

# Field of Submucosal Endoscopy

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Submucosal endoscopy (third-space endoscopy) can be defined as an endoscopic procedure performed in the submucosal space. This procedure is novel and has been utilized for delivery to the submucosal space in a variety of gastrointestinal diseases, such as a tumor, achalasia, gastroparesis, and subepithelial tumors. The main submucosal endoscopy includes peroral endoscopic myotomy, gastric peroral endoscopic myotomy, Zenker peroral endoscopic myotomy, submucosal tunneling for endoscopic resection, and endoscopic submucosal tunnel dissection. Submucosal endoscopy has been used as a viable alternative to surgical techniques because it is minimally invasive in the treatment and diagnosis of gastrointestinal diseases and disorders.

submucosal endoscopy

third space endoscopy

peroral endoscopic myotomy (POEM)

endoscopic submucosal dissection (ESD)

## 1. Introduction

Over the past decades, endoscopy has developed from being a diagnostic tool to a therapeutic tool. Gastrointestinal endoscopy has made great progress through the development of the endoscopic submucosal dissection (ESD) technique. Technical advances in endoscopy were inspired by the concept of natural orifice transluminal endoscopic surgery (NOTES) <sup>[1][2]</sup>. NOTES is a novel technique that involves the invasion of “the mucosa and submucosa to the muscle layer” with a flexible endoscope by making full use of the ESD technique. A major concern regarding NOTES was the safety of access to the peritoneal cavity and the secure closure of the entry point into these spaces. Sumiyama et al. developed submucosal endoscopy with a mucosal flap safety valve (SEMF), in which the peritoneal cavity could be accessed using a submucosal tunnel and the defect closed by using the mucosal flap <sup>[3]</sup>. This concern has been overcome with the introduction of the SEMF. Thus, the significance of the submucosal space as an operating field was realized. Submucosal endoscopy, also called third-space endoscopy, can be defined as an endoscopic procedure performed in the submucosal space or third space. This procedure is a novel operating field and has been applied in clinical procedures recently <sup>[4]</sup>. Submucosal endoscopy utilizing the SEMF technique has been utilized for delivery to the submucosal space and the peritoneal or mediastinal cavity in a variety of gastrointestinal diseases such as a tumor, achalasia, gastroparesis, and subepithelial tumors. This technique is divided roughly into ESD and peroral endoscopic myotomy (POEM). The current applications and evidence regarding submucosal endoscopy while exploring the possible future clinical applications in this field.

## 2. Expert Opinion

Submucosal endoscopy has emerged as a novel operating field for interventional endoscopy, and its use has significantly increased over the past decade. The main reason is that submucosal endoscopy adopts the concept of SEMF. SEMF has enabled endoscopists to safely utilize the submucosal space. SEMF has become a breakthrough in the diagnosis and treatment of diseases that, to date, have an unknown region. POEM is an established initial treatment modality for achalasia using the submucosal space. The emergence of the concept of POEM in the submucosal space has dramatically evolved not only the treatment but also the diagnosis of diseases. Subsequently, POET/STER has been developed for the excision of subepithelial tumors from the esophagus and stomach. The other indications for submucosal endoscopy include refractory gastroparesis and ZD. G-POEM/POP and D-POEM/Z-POEM have been developed for patients with refractory gastroparesis. Moreover, ESTD/PCM was derived from ESD for the management of early gastrointestinal cancer. Recently, the submucosal tunneling technique has been applied not only in treatment but also in diagnosis. Submucosal tunneling biopsy has recently emerged. All submucosal endoscopic procedures use a similar technique to the submucosal tunneling technique. The submucosal tunneling technique is yet to be established and validated, and therefore, submucosal endoscopic procedures are likely to become popular in the near future. Although submucosal endoscopy is largely safe, and previous studies seem to yield promising results regarding all submucosal endoscopic procedures, some issues need to be resolved to facilitate these procedures. Regarding efficacy, evidence is lacking and limited for the majority of these procedures. It is possible that problems, such as adverse events, will surface with more time and the accumulation of data, such as from GERD after POEM. In particular, randomized studies and long-term follow-up data are yet to be accumulated, except those regarding POEM. There is a pressing need for additional meaningful data that can appropriately position these procedures. Therefore, as these procedures become increasingly common, it is necessary to address the issues of training, and further guidelines will be necessary. These procedures are not easy to learn as there are differences between Asia and other regions, even in ESD skill levels. Submucosal endoscopy is a complex procedure based on surgical principles. Nevertheless, these procedures are performed by not only surgeons but also endoscopists. Therefore, it is necessary to construct optimum training systems such as animal models and observerships at expert centers. In particular, endoscopists have to perform the procedure in close contact with surgeons when treating patients. After all, submucosal endoscopy is a less invasive procedure than surgery but is still somewhat invasive to the patient. Hence, the indications for these procedures must be decided strictly, and it is necessary to create guidelines. In the future, the concept of “inside and outside of the gastrointestinal tract” will lose practicality in endoscopic treatment, and it will become possible to diagnose and treat gastrointestinal diseases and disorders with an optimum approach and with minimal invasion while freely moving in the lumen and peritoneal cavity. Thus, it may be useful for investigating diseases for which the cause is unknown. In addition, improved devices and techniques may reduce procedure-related complexities and allow the endoscopist to perform these procedures more easily. As the understanding of these procedures improves, the future of submucosal endoscopy could hold promise in diagnostic as well as therapeutic endoscopy.

## 3. Highlights

POEM has become the standard radical treatment for esophageal achalasia and related disorders as it is less invasive and has a higher curative effect than conventional therapeutic methods such as LHM. POET/STER is a novel treatment modality involving endoscopic enucleation of subepithelial tumors of the upper GI tract without full-thickness perforation. G-POEM/POP is technically feasible in patients with gastroparesis using myotomy. D-POEM/Z-POEM has been established recently as an effective method for complete septal dissection using a submucosal tunneling approach. Submucosal tunneling biopsy is a safe and effective method with a direct visual control of the region of interest. ESTD/PCM is a novel approach to safer and easier resection of cancer even with severe submucosal fibrosis. In the near future, submucosal endoscopy holds promise of breakthrough in the diagnosis and treatment of gastrointestinal diseases and disorders.

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