\pm$  0.4%; (2) surgery was indicated for noncurative ESDs in 7.4%  $\pm$  1.9% versus 5.2%  $\pm$  0.7%; and (3) local recurrence of cancer was observed in 1.5%  $\pm$  0.9% versus 0.3%  $\pm$  0.1%, and progressive disease in 0 versus 0.4%  $\pm$  0.2%. There were no significant differences in SAE rates among the subgroups or in the comparisons of the 3 subgroups (initial vs competent vs professional category).

### DISCUSSION

The main goal of this ESD training program in Salzburg was a high number of referral centers that start and implement ESD with low risk in an unsupervised fashion, according to a subsequent detailed strategy.<sup>2</sup> To this end, principles and guidelines developed in Japan were conveyed by leading Japanese experts. This primer course program conveyed awareness for the 2 learning curves: (1) accurate endoscopic staging of early neoplasias for correct ESD indication; and (2) knowledge and



**Figure 3.** Adverse outcome during implementation of endoscopic submucosal dissection (ESD). The cross-sectional survey is split into initial category ( $\leq 30$  ESDs [red]; total 420 ESDs; follow-up 18  $\pm$  2.6 months) versus competent and professional category ( $>30$  ESDs [dark green]; total 5676 ESDs; follow-up 59  $\pm$  5 months, initial phase of centers included). There were no significant differences between the 2 groups or between the 3 categories in total subgroup analyses. \*Mortality indicates percent per category.

basic training for acquisition of electrosurgical ESD skills and for the logistic requirements to implement a new ESD center.<sup>2</sup> The reference material was continuously updated (endoscopic atlas; per website, syllabus, lectures, and video cases). We

registered only highly experienced senior candidates, to reduce the risk of AEs, and preferred newly recruited referral centers, to minimize repetitive participation or additional candidates from recruited centers. To foster ESD skills, we strongly recommended continued hands-on training *ex vivo*, expert observation, sabbatical at ESD centers in Japan, or ESD performance under teaching assistance by a Japanese expert.<sup>2,46</sup> As collaborators in a joint effort to establish an ESD supply network (Supplementary Table 1), the participants were encouraged to perform unsupervised implementation of ESD based on best case-volume according to prevalence of indications and step-up of technical challenge.<sup>2</sup>

What are the merits of the retrospective survey on this program? Categorical feedback information was available for 91% of the 135 participating centers (30% zero ESDs; 7% published ESDs; and 54% with ESD survey data) detailing a supply network of 83 ESD centers (61%). The 79 (59%) started or implemented ESD centers had been set up on zero or initial (89.5%) or early competent (10.5%) prior ESD experience (Fig. 1). Hence, this course program was an effective ESD start-up primer for referral centers.

The questionnaire data on unsupervised implementation cover 91% (72 of 79) of the started or implemented ESD centers. All stated they use ESD indications according to JGES,<sup>2</sup> qualified analysis of specimens, and a prospective register for ESD-ITT. The questionnaire only asked for core parameters of the implementation strategy, such as basic performance (organ distribution, *en bloc*-ESD/hybrid ESD/piecemeal EMR) and SAEs relevant for the patients. Hence, these cross-sectional data seem representative for the implementation of ESD centers.

Unsupervised implementation of clinical ESD was prevalence based, mainly on colorectal lesions (66% → 72%), with a step-up approach on colonic (9% → 32%,  $P < .05$ ) and esophageal (6% → 15%) neoplasias, and nevertheless with a low-risk scenario: low rates of 30-day mortality, long-term morbidity and surgical repair, and satisfactory oncologic outcome, such as need for oncosurgery and local recurrence of cancer after ESD-ITT (Fig. 3). Overall, these SAE rates are barely higher than those reported from East Asia.<sup>47,48</sup> ESGE guidelines advise against performance of ESD in the colon during the implementation period, mainly because colonic ESD is more difficult and carries a higher risk of perforation.<sup>1,49,50</sup> However, the ESGE curriculum for ESD training did not recognize the safety of prospective European case series of colorectal ESD.<sup>42,43,45,50-52</sup> Most colonic perforations are small and well managed with endoscopy, whereas rare delayed perforations require surgical repair.<sup>43-45,53-57</sup> In prevalence-based ESD learning curves, colonic ESD is as safe as rectal and gastric ESDs (<1% surgery for overall 8%-12% AEs).<sup>56-58</sup>

The rate of *en bloc* ESD in starting centers (64%) was as low as published for initial learning of colorectal ESD<sup>22,58,59</sup> but in the professional category (88%) nearly reached the East Asian standard (>90%).<sup>47,48</sup> ESD-ITT included a high rate of hybrid ESDs (26%) on the initial category versus

significantly less on competent (13%) and professional (7.5%) categories. Hybrid ESDs were considered responsible for the high rate of AEs (eg, bleeding, perforation) in a meta-analysis that has not distinguished hybrid ESD performed for technical reasons versus hybrid ESD for managing AEs of ESD.<sup>48</sup> Our faculty, however, had recommended hybrid ESD for self-completion of difficult ESD-ITT.<sup>60</sup> The high rate of hybrid ESD does not correspond to the low rate of AEs but matches the similar rate of failed self-completion (20%-35%) for supervised learning of ESD in Japan.<sup>54,55</sup>

Limitations of this cross-sectional survey are as follows: (1) retrospective exploratory design with potential reporting bias, (2) unknown additional success factors, and (3) missing items such as measured training efficiency, organ-specific ESD subgroup analysis, and curative resection data.

The retrospective exploratory design of the survey only shows subsequent successful implementation of ESD centers but no causal relationship. Course participation (with hands-on training) was priming for the program strategy.<sup>2</sup> Reporting bias is possible in such surveys but less likely in the presence of prospective data registers and match of the survey data with the rates of *en bloc* ESD and SAE of Western ESD series.<sup>27,28,32-34,43,48,52,56,61</sup>

These findings should be interpreted with caution: the low-risk implementation of ESD centers depends on additional success factors<sup>2</sup>: conscious selection of the center's most experienced endoscopist, check list for risk precautions, and self-evaluation of performance during unsupervised ESD-ITT.<sup>2,58</sup>

The hands-on course was not designed to measure the efficiency of individual skills training because of the scheduled rotation of the trainees during ongoing ESD procedures (but achieved an average number of 4-5 procedures).<sup>3</sup> Nevertheless, during the first year after the course in 2009, the ESD case load (total, colorectal, and esophageal) had more than tripled, and the trainees with highest perforation rate did not start clinical ESD.

Subgroup analysis only shows a nonsignificant trend for lower rates of SAEs (surgical repair, morbidity; oncosurgery, recurrence of cancer) in competent and professional categories. Organ-specific SAE rates were not significantly different due to small differences and small sample sizes, confirming the overall low risk of SAEs during implementation of CR-ESD.

This survey only inquired onco-surgery done for non-curative ESD (as surrogate indicator for correct lesion selection) rather than histologic CR. An ESGE curriculum training course program (2013-2019) of the same hands-on format based on gastric and esophageal hybrid knife-ESD with exclusively European teachers reported more successful implementation of clinical ESD: competence was achieved with 10 ESDs followed by professional ESD performance (CR >80%) at 10 to 20 ESDs and 20 to 30 ESDs.<sup>62</sup> That questionnaire was much more detailed, but data are based only on 19 participants despite >250 training slots (ie, <10%

surveyed). Such rapid progression to competent and professional ESD contrasts with much longer ESD learning curves worldwide.<sup>2,25-27,42-45,48,53,54,56,57,61,63</sup>

Our survey data support the feasibility and safety of prevalence-based colorectal implementation of ESD, as shown by individual learning curves of mainly course participants.<sup>42,43,52,56,57,64</sup> Beyond that, CR is the main indicator for professional status of ESD centers.<sup>2</sup> The CR rates (65%-75%) reported from Europe are significantly lower than for professional centers of Japan (80%-89%),<sup>22,26,28,32,41,47,61,63,65,66</sup> mainly due to less accurate endoscopic indications, including deep submucosa-invasive cancers indicated for surgery/not for ESD.<sup>2,26,61,63</sup> Unfortunately, European guidelines still recommend evaluation of en bloc ESD specimens with the surrogate standard of “low-risk resection,” “local risk resection,” and “high-risk resection,”<sup>49,50</sup> which is the standard for evaluation of piecemeal EMR<sup>58</sup> but conceals the merit of en bloc ESD to the patients (ie, histopathologic CR of early GI cancer).<sup>4,10,11</sup>

We therefore recommend stringent application of the JGES criteria to ESD-ITT, including the validated indication criteria for “ESD with curative intention,” “ESD with diagnostic intention,” and “out of ESD indication” (ie, “indication for surgical resection with lymphadenectomy”) as well as the histopathologic standard “curative resection.”<sup>4,10,11</sup> ESGE and National Societies will have to focus guidelines and curriculum courses on professional curative rates (80%-90%) for ESD with curative intention.

In conclusion, these survey data support the feasibility and safety of prevalence-based implementation of the ESD procedure mainly in the colorectum, provided the endoscopist is experienced in endoscopic indication, electro-surgical technique, and knowledge regarding ESDs. This approach facilitates further implementation and advancement of ESD centers in the West.

## DISCLOSURE

The following authors disclosed financial relationships: T. Toyonaga: Royalties or licenses from Olympus and Fujifilm. N. Yahagi: Consulting fees from Olympus, Fujifilm, and Boston Scientific; and patents planned, issued, or pending for Olympus, Pentax, and Boston Scientific. A. Ziahebi: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from LAMS; honoraria for HBP expert meetings; and honoraria for online presentation (“Treatment of superficial colorectal neoplasia”). D. Neureiter: Consulting fees from Boehringer Ingelheim Pharma GmbH & Co. (Germany) and Lilly (Austria). H. Seifert: Honoraria from ERBE for tutoring ESD workshops. G. Kaehler: Grants or contracts from Micotech Europe GmbH, Baxter, GBUK, Erbe Elektromedizin GmbH, and Medi-Globe GmbH; payment

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*Abbreviations:* AE, adverse event; CR, curative resection; ESD, endoscopic submucosal dissection; ESD-ITT, ESD intention-to-treat; ESGE, European Society of Gastrointestinal Endoscopy; JGES, Japan Gastroenterological Endoscopy Society; SAE, severe adverse event.

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\*Members of the ESD Workshop Expert Training Group are listed in [Supplementary Table 1](#) (available online at [www.igiejournal.org](http://www.igiejournal.org)).

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Current affiliations: Department of Endoscopy, Saku Central Hospital Advanced Care Center, Saku, Japan (1); Division of Research and Development for Minimally Invasive Treatment, Cancer Center, Keio University School of Medicine, Tokyo, Japan (2); Spécialités Digestives, Hôpital Edouard Herriot, Medical University of Lyon, Lyon, France (3); Department of Internal Medicine I, University Hospital (4); Center for Physiology, Pathophysiology and Biophysics, Institute of Physiology and Pathophysiology (5); Institute of Pathology, University Hospital (9); Paracelsus Medical University, Salzburg, Austria; Department of Endoscopy, Kobe University Hospital, Kobe, Japan (6); Department of Gastroenterology and Hepatology, Gunma University Hospital, Maebashi, Japan (7); Endoscopy Center, Kepler University Hospital, Linz, Austria (8); Veterinary Practice, Altheim, Austria (10); Department of Medicine–Gastroenterology, University Hospital Oldenburg, Oldenburg, Germany (11); Endoscopy Center, Surgical Clinic, University Hospital Mannheim, University Heidelberg, Heidelberg, Germany (12); Endoscopy Unit, Cancer Hospital, Privolzhsky Research Medical University, Nizhny Novgorod, Russian Federation (13); Institute for Digestive Health and Liver Disease, Mercy Medical Center, University of Maryland, Baltimore, Maryland, USA (14); Department of Gastroenterology, University Hospital Augsburg, Augsburg, Germany (15); Department of Gastroenterology, Vivantes Hospital Berlin-Friedrichshagen, Berlin, Germany (16).

Reprint requests: Frieder Berr, MD, PhD, Department of Internal Medicine I, University Hospital Salzburg, Paracelsus Medical University, Mueller Hauptstrasse 48, 5020 Salzburg, Austria. E-mail: [frieder.berr@pmu.ac.at](mailto:frieder.berr@pmu.ac.at).

## SUPPLEMENTARY APPENDIX 1. ADDITIONAL DETAILS OF THE ANNUAL ESD WORKSHOP PROGRAM

Each annual endoscopic submucosal dissection (ESD) Workshop has been a priori approved as scientific project by the governmental Ethics Committee and Animal Ethics Committee (Bundesministerium für Wissenschaft, Forschung und Wirtschaft, Vienna, Austria; BMWF 66.012/0006-II/10b/2009 through 66.019/0029-WF/V/3b/2018) and since 2017 as third-party organized procedure training by the Conference Vetting System of Ethical MedTech Europe ([www.ethicalmedtech.eu](http://www.ethicalmedtech.eu)). The ESD workshops and Updates were operatively organized by the authors located in Salzburg, Austria, on a not-for-profit basis. Funds for total costs (including accommodation) had been raised from participant fees (40%-63%), donations of a charitable foundation (5%-25%), and unrestricted educational grants (28%-35%) by the endoscopic and pharmaceutical industry.

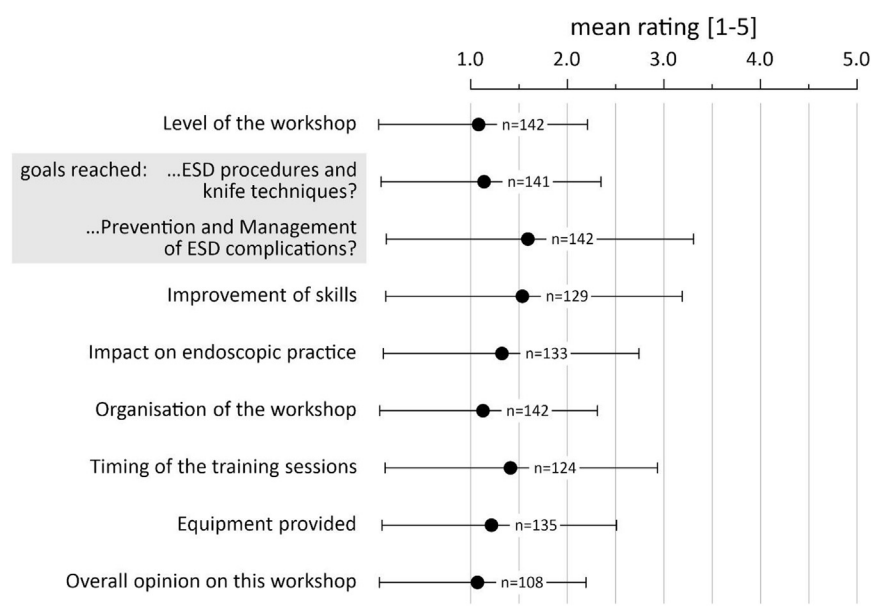
Description of the annual ESD Training Workshop and Update is given in the Methods and for year 2009 in detail elsewhere.<sup>1</sup> From 2010 on, the attendees were multinational, selected in accordance with European Society of Gastrointestinal Endoscopy (by T.P.), and ESD adverse events were no longer fatal (ie, no perforation-induced pneumothorax). Since 2010, we focused training on the colorectum, to allow for a step-up approach of ESD implementation in the colorectum, and improved the structured training program (with 2 parallel training stations per session) for management of bleeding (in heparinized animals), and prevention and management of (intentional) perforation with different techniques (clipping  $\pm$  loop trick; over-the-scope clip; and endo-suturing). The 4 hands-on sessions (days 1 and 2) were each started with a 20-minute live demonstration (knife-type ESD; endo-clipping/suturing) by a top expert. In the meantime, stomach or large bowel down from the splenic flexure were cleaned from residual mucus or contents and areas similar to lesions marked with electrocoagulation points by the respective tutor. After a short break to allocate the training teams, the ESD hands-on training was run for 4 hours with teams of 3 participants

per training station: every 20 minutes, exchange of the operator; every hour move to next working station. Supervision and individualized instruction on the ESD technique were provided by the top experts from Japan and experts from Europe and the United States at the parallel stations. ESD specimens were taken to the pathologist to document with image, sizes, ESD type and duration, and adverse events. In the afternoon session, the teams passed through the corresponding row of training stations. Only very common knife types with cutting direction from near side to far side (Hook-(J-), Dual-(J-), Hybrid-, and Flush-knife BT) had been chosen, because learners had been warned of perforation when using knives with cutting direction from far side to near side.<sup>2</sup> In the stomach, distal colorectum, and, for skilled teams, distal esophagus, different techniques were practiced (as explained in the syllabus): en bloc ESD using initial circumferential incision, partial circumferential incision, tunneling- and pocket-creating method, and hybrid ESD (with final snaring in 1-3 pieces).<sup>3</sup>

Audiovisual recordings of lectures, quizzes, and live demonstrations of the Update (on day 3) were year-on available ([www.gastroenterologie-salzburg.at](http://www.gastroenterologie-salzburg.at), resp. since 2019 for self-learning selected under [www.early-cancer.eu](http://www.early-cancer.eu)). Few of the lectures and the syllabus (last updated in 2020) are available only with password on request from the corresponding author. All updates in course program and supporting material were revised according to Japan Gastrointestinal Endoscopy Society recommendations by 2 of the authors (T.O. and N.Y.).

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**Supplementary Figure 1.** Results of endoscopic submucosal dissection (ESD) workshop evaluation 2009 to 2018. Numeric data from a structured questionnaire ([Supplementary Appendix 1](#)) which was handed out to all participants in the ESD workshops between 2008 and 2019 are summarized as mean values  $\pm$  95% confidence interval. *n* indicates the number of responses received for each item.

**SUPPLEMENTARY TABLE 1. Collaborators of the ESD Workshop Training Group (responding centers)**

Ulrich Halm, Parkklinikum Helios, Leipzig, DE	Oliver Möschler, Marienhospital, Osnabrück, DE
Heinrich Schulz, KH St Josef Bremen, Bremen, DE	Sandro Sferrazza, Univ Hosp. St Chiara, Trento, IT
Edouard Chabrun, CHU Bordeaux, Bordeaux, FR <sup>1</sup>	Boris Pekarek, National Oncology Ctr., Bratislava, SK
Franck Cholet, CHU de la Cavale Blanche, Brest, FR	Orhan Kursat Poyrazoglu, Firat UH, Elazig, Anatolia, TR <sup>6</sup>
Henrik Thorlacius, Skane UH, Lund Univ., Malmö, SE	Bulent Baran, Townsville Univ. Hosp., Townsville, Queensland, AUS
Franz-Ludwig Dumoulin, Gemeinschafts-KH Bonn, DE	Andreas Mayer, Landsteiner UK, LKH, St Pölten, AT
Alberto Herreros de Tejada, Porto de Hierros UH, Madrid, ES	Barbara Tribl, AKH, Wien, Med Univ Wien, Wien, AT
Cezary Łozinski, Cancer Institute Poznań, Poznań, PL	Martin Goetz, Univ. Klinikum, Tübingen, DE <sup>7</sup>
Fabrice Caillol, Institut Paoli Calmettes, Marseille, FR	Dieter Plamenig, KH Barmherzige Brüder, St Veit, AT <sup>8</sup>
Michał Szychalski, Medical University of Lodz, Lodz, PL	Tilman Pickartz, Univ. Klinikum, Greifswald, DE
João C. Santos-Antunes, Univ Hosp S. João, Porto, PG	Chris Hayward, Plymouth Univ. Hosp., Plymouth, UK
Manfred Lutz, Caritasklinikum St Theresia, Saarbrücken, DE	Frank Grünhage, Rhein KH, Dormagen-Grevenbroich, DE <sup>9</sup>
Katrin Bermoser, KH Hall in Tirol, AT <sup>2</sup>	Tarek Qutob, City Hospital, Amman, JD
Andreas Schäfer, Alfried-Krupp Krankenhaus, Essen, DE	Tom Seerden, Amphia Hospital, Breda NL
Yann LeBaleur, CHU Henri Mondor, Paris, FR <sup>3</sup>	Volker Schmitz, KH Bad Kreuznach, DE
Harold Jacob, Haddassah UH, Ein Karem, Jerusalem, IL	Reiner Wiest, Inselspital, Univ. Bern, Bern CH
Hans-Peter Allgaier, Diakonie KH Freiburg, DE	Arthur Hoffman, HeliosH-Schmidt KH Wiesbaden, DE
Gerhard Kleber, Ostalb Klinikum, Aalen DE	Thomas Flatz, LKH Feldkirch, Feldkirch, AT
Ingo Steinbrück, Asklepios KH Hamburg-Altona, DE <sup>12</sup>	Henrik Horvath, Bürgerspital, Solothurn, CH <sup>10</sup>
Alberto Tringali, Ospedale Conegliano, Conegliano, IT	Edi Viale, Ospedale San Raffaele, Milan, IT
Thomas Flatz, LKH Feldkirch, Feldkirch, AT	Michaela LaRoche, Diakonie KH Kassel, DE
Christian Österreicher, Hanusch KH, OEGK, Wien, AT	Jan Peveling-Oberhag, Robert Bosch KH, Stuttgart, DE
Anton Glas, Klinikum Passau, Passau, DE	Maridi Aerts, ZU Univ Hospital, Brussel, BE
Robert Schroder, Gellre Hospital, Apeldoorn, NL <sup>4</sup>	Eyal Gal, Kaplan Medical Ctr, Tel Aviv, IL
Achim Lutterer, Klinikum Karlsruhe, Karlsruhe, DE	Daniel Doykov, Univ Hospital Kaspela, Plovdiv, BGR
Edris Wedi, Univ Hosp Göttingen, Göttingen, DE <sup>13</sup>	David Allerstorfer, KH Rudolfinum, Vienna, AT
Michael Anzinger, KH Barmherzige Brüder, München, DE	Gerd Bodlaj, KH Barmherzige Schwestern, Wien, AT
Philip Boger, UH Southampton, Southampton, UK	Romualdas Maskelis, Lithuan. Nat. Cancer Ctr Vilnius, LT
Stepan Suchánek, Milit. Hosp, Charles Univ, Prague, CZ	Varvara Vassiljeva, Hospital Arlon, Arlon, BE
Arthur Laquière, Hopital-NORD, Marseille, FR	Nikos Kapetanakis, Gastro Med Ctr, Volos, GR
Sarveson Rajkumar, Royal Stoke UH, Stoke-on-Trent, UK	Beate Appenrodt, UK Saarland Homburg, DE <sup>11</sup>
Maciej Rupinski, Marie Curie Oncology Center, Warsaw, PL	Miguel Moura, Santa-Maria-UH, Lisboa, PG
Terry Jue, Kaiser Permanente Hosp, San Francisco, USA <sup>5</sup>	Barbara A. Bastiaansen, Acad Med Ctr, Amsterdam, NL
Mohamed Barawi, UH Wayne State University, Detroit, MI, USA	Neven Barsic, Univ Hosp Zagreb, Zagreb, HR
Christoph Schlag, KH re-dr Isar, Tech.Univ, München, DE <sup>14</sup>	Vinzent Zimmer, Marienhaus Klinik Neunkirchen, DE

ESD, Endoscopic submucosal dissection.

Current affiliations are as follows:

<sup>1</sup>Clinique de l'Anjou, Angers, FR.

<sup>2</sup>LeopoldinuMED Hall in Tirol, AT.

<sup>3</sup>Hôpital Paris Saint-Joseph, Paris, FR.

<sup>4</sup>Nij Smellinghe Ziekenhuis, Drachten, NL.

<sup>5</sup>Mayo Clinic, Phoenix, AZ, USA.

<sup>6</sup>Aydin University Hospital, Istanbul, TR.

<sup>7</sup>Med. Klinik IV, Kliniken Böblingen, Böblingen, DE.

<sup>8</sup>Spittal a.d. Drau, AT.

<sup>9</sup>KRH Klinikum Siloah, Hannover, DE.

<sup>10</sup>Klinik Linde, Biel, CH.

<sup>11</sup>St. Elisabeth-Krankenhaus, Köln, DE.

<sup>12</sup>Diakonie KH Freiburg, DE.

<sup>13</sup>Sana Kliniken, Offenbach, DE.

<sup>14</sup>Universitätsspital, Zürich, CH.

**SUPPLEMENTARY TABLE 2. Basic questions of the survey questionnaire “Implementation of ESD technique by participants of ESD Workshops (2009-2018)”**

Participation in ESD Workshop <i>in the year(s)</i>	.....	
Affiliation:	.....	
<b>Center structure</b>	YES	NO
• Endoscopic resection	...	...
• Laparoscopic visceral surgery	...	...
• GI pathologist/specimen analysis	...	...
• In serial sections (2 mm)	...	...
• Depth of submucosal invasion (μm)	...	...
• ESD indications according to JGES*	...	...
<b>ESD performance</b>		
Total no. of ESD n = ...	since (month/year): .... / ....	
ESD in year 2017: n = .... (resp. in year 2018)		
Fraction (%) of all ESD:		
• Rectal ESD	... %,	<i>malignant lesions†</i> : ...% of colorectal ESD
• Colonic ESD	... %	
• Gastric ESD	... %	
• Esophageal ESD	... %	
Fraction (%) of ESD intention-to-treat		
• ESD en bloc	... %	
• Hybrid-ESD‡	... % (final snaring, 1-3 pieces)‡	
• Conversion to piecemeal-EMR	... %	
ESD with diagnostic intention ...%		
Severe adverse events of all ESD (n):		
• Surgery for ESD adverse event	n = ...	
• 30-day mortality	n = ...	
• Long-term morbidity from ESD	n = ...	(impairment: .....)
<b>Follow-up program after ESD</b>		
• Prospective data file (in your center)	YES... NO ...	
• Follow-up recommended (to referring physician)	YES... NO ...	
• Surgery recommended for cure (for noncurative ESD)	n = ...	
• Local/nodal recurrence of cancer after ESD	n = ...	
• Progressive disease after ESD of cancerous lesion	n = ...	

ESD, Endoscopic; JGES, Japan Gastrointestinal Endoscopy Society.

\*Compare Tab 1 in reference [2].

†Cancer and high-grade intraepithelial neoplasia.

‡Defined as final snaring in 1-3 pieces (Toyonaga T, Man IM, Morita Y, et al. The new resources of treatment for early stage colorectal tumors: EMR with small incision and simplified endoscopic submucosal dissection. Dig Endosc. 2009;21[Suppl 1]:S31-759).

**SUPPLEMENTARY TABLE 3. Sponsors of the endoscopic and pharmaceutical industry**

## Major sponsors:

Olympus Europe, Hamburg, DE  
 FUJIFILM Europe GmbH, Ratingen, DE  
 ERBE Elektromedizin GmbH, Tübingen, DE  
 Leonie Wild Foundation, Heidelberg-Eppelheim, DE

## Other sponsors:

3-D Matrix EMEA-BV, Hoofddorp, NL	Abbot GmbH, Vienna, AT
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Peter Pflugbeil GmbH, Zorneding, DE	Roche Austria GmbH, Onkologie, Vienna, AT
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Reinhard Di Lena GmbH, Donnersbach, AT	Sanofi-Aventis, Österreich, Vienna, AT
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Werfen Austria GmbH, Vienna, AT	Zymed GmbH, Vienna, AT