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ESD training: A challenging path to excellence

Herreros de Tejada A. ESD training

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**Abstract**

Endoscopic submucosal dissection (ESD) has important advantages against Endoscopic mucosal resection (EMR) for early gastrointestinal neoplasia treatment, but its difficult learning curve and associated risks have constrained its wider expansion. ESD training includes comprehensive study of ESD basics, attending live cases and performing initial interventions in animal models, ideally under expert supervision. Mentoring methods in Japan and other Asian countries are reviewed, with special concern in the conditions recommended for trainees to engage in an ESD program and achieve competence. Animal training is usually based on the well-known porcine model. *Ex vivo* models for esophageal, gastric and rectal ESD are cheap and easy to set up, whereas *in vivo* training requires especial settings and veterinarian support. Nevertheless, it is advisable to gain experience in the live pig, where conditions are similar to human, before moving to real patients. Particular attention is focused on colorectal ESD (CR-ESD), one of the most difficult locations for this technique. Since most of the potential lesions for ESD in Western countries are located in colon or rectum, excellence in training is of paramount importance for successful outcomes in CR-ESD in the West.

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**Key words:** Endoscopic submucosal dissection; Training; Early neoplasia; Animal model; Colorectal

**Core tip:** This mini-review focuses on endoscopic submucosal dissection (ESD) training. ESD is a relatively novel advanced technique used for en-bloc resection of gastrointestinal early neoplasia. ESD training has become a challenge for Western endoscopists due to several factors: low detection rate of early gastric cancer, the perfect scenario for starters; lack of experts in the technique for adequate tutoring; and finally, most of the target lesions in Western countries are colorectal neoplasias, representing the highest peak of difficulty in ESD. We will review some of the most important steps that could shape a training program in ESD, including animal training. Particular attention is focused in colorectal ESD.

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**INTRODUCTION**

Oncology field is already an important area of development for gastroenterologists[[1](#_ENREF_1)], since diagnosis and/or treatment of early gastrointestinal neoplastic lesions is crucial for prevention and cure. Management of lesions with low risk of lymph node metastasis usually comprises *classic* polipectomy and endoscopic submucosal resection (EMR). EMR has demonstrated good results dealing with esophageal, gastric, duodenal and colorectal lesions[[2-5](#_ENREF_2)]. Ideal targets include flat lesions (Paris Classification 0-IIa and 0-IIb) less than 2 cm, though piece-meal resection is also possible with acceptable outcomes[[2](#_ENREF_2),[6](#_ENREF_6)]. Endoscopic submucosal dissection (ESD) is a late step forward in therapeutic endoscopy for early gastrointestinal neoplasia[[7](#_ENREF_7)], and it has become a standard of care not only in Japan, when it originated in the late-1990s, but also in some other countries and regions[[8-17](#_ENREF_8)]. ESD has also spread in its indications: gastric, esophageal, colorectal, duodenal and even hypofaringeal early neoplasia are potential targets, with excellent results[[18](#_ENREF_18)]. New and exciting areas of research for ESD are being explored nowadays, like the treatment of submucosal tumors[[19](#_ENREF_19),[20](#_ENREF_20)] (Figure 1).

The main advantages of ESD compared to EMR are: higher en-bloc and R0 resection rate[[21-23](#_ENREF_21)], with decreased local recurrence, no limitation due to size of the lesion in certain circumstances and superior pathological assessment of the cancer invasion in the specimen[[24](#_ENREF_24),[25](#_ENREF_25)]. Nevertheless, ESD is associated with a higher risk of severe complications (bleeding and perforation) (Figure 2), in addition to a particular difficult and lasting learning curve[[21](#_ENREF_21),[26-28](#_ENREF_26)]. The latter, together with the lack of experts available for tutoring, are the most important constricting factors for a wider expansion of ESD in Western countries[[11](#_ENREF_11)]. Another circumstance also contributes to the low penetration of ESD in western areas: there is a lower gastric cancer incidence, with lower proportion of early gastric cancer diagnosed during upper endoscopy procedures[[13](#_ENREF_13),[29](#_ENREF_29)]. Those are the ideal cases for initial training in human ESD, as recommended by experts[[9](#_ENREF_9),[18](#_ENREF_18),[30](#_ENREF_30)]. Unfortunately this painful scenario for training is aggravated by the fact that many potential lesions for Western endoscopists to perform ESD are mostly found in colon and rectum, a particular challenging location, even for Japanese experts[[31](#_ENREF_31),[32](#_ENREF_32)]. We will review some of the most important aspects of ESD training, with a particular section focused on colorectal ESD (CR-ESD).

**JAPANESE EXPOSURE: THE ORIGINAL SOURCE**

ESD was initially developed in Japan, and Japanese experts have propelled this technique to its highest standards and excellent outcomes[[33](#_ENREF_33),[34](#_ENREF_34)]. In Japan, the usual way of teaching new apprentices in ESD has traditionally consisted on supervised ESD procedures by senior endoscopists in referral centers (Figure 3). This scheme seems to have worked well in recent years, but as the number of physicians performing ESD and its indications are rising, it seems that even in Japan some kind of standardized ESD training program for teaching centers is needed[[35](#_ENREF_35)]. Most of the candidates should have demonstrated advanced skills in therapeutic upper and lower endoscopy, as well as extensive knowledge of early neoplasia endoscopic assessment. Moreover, many mentors do consider aptitudes like perseverance, competence in dealing with stressing situation and awareness of own limitations on their mentee selection process.

Gastric ESD is contemplated as the first step in ESD career, since easier position and thin wall facilitates ESD approach with lower risk of perforation. Screening programs in gastric cancer have boosted the detection and knowledge of early gastric cancer in Japan[[36](#_ENREF_36)]. Basic competence in terms of en-bloc resection and complication rate could be reached after 30 human gastric cases have been completed under expert supervision[[28](#_ENREF_28),[37](#_ENREF_37)]. Tsuji et al have described excellent results for trainees who completed 27-30 gastric ESD after having attended 40 cases and later completed 20 cases of post-ESD preventive coagulation[[38](#_ENREF_38)]. A recent study suggest that expertise similar to well-experienced endoscopists could be achieved after having completed 80 cases, including lesions within extended criteria (ulceration, large size…)[[39](#_ENREF_39)]. Some suggested criteria for skill advances monitoring are speed, size and en-bloc resection rate[[28](#_ENREF_28)], but also location in the stomach is a decisive factor, with more difficult cases in the body and fundus[[10](#_ENREF_10),[39](#_ENREF_39)].

For many foreign physicians with interest in ESD, Japanese teaching centers are a good opportunity for first-hand exposure in its “natural” environment[[40](#_ENREF_40)]. They can experience live how the experts perform high quality diagnostic evaluation of target lesions and perform ESD. Essential knowledge to acquire includes but is not limited to: dye and digital chromoendoscopy, magnification endoscopy, marking and initial approach to lesions, step by step ESD procedure, tools and devices, management of minor and major complications, post-ESD surveillance and specimen fixation and pathological assessment. Overseas endoscopists are not usually allowed to do hands-on training in humans in Japan, yet they can still practice ESD in animal model with the unique opportunity of onsite expert supervision[[41](#_ENREF_41)] (Figure 4). Furthermore, it is possible to invite Japanese experts to Western centers to get tutoring support for initial ESD approach[[42](#_ENREF_42), [43](#_ENREF_43)] (Figure 5).

In recent years a relevant progress in ESD have been observed in other neighboring countries in southeast Asia, mainly in South Korea[[10](#_ENREF_10),[44](#_ENREF_44)] and China[[45](#_ENREF_45)]. In South Korea it has been described that eligible trainees with 2-year experience in endoscopy must observe 30-40 ESD cases to follow all steps of the procedure, including fixation of the specimen once completed; afterwards, the fellows would serve as assistant with knifes to an expert endoscopist for 15-20 cases, before being granted to start ESD with small lesions in the antrum under close supervision[[46](#_ENREF_46)]. As an additional reinforcement, the national Korean ESD group conducts an *ex vivo* hands-on course for trainees[[30](#_ENREF_30),[47](#_ENREF_47)]. In the near future we can expect also high quality expert groups in Korea offering additional opportunities for ESD training to overseas trainees.

**ANIMAL TRAINING: THE WILD EXPERIENCE**

Training in animal model is probably the best way to overcome some of the limitations in learning ESD[[41](#_ENREF_41),[48](#_ENREF_48)]. Such a difficult technique must not be attempted in humans unless supervised by certified experts, or after an intensive animal training program has been completed and satisfactory outcomes have been achieved. The porcine model is similar to human anatomy, not expensive and widely accessible[[46](#_ENREF_46)]. Reports of ESD in other species are scarce[[16](#_ENREF_16), [49](#_ENREF_49)], including a description of human excised portion from sleeve gastrectomy[[50](#_ENREF_50)]. Most studies have demonstrated the usefulness of the porcine *ex vivo* and *in vivo* for initial competence achievement in ESD, where regular endoscopes can be used and anatomic similarities in esophagus and stomach facilitates the approach[[43](#_ENREF_43),[45](#_ENREF_45),[48](#_ENREF_48),[51](#_ENREF_51),[52](#_ENREF_52)]. The trainee can experience early steps of ESD process (marking, circumferential cutting and submucosal dissection), together with management of complications such as perforation and bleeding (only *in vivo* model). Some suggested criteria for skill advances monitoring are speed and en-bloc resection rate[[53](#_ENREF_53),[54](#_ENREF_54)]. An animal training program in ESD requires appropriate settings and dedicated endoscopy equipment and material (Figure 6), all of which is not commonly accessible to many trainees in their institutions. Some endoscopists attend special courses in ESD to get access to animal training, with good results in terms of skill improvement[[43](#_ENREF_43), [45](#_ENREF_45)].

***Ex vivo model***

Harvest porcine organs like esophagus and stomach are easy to set, cheap, and there is no need for veterinarians or anesthesia[[37](#_ENREF_37),[40](#_ENREF_40),[46](#_ENREF_46)]. It is not acceptable to start in the live animal before having familiarized with maneuvers and initial steps of ESD. Perforation and associated mortality are common in live animals for those novices with no experience at all[[45](#_ENREF_45)]. The fresh harvest organ should be intensively cleaned before attaching proximal esophagus to an insertion tube inside a plastic box or placing the organ in a plastic model. Similar setting has been described for porcine harvest rectum (Figure 7), with good results for CR-ESD[[55](#_ENREF_55)]. Although these models do not reproduce real *in vivo* conditions, like spontaneous motility, bleeding and tissue reaction to injection and electrocautery, the trainee can practice special maneuvers, injection, circumferential cutting and dissection. This initial phase is a good opportunity to familiarize with different knives and devices. Insulated type are recommended for the naïve trainee, since non-insulated knifes may be associated with higher perforation risk[[45](#_ENREF_45)]. It is recommended that the novice should get acceptable en-bloc resection and perforation-free results, before stepping up to live animals[[48](#_ENREF_48)]. General recommendation for the trainee is to initiate ESD in porcine stomach, starting in antrum, and then progressing according to an increasing difficult gradation to the body, the greater curvature, the lesser curvature and the fundus[[43](#_ENREF_43)]. Afterwards the trainee might practice in more demanding locations like the esophagus o rectum, for which specific *ex vivo* model preparation has been described elsewhere[[51](#_ENREF_51),[55](#_ENREF_55)].

***In vivo model***

The *in vivo* model is the natural and ethically accepted next step, after a sufficient period of training in the *ex vivo* model. Using live pigs require support from veterinarians to provide preparation of the animal (24-48 h fasting is advisable); general anesthesia and euthanasia/follow-up care of the animal after procedures are completed (Figure 8). The sense of reality increases when performing ESD in live animal, with physiological reactions, including motility, mucosal secretions, bleeding and abdominal distension. In survival studies we can check for perforation closure outcomes and post-ESD scars, which can give a chance for practicing ESD in difficult scenario (severe fibrosis, ulceration) afterwards. This simulation can also be set up in *ex-vivo* model using banding and snare transection[[56](#_ENREF_56)], but a more realistic approach seems to be the live animal. Once the trainee has gained enough experience in the stomach, he/she could move forward to the esophagus or the rectum-colon. Whereas the former requires similar setting to the gastric, rectum and colon demand an intensive preparation with bowel cleaning agents, and frequently additional rectal water infusion of the rectum[[40](#_ENREF_40)](Figure 9).

**IMPROVING YOUR SKILLS: WISE ADVICES FROM EXPERTS**

There are some general advices for endoscopists already performing ESD in humans that should be kept in mind. Good field of vision and situation of the scope in relation to the target lesion are of paramount importance. The endoscopist must know how to change the patient´s position to get the best of gravitational counter traction and clear view to facilitate the access to the submucosal layer[[57](#_ENREF_57)]. Managing accurately retroflex position is particularly important when performing gastric ESD, where fundus and body locations usually require such approach. Getting used to dissect while positioning in such “inverted” fashion will demand hours of hard training, ideally in the animal model setting. It has been suggested that the appropriate level for dissection is depth to be beneath vascular network and above the muscle layer, so to reduce bleeding events during ESD as well as the risk of positive vertical margin[[58](#_ENREF_58)]. A similar recommendation is also true for those lesions with severe fibrosis, and if possible, we should try to create a nice flap starting far from the lesion border. Good quality of field of vision is paramount, and experienced endoscopists do recommend performing a careful and systematic hemostasis of bleeding points, or even better, appropriate preventive hemostasis of visible vessels[[59](#_ENREF_59)]. Special care should be put on the systematic coagulation of all visible vessels in the resection site after completed the resection[[58](#_ENREF_58)]. Animal training has been essential for introducing ESD practice in Western countries[[40](#_ENREF_40), [42](#_ENREF_42)], but it also plays an important role for those endoscopists engaged in human ESD that still need to increase the load case in order to increase their skills, so they can face difficult ESD locations (colon, gastric fundus…). Another aspect we should bear in mind in the great importance of preserving a complete and systematic registry of all ESD cases, so short and long term outcomes/adverse events in our series could be analyzed[[11](#_ENREF_11)].

**COLORECTAL ESD (CR-ESD): THE HIGHEST PEAK**

Whereas gastric ESD has become a standard procedure in Japan and other Asian countries long time ago, CR-ESD is still a challenging procedure, even for Japanese experts. Most of the experience in CR-ESD comes from large studies in Japan[[34](#_ENREF_34),[60-62](#_ENREF_60)]. Eligible flat colorectal lesions for ESD are increasingly diagnosed in Japan and western countries[[63-65](#_ENREF_63)], and the will rise even more in the near future with expansion of colorectal screening[[66](#_ENREF_66),[67](#_ENREF_67)]. Absolute indications for ESD in Japan include: LST-NG > 20 mm, LST-G mixed type > 40 mm and any lesion with severe fibrosis (due to EMR, biopsies or inflammatory bowel disease)[[34](#_ENREF_34),[60](#_ENREF_60),[68](#_ENREF_68)] (Figure 10). There is controversy regarding the adoption of CR-ESD due to the high risk of failure and complications, and since EMR appears to be good enough for management of colorectal sessile non-invasive neoplasia[[2](#_ENREF_2)], there are advocates for exploring alternative hybrid techniques with ESD steps associated to EMR[[69](#_ENREF_69)].

The learning curve for CR-ESD has been analyzed in several studies. Apparently, up to 80 cases might be needed to complete before getting excellent results (en-bloc and R0 resection)[[70](#_ENREF_70)]. Sakamoto *et al*[[71](#_ENREF_71)] reported progressive learning curve by 2 trainees supervised, reaching competence level after 30 CR-ESD. Other authors have recommended a caseload of 20 or 30 gastric ESDs before attempting CR-ESD[[60](#_ENREF_60),[72](#_ENREF_72)]. It is possible that this learning curve could be reduced if additional training is completed in the animal model, while performing the first human cases in the rectum, where maneuverability is easier and perforation has less impact in the patient[[32](#_ENREF_32)]. In the learning process of CR-ESD, it might be acceptable to approach to smaller lesions in rectal location (relative indication for ESD) in order to gain experience and avoid despair[[27](#_ENREF_27),[32](#_ENREF_32)].

A recent European position statement in ESD recommended steps that should be taken to acquire good skills in CR-ESD, following a progressive training, mainly in animal model, and keeping a record track[[11](#_ENREF_11)]. There are some series of CR-ESD in European centers, which show inferior outcomes, slower progression and limitation to distal locations than Japanese counterparts[[27](#_ENREF_27),[73](#_ENREF_73),[74](#_ENREF_74)]. Still, results are encouraging, and a recent report showed acceptable R0 and en-bloc resection rates in rectum and colon after 5 and 20 cases respectively[[42](#_ENREF_42)]. Some Japanese experts reassure that inexperienced western endoscopists should not try CR-ESD in lesions with significant fibrosis or larger than 40 mm during the first 30-40 cases[[32](#_ENREF_32)].

***Selected tips for CR-ESD***

Adequate positioning and high risk of perforation are the main limitations when trying to perform successful CR-ESD. You will learn from each of your cases, and you should be prepared to face complications calm enough to manage them and move forward. Here are some general advices for starters I would recommend from my limited personal experience: (1) Ask for proper advice from experts when planning CR-ESD: It might be very useful to send pictures and/or video clips of the lesion beforehand to an expert, so you can get recommendations: eligible for ESD, suitable or not for your level of experience, tips for approaching, *etc*; (2) Consider general anesthesia for CR-ESD. You may spend many hours when approaching difficult locations, and regular soft breathing moves can help you getting the scope stabilized and avoid unexpected bowel movements than could facilitate unintentional perforation. Extended deep sedation with regular drugs (propofol, midazolam, pethidine…) might induce the patient to experience intense snoring, resulting in bowel “bouncing” that makes ESD hard enough; (3) Have some rest. When performing ESD, any minor mistake can waste all your work, so it is essential to be fresh and alert. This is not easy after some hours of tense concentration, most of all in the initial period of training, when CR-ESD takes so long. You should consider a break after 75-90 min of procedure, when the time of reaction and concentration level may start to decline; and (4) Do record all your procedures, so you can be able to review your mistakes. It is especially useful to watch those moments prior to unintentional perforation, so you can learn what not to do next time. Most of the time it is a question of excessive push of the knife or wrong direction approach.

**CONCLUSION**

ESD is an advanced technique for early neoplasia treatment in continuous expansion, with important advantages against EMR. However, the difficult learning curve is still the main restricting factor. Training in ESD is a long and hard journey, that will require comprehensive study of the ESD essentials, attending live cases, completing an animal training program using both *ex vivo* and *in vivo* models, and finally moving to human cases under close expert´s supervision. For Western endoscopists this journey will be particularly arduous, with CR-ESD as the foremost challenge. And yet, most of their potential candidates for ESD are and will probably be colorectal early neoplasias. Intensive preparation with all available means of training is key for actual and future trainees initiating ESD. As quoted by Prof. Toyonaga, “…ESD can be a superb treatment method that is extremely beneficial for patients when the quality is well secured…”[[58](#_ENREF_58)]. In other words, ESD in an excellent technique, and there is no substitute for excellence in ESD training.

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**Figure 1 Rectal neuroendocrine tumor.** A: Specimen fixed after successful endoscopic submucosal dissection; B: HE × 10. Neuroendocrine tumor, 6 mm largest diameter. Free lateral and depth margins (R0)

**Figure 2 Small perforation (blue arrow) in the anterior wall of the stomach after ESD of intramucosal adenoCa (T1a, R0).**

**Figure 3** **Professor Toyonaga supervising human endoscopic submucosal dissection case performed by young trainee.** Kobe University Hospital, Japan.

**Figure 4 Dr. Morita supervising live animal endoscopic submucosal dissection case performed by trainee (Dr. Herreros de Tejada).** 2nd KOBE International endoscopic submucosal dissection and EUS-FNA Hands-on-Seminar Kobe University Hospital, Japan.

**Figure 5 Dr. Morita supervising human rectal endoscopic submucosal dissection case performed by trainee (Dr. Herreros de Tejada**). International endoscopic submucosal dissection Live Madrid 2013 Clinical and Hands-on Course. Puerta de Hierro University Hospital, Madrid, Spain.

**Figure 6 Operating room with equipment ready for endoscopic submucosal dissection.** Animal Research Lab. Research Institute. Puerta de Hierro University Hospital, Madrid, Spain.

**Figure 7 Fresh harvest porcine stomach (A) and rectum (B) attached inside a plastic box for *ex vivo* model.** Animal Research Lab. Research Institute. Puerta de Hierro University Hospital, Madrid, Spain.

**Figure 8 Gastric endoscopic submucosal dissection performed in live pig under general anesthesia.** Animal Research Lab. Research Institute. Puerta de Hierro University Hospital, Madrid, Spain.

**Figure 9 Preparation for rectal endoscopic submucosal dissection with intensive rectal water infusion of the rectum.** Animal Research Lab. Research Institute. Puerta de Hierro University Hospital, Madrid, Spain.

**Figure 10 Colorectal-Endoscopic submucosal dissection specimen fixed: LST Granular mixed type, 60 mm longest diameter located in descending colon.** Puerta de Hierro University Hospital, Madrid, Spain.