

ENDOSONOGRAPHY IN SUBEPITHELIAL LESIONS OF THE DIGESTIVE TRACT: DIAGNOSIS AND MANAGEMENT UPDATED 2025



Subepithelial lesions (SELs) are a relatively frequent finding on endoscopy, with an estimated prevalence of 0.3–1.4% in endoscopic studies.⁽¹⁾ Their accurate characterization has implications that help us determine prognosis, risk of malignancy, need for surveillance, and therapeutic options. Endoscopic ultrasound (EUS) has become established as the most precise method for defining the layer these lesions involve, their echogenicity, margins, relationship with neighboring structures, and the possibility of obtaining a histological sample.⁽²⁾ They even help us determine if the lesion identified as an SEL is actually an extrinsic compression.

Recent advances in high-frequency EUS, elastography, high-sensitivity Doppler, contrast-enhanced ultrasound (CE-EUS), and endoscopic resection techniques (ESD, STER, EFTR) have transformed the approach to these lesions.

In particular, the period 2023-2025 has generated relevant evidence, especially in GIST and other subepithelial lesions.

The layer of origin is very important, because the originating cells and the type of tumor depend heavily on it.

- **LAYER 1** surface epithelium or mucosa → mucous cysts or artifacts.
- **LAYER 2** muscularis of the mucosa → hemangiomas, superficial leiomyomas, GIST.
- **LAYER 3** submucosa → lipomas (hyperechoic), granular cell tumors, cysts.
- **LAYER 4** muscularis propria → GIST, leiomyomas, schwannomas; the most relevant layer.
- **LAYER 5** serosa or extrinsic structures → external compressions (spleen, pancreas, vessels, kidney, liver).

The EUS is the standard for identifying the layer with an accuracy >90%.⁽³⁾

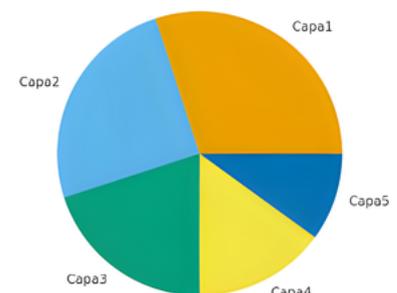


Figure 2: Frequency distribution of LSE according to organ layers (1-5).

GENERAL CLASSIFICATION OF SUBEPITHELIAL LESIONS

According to the ultrasound layer of origin (EUS)



Figure 1: Shows the different layers of the digestive tract wall. It should be noted that the intrathoracic esophagus and the rectum below the peritoneal reflection do not have a serosa.



Figure 3: Distribution of injury types according to the layer of involvement.

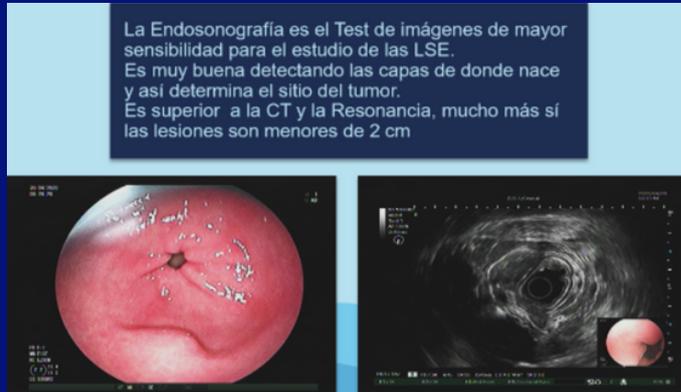


Figure 4: Shows on the right a radial EUS with a second layer lesion that is small and easily classifiable by this method.

CURRENT ROLE OF EUS IN THE DIAGNOSIS OF LSE

Diagnostic accuracy

In a 2024 meta-analysis by Ryou et al, published in Endoscopic Ultrasound, EUS was shown to have a sensitivity of 92% for determining the layers of origin, 85% for differentiating mesenchymal tumors, and 78% for predicting malignancy in GIST, when combining morphological criteria plus CE-EUS (contrast-enhanced EUS) (4).

EUS elastography allows for the differentiation of lesions based on stiffness. There are qualitative and quantitative elastography methods. Qualitative elastography uses color analysis, with blue indicating hard or rigid tissue, green indicating soft tissue, and a mixture of blue and green indicating heterogeneity. Quantitative elastography measures the stiffness index or strain ratio (SR). In GIST, this value ranges from 3 to 8. High-risk tumors are considered to have a SR above 7, and low-risk tumors below 3. Generally speaking, for the purpose of interpretation, a lesion larger than 2 cm with an SR greater than 3 should be biopsied with a fine-needle aspiration biopsy (FNAB).

RELEVANT MORPHOLOGICAL CRITERIA

Important factors for considering whether or not malignancy is present. These are more relevant to GISTs, and include:

Size >2 cm: is one of the strongest predictors. Previously we had a larger measurement, but in the last two years this is the size that suggests the possibility of malignancy (4-6).

Irregular borders: Suggests infiltrative and high-risk growth, especially in GIST(14).

Heterogeneity: This refers to hypo- and hyperechoic areas, necrosis, or degeneration. For Vadararajulu, this is a marker of aggressiveness (19).

Presence of internal cysts: These are anechoic areas within the lesion that are due to necrosis, cyst degeneration, or cavitation; they tend to be benign. They are more commonly seen in lesions larger than 20 mm (1-13).

Calcifications or ulceration of the overlying mucosa: these are indicative of malignant tumor activity. It is an important marker in gastric GISTs and calcifications are equally important (12-14-16).

ELASTOGRAPHY (EUS-EG)

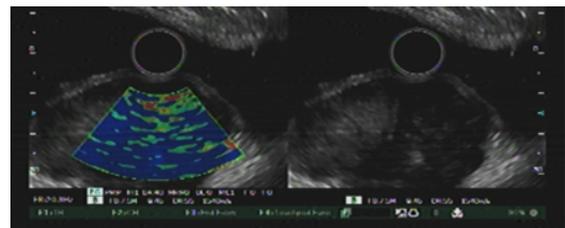


Figure 5: Elastography of a gastric GIST lesion. The colors are clearly visible, and qualitatively we can say that it is a lesion with a predominance of hardness and softer areas of heterogeneity.

SAMPLING TECHNIQUES IN SUBEPITHELIAL LESIONS (2025)

FNA vs FNB

The literature from 2023–2025 is conclusive: FNB outperforms FNA in sensitivity and accuracy for LSE.

- Sensitivity : 92% FNB vs 72% FNA.
- GIST diagnosis: 88% vs 62%.⁽⁸⁷⁾

ELASTOGRAPHY-GUIDED SAMPLING AND CE-EUS

Elastography should often be performed as it optimizes the puncture site and increases the yield of viable tissue. The 2023–2024 Lyon Series reported a 15% improvement in sample acquisition with this aid.⁽⁸⁾

Many countries do not have IV contrast and therefore its important use is reported for those that do.

The overall risk of complications during puncture is low (<1%), with minor bleeding and exceptional perforation being the most common occurrences.⁽⁹⁾

ECOENDOSCOPIC CONTRAST (CE-EUS)

It has become very important, and before describing it, we must discuss the washout effect. This means that when staining is applied to tissue, the arterial phase immediately absorbs the medium, but under the described effect, it disappears more quickly compared to the surrounding tissue, indicating an abnormality in vascularization. The main types of LSE (5-6-8) appear as follows:

- GIST: arterial hyperenhancement + early wash-out.
- Schwannoma: homogeneous enhancement without wash-out.
- Leiomyoma: moderate, stable enhancement.

A 2024 prospective multicenter study (Molina-Infante et al.) showed a 12–18% increase in diagnostic accuracy when CE-EUS is added to conventional EUS.⁽⁶⁾

SPECIFIC ULTRASOUND CHARACTERISTICS BY TUMOR TYPE

LIPOMA

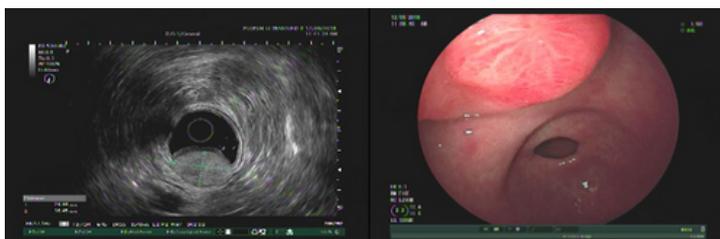


Figure 6: Lipoma in the stomach: Macroscopically, it appears yellowish and smooth. The cushion sign is positive. On EUS, a hyperechoic lesion of the third layer is clearly visible. No signs of malignancy are seen.

It is a Layer 3 lesion, hyperechogenic, with well-defined borders. It does not require biopsy or monitoring. Ultrasound plus clinical evaluation provides a definitive diagnosis in >95%.⁽¹⁰⁾

GRANULAR CELL TUMOR (GCT)

- Submucosal (3rd echolayer), isoechoic, homogeneous.
- <2% risk of malignancy.
- Annual surveillance if <1 cm; consider resection if >2 cm.⁽¹¹⁾

LEIOMIOMA

- The muscularis propria, or muscularis mucosae, is affected and appears homogeneous and hypoechoic. It is more common in the esophagus.
- Usually asymptomatic; resection if symptoms are present or the growth is large.⁽¹²⁾

SCHWANNOMA

It is from layer 4, homogeneous hypoechoic, with a characteristic peripheral hypoechoic halo.

- CE-EUS with persistent homogeneous enhancement.
- Low aggressiveness.⁽¹³⁾

GIST (GASTROINTESTINAL STROMAL TUMOR)

Key EUS findings



Figure 7: Layer IV lesion, showing areas of degeneration indicated by the arrow. GISTs are hypoechoic, sometimes heterogeneous, and may or may not have irregular borders, internal cysts, or intense vascularity. A size >2 cm increases the risk of malignancy. (14)

EUS-BASED MALIGNANCY PREDICTION SCORE IN GIST. (15)

The score published by Cho JW, et al. Gut. 2024, integrates five morphological variables observed by endosonography, which correlate with high mitotic risk and malignant behavior. Each criterion adds points, and the total score classifies the risk.

TUMOR SIZE

- 2–3 cm → 1 point
- 3–5 cm → 2 points
- >5 cm → 3 points

Size is the strongest single predictor of score.

IRREGULAR OR LOBED BORDERS → 1 POINT

The irregularity correlates with infiltrative pattern and loss of pseudotumoral capsule.

INTERNAL HETEROGENEITY → 1 POINT

Presence of hypo- and hyperechoic areas that indicate necrosis, hemorrhage, or degeneration.

INTRALESIONAL CYSTS → 1 POINT

Consistent marker of intermediate or high-risk tumors.

CALCIFICATIONS OR MUCOSAL ULCERATION → 1 POINT

Sign of chronicity and tumor aggressiveness.

TOTAL SCORE AND ITS MEANING

Total score	Risk of malignancy	Recommended conduct
0–1 points	Very low	Periodic EUS surveillance
2–3 points	Intermediate risk	Consider FNB or resection depending on location
≥ 4 points	High risk	Indicated resection (endoscopic or surgical)

DIAGNOSTIC PERFORMANCE OF THE SCORE

- Sensitivity: 84–89%
- Specificity: 72–78%

It significantly improves discriminative ability compared to using a single isolated criterion.

The score was validated in cohorts from Asia and Europe, and is proposed as a standardized tool for preoperative stratification (15)

INDICATIONS FOR RESECTION

- > 2 cm
- Significant growth
- High-risk suspicion
- Symptoms
- Patient preference

THERAPY

- ESD, STER and EFTR for 1–3 cm lesions in expert hands (risk of leakage 3–6%).
- Laparoscopic surgery for lesions >3–4 cm.⁽¹⁶⁾
- TKI (imatinib, avapritinib) if high risk and surgical resection is contraindicated or specific mutations.

SUBEPITHELIAL NEUROENDOCRINE TUMORS (NETS)

They appear as hypoechoic areas of the 2nd or 3rd echo layer, they are regular, the submucosa may appear thickened.



Figure 8: Gastric NET-type lesion, which is clearly seen on EUS.

- Prominent hypervascularity in CE-EUS. It is in this type of tumor where staining is most commonly used.
- EUS defines muscle size and engagement (key to T1 vs T2).⁽¹⁷⁾
- Endoscopic resection if <10 mm without muscle invasion; surgery if >20 mm.

LSE EXTRAMURALES

- Bazo
- Vasos esplénicos
- Lóbulo hepático izquierdo.
- Vesícula biliar
- Colon
- Páncreas



Además las lesiones patológicas como tumores, abscesos, pseudoquistes pancreáticos, quiste renal, leiomiomas uterinos, aneurismas y adenopatías pueden algunas veces ser identificadas como compresiones extrínsecas en el estómago.

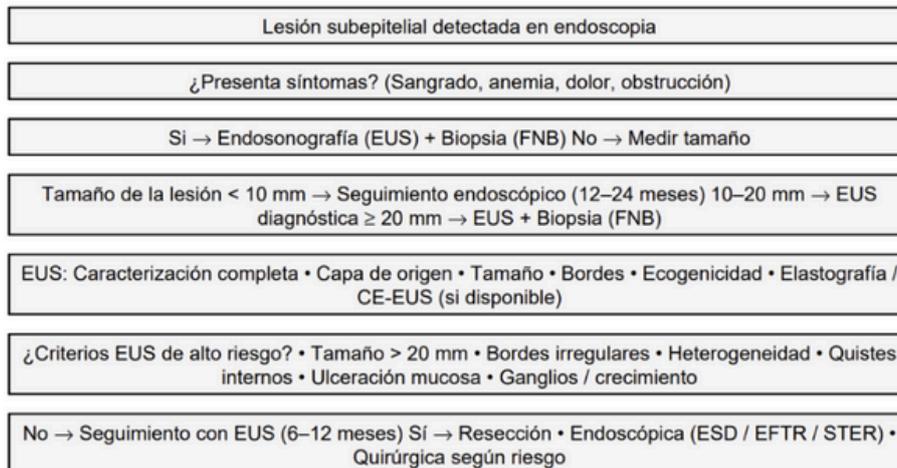
EXTRINSIC INJURIES THAT MIMIC SLI

RECOGNIZE COMPRESSIONS BY:

- Pancreas (antrum)
- Splenic artery
- Base
- Mediastinal cysts

EUS avoids unnecessary resections.⁽¹⁸⁾

Algoritmo 2025 – Manejo de Lesiones Subepiteliales (LSE)



1. Endoscopy identifies LSE >5 mm
2. EUS to define layer + pattern
3. According to the findings:
 - Lipoma / cyst → No biopsy / no follow-up
 - Layer 4 <2 cm no risk data → monitoring 6–12 months
 - Layer 4 >2 cm or risk criteria → FNB
 - Confirmed diagnosis
 - Small leiomyoma → monitoring
 - Schwannoma → selective resection
 - GIST <3 cm → ESD/STER/EFTR
 - GIST >3–4 cm → surgery
 - NET according to size/endoscopic ultrasound

KEY POINTS 2025

- EUS + CE-EUS + elastography is the most accurate tripod in Layer 4 lesions.
- FNB is the standard sampling technique.
- GISTs > 2 cm can be managed by advanced endoscopy in expert centers.
- EUS reduces unnecessary surgeries by up to 60%.⁽¹⁹⁾

LITERATURE

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VIDEOS OF THE MONTH



ELUXEO 8000
SYSTEM

ARTICLE OF THE MONTH

Endosonografía en lesiones subepiteliales: actualización 2025

This is one of the references consulted. The article is a compendium of guidelines and articles on the subject.

Polkowski M, et al, Endoscopic Ultrasound – guided diagnosis and management of subepithelial lesions : ESGE Guideline .Endoscopy 2022; 54:422-429.

Subepithelial lesions of the digestive tract require a systematic approach that combines endoscopy, endoscopic ultrasound (EUS), and, when appropriate, histological sampling. Recent innovations such as contrast-enhanced endoscopic ultrasound (CE-EUS), elastography (EUS-EG), and next-generation fine-needle aspiration (FNB) needles have significantly improved diagnostic accuracy, especially in tumors of the muscularis propria such as GISTs, leiomyomas, and schwannomas.

EUS allows for precise determination of the layer of origin (>90%), a crucial aspect for risk stratification. Morphological criteria such as size, borders, heterogeneity, internal cysts, and ulceration remain the cornerstones for predicting aggressiveness. CE-EUS adds value by differentiating specific enhancement patterns: arterial hyperenhancement with washout in GISTs, homogeneous enhancement in schwannomas, and stable moderate enhancement in leiomyomas.

Histological sampling using fine-needle aspiration biopsy (FNAB) offers superior diagnostic accuracy rates (>90%) compared to fine-needle aspiration biopsy (FNA), establishing itself as the ideal method for lesions >2 cm or those suspected of being high-risk. Management depends on individual characteristics: surveillance for small, benign lesions, endoscopic resection for GISTs >2 cm or confined neuroendocrine tumors, and surgery for larger or high-risk lesions.

Overall, by 2025, EUS is positioned as the most comprehensive and accurate tool for assessing spinal cord injuries, optimizing outcomes and reducing unnecessary interventions. Its role will continue to expand with new imaging techniques and minimally invasive approaches.