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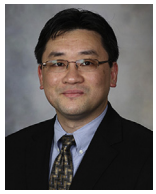
# Endoscopic Full Thickness Resection



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**Recent advances in minimally invasive endoscopic approaches have pushed the boundaries of well-established resection techniques for therapeutic and diagnostic applications. Endoscopic full thickness resection techniques are a key development in the management of challenging epithelial and subepithelial lesions that are not amenable to conventional endoscopic resection methods and previously required a surgical approach. Endoscopic full thickness biopsy represents a paradigm shift in tissue acquisition and will enhance our understanding of the pathophysiology, and guide therapy, of gastrointestinal neuromuscular diseases, as well as other inflammatory and neoplastic conditions. This review highlights current tools and techniques available for endoscopic full thickness resection and biopsy, as well as outcomes from such interventions.**

*Keywords:* Endoscopic Full Thickness Resection; Full Thickness Resection Device; Subepithelial Lesions; Submucosal Tunneling Endoscopic Resection.

Standard polypectomy, endoscopic mucosal resection, and endoscopic submucosal dissection are established techniques for the resection of superficial neoplasms involving the mucosa and submucosa of the gastrointestinal (GI) tract.[1] The efficacy and safety of these procedures are hindered in the setting of non-lifting epithelial lesions due to severe fibrosis and scarring, subepithelial lesions (SELs) arising from the muscularis propria (MP), and lesions in locations that are difficult to access or at high risk of adverse events (eg, within a diverticulum). The introduction of endoscopic full thickness resection (EFTR) techniques has provided a less invasive treatment alternative for many of these lesions that would have required a surgical approach otherwise. While laparoscopic assistance can be of value for selected lesions during EFTR, many of these lesions can be resected by endoscopic techniques alone. These techniques include clip-assisted EFTR, standard (direct) resection of the lesion followed by closure of the defect ("exposed" EFTR), and lesion resection via the submucosal tunneling approach ("non-exposed" or "neo" EFTR).[2]

Although EFTR implies resection through all layers of the GI wall, in practice the term is also used to include removal of intramural lesions without complete breach of the gut wall (eg, resection of a tumor originating from the MP with preservation of the uninvolved adventitia or serosa). These partial thickness resections have been labeled "endoscopic muscularis dissection," "endoscopic enucleation," "endoscopic submucosal excavation," and "endoscopic muscularis excavation," to name a few,[3] and are included under the umbrella term *EFTR* for the purpose of this review.

Conventional endoscopic pinch biopsies are non-diagnostic for neuromuscular disorders and other conditions that involve the deep layers of the GI tract. However, a safe and effective method that can capture the entire GI wall to include the MP has eluded us until the advent of endoscopic muscle biopsy techniques.[4,5] In order to standardize nomenclature, we propose using the terms *endoscopic full thickness biopsy* (EFTB) and *endoscopic full thickness resection* (EFTR) to clearly differentiate between diagnostic and therapeutic applications, respectively.

## Therapeutic Applications

### Rationale

EFTR is increasingly being performed for the removal of select subepithelial and epithelial lesions that are not amenable to conventional resection techniques. For particular lesions, such as GI stromal tumors (GISTs), EFTR offers important diagnostic advantages over endoscopic ultrasound (EUS)–guided fine-needle aspiration or biopsy with regard to procurement of adequate material for definitive

***Abbreviations used in this paper:*** **CI, confidence interval; EFTB, endoscopic full thickness biopsy; EFTR, endoscopic full thickness resection; EUS, endoscopic ultrasound; FTRD, full thickness resection device; GI, gastrointestinal; GIST, gastrointestinal stromal tumor; MP, muscularis propria; OTS, over-the-scope; SEL, subepithelial lesion; STER, submucosal tunneling endoscopic resection.**

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diagnosis and for determination of malignant potential (ie, mitotic index). Moreover, indefinite periodic examinations without definitive diagnosis are costly and emotionally burdensome for some patients, and the therapeutic value of EFTR in this setting cannot be overstated. According to the National Comprehensive Cancer Network guidelines, gastric GIST >2 cm should undergo resection, whereas treatment options for incidental GIST <2 cm without high-risk features on EUS include resection or surveillance.[6] The surveillance approach, however, raises concerns about patient compliance, cost-effectiveness, risk associated with repeated endoscopic procedures, and delay in therapy of potentially malignant lesions.

Although endoscopic resection of SELs involving the MP was previously considered a contraindication owing to a high perforation rate, the refinement in resection tools and closure devices, as well as increased experience with EFTR techniques, have minimized this adverse event. In particular, confidence in closure has allowed full thickness resection and biopsy techniques to progress forward in a safe and effective manner. Furthermore, an intentional perforation is expected for some EFTR procedures and should not be viewed as an adverse event, as long as it can be sealed effectively intraprocedurally. In the era of EFTR, reclassification of adverse events for invasive procedures should be pursued to differentiate inconsequential and inevitable events from true adverse events impacting outcomes.

Relative to thoracoscopic or laparoscopic interventions, EFTR is the least invasive modality along the spectrum of minimally invasive procedures, and is better suited for the removal of SELs at particular locations, such as the esophagogastric junction, where laparoscopic surgery is challenging. However, EFTR should be performed by appropriately trained advanced therapeutic endoscopists. Similar to other advanced resection procedures, such as peroral endoscopic myotomy for achalasia, no standardized protocol for training and assessment of competence is currently available. Future GI societal guidelines will be instrumental in directing training and evaluation of competence.

### *Pre–Endoscopic Full Thickness Resection Assessment*

The location, size, and features of the lesion determine, for the most part, resectability and the type of EFTR procedure most suitable to accomplish the task. EUS plays an important role in identifying benign incidental lesions that do not necessitate resection (eg, duplication cyst, lipoma) and in characterizing SELs, including size, layer of origin, growth pattern (intra- vs extraluminal), involvement of adjacent structures and regional lymphadenopathy.[7] Lesions with high-risk features on EUS that suggest malignancy (eg, irregular border, cystic spaces, heterogenous echotexture, and suspect lymph nodes) would preclude removal of these lesions via EFTR.[8]

For SELs arising from the MP, assessment of the degree of lesion attachment with this layer may predict completeness of tumor resection. In one study, successful R0 resection (negative deep and lateral margins) was predicted by the observation of only narrow or no lesion attachment with the underlying fourth hypoechoic layer (MP) at EUS (odds ratio, 35.0; 95% confidence interval [CI], 3.7–334.4; $P = .001$).[9] Other factors, such as tumor location, histopathology, and size, were not statistically associated with complete resection. It should be noted, however, that EUS was only 73% accurate in determining the tumor's layer of origin, and so the intended resection approach based on EUS findings may need to be altered at the time of the procedure.

In addition to EUS, computed tomography is recommended for evaluation of SELs because the combination of these techniques was superior to EUS alone at predicting the endoscopic maneuvers needed for lesion resection in a randomized trial.[10] In the presence of large SELs (>3 cm), computed tomography is indicated for assessment of metastasis or invasion beyond the gut wall.

## Endoscopic Full Thickness Resection Techniques

### *Clip-Assisted Endoscopic Full Thickness Resection*

In general, EFTR involves resection of a lesion followed by defect closure using mechanical clips or endoscopic suturing. Over-the-scope (OTS) clip-assisted EFTR is an emerging "close then cut" technique that can provide full thickness resection of epithelial and subepithelial lesions throughout the GI tract, a potentially safer alternative that involves securing the defect before resection.

**Indications.** Select non-lifting epithelial lesions (eg, adenoma) that are associated with severe fibrosis from prior attempts at resection and small SELs, including neuroendocrine tumors and GISTs, may be considered for clip-assisted EFTR. The size of the lesion that can be targeted with this technique is dependent in part on the diameter of the OTS cap utilized. In general, OTS clip-assisted EFTR is suitable for lesions that are <1 cm in the upper GI tract and <2 cm in the colorectum. Clip-assisted resection for lesions within the appendiceal orifice and in the presence of a native appendix should be avoided due to risk of provoking appendicitis. The role of OTS clip-assisted EFTR for early T1 cancers and lesions >2 cm in size deserves further study.

**Devices and techniques.** Both non-dedicated and dedicated OTS clip devices have been used for clip-assisted EFTR.

**Non-dedicated devices.** The 2 non-dedicated OTS clip devices include the Padlock clip (US Endoscopy, Mentor, OH) and the OTSC (Ovesco Endoscopy AG, Tübingen, Germany).

The Padlock clip is a star-shaped nitinol ring with 6 inner needles that is premounted on a cap. It has proprietary radial compression technology that facilitates circumferential tissue apposition (Figure 1*A*). The clip is available in 2 sizes: the Standard Padlock fits a 9.5- to 11-mm diameter endoscope while the Padlock Pro-Select fits an 11.5- to 14-mm endoscope. Both clips have a cap diameter of 11 mm that allows for atraumatic intubation, particularly via the oral route, and the cap depth or tissue