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Ospedale Santa Maria della Misericordia

LE BASI FUNZIONALI DELL'ECOGRAFIA E DELL'ECOENDOSCOPIA

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Elastografia in Ecoendoscopia

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Introduction

- Tissue **stiffness** is closely related to its **biological characteristics**

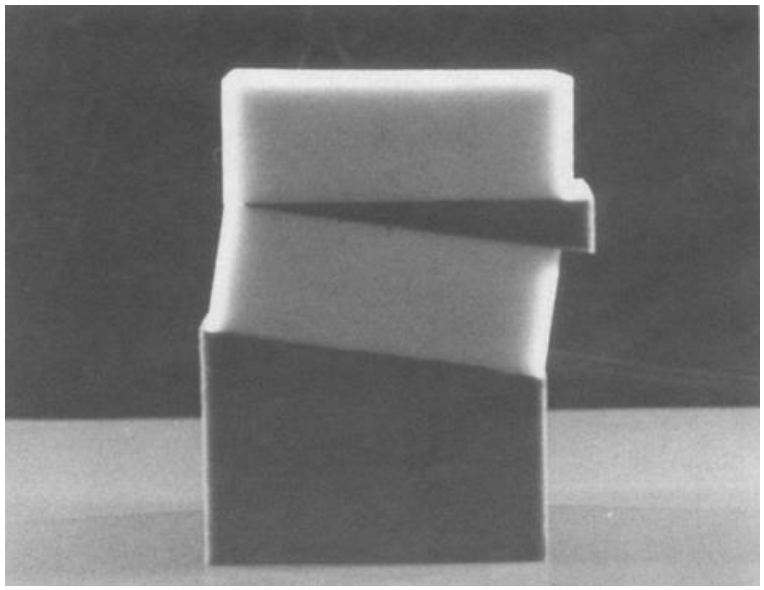


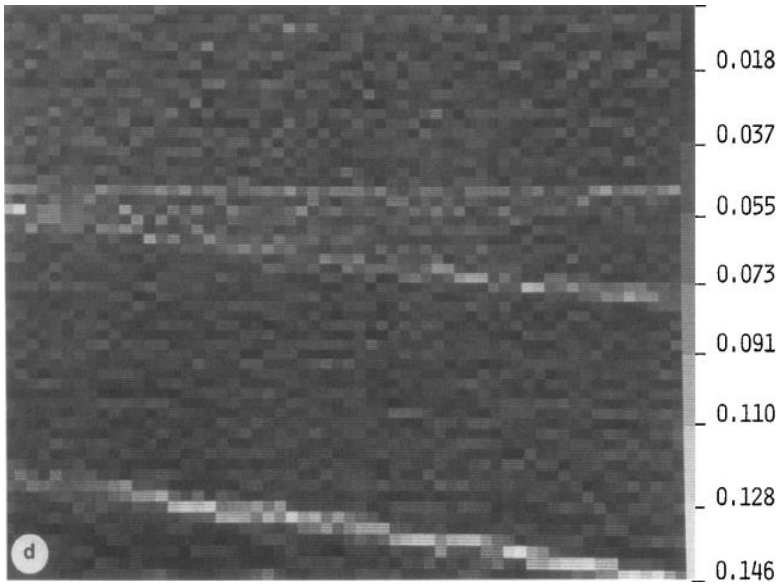
The evolution of imaging techniques has added elastography to physical palpation, a sort of "palpation by imaging," which allows real-time estimation of tissue stiffness.

Dietrich CF et al, Endoscopic US 2020

Introduction

- **In 1991, Ophir Equate first invented a model of ultrasound (US) elastography overcoming the weakness of subjectivity by manual palpation**



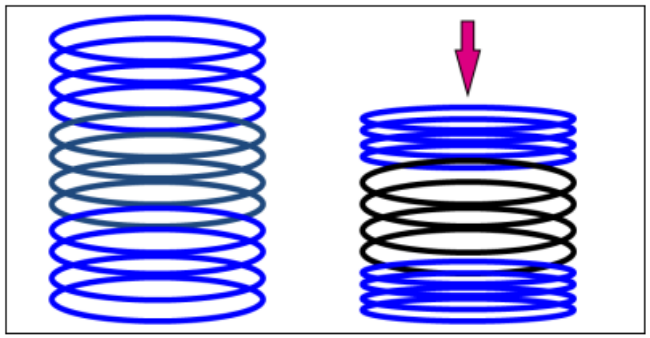


a. Measurement of global elastic modulus of foam blocks

Three types of reticulated open cell polyester foam samples were cut into 14 X 14 X 5 cm blocks. Type I was a black foam with a porosity of ~ 80 ppi (pores

Ophir J et al, Ultrason Imaging 1991

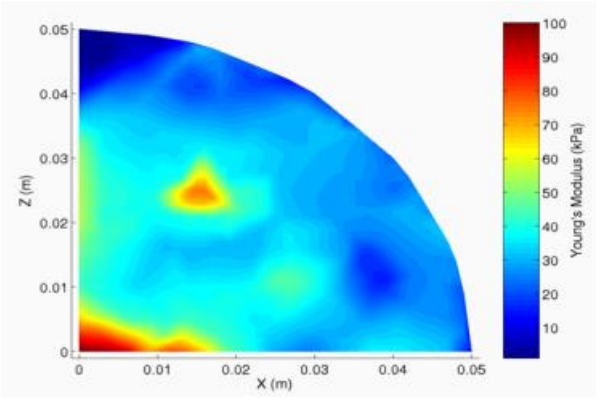
What is Elastography?



- Elastography is an imaging modality for the **real-time evaluation of tissue stiffness by its response to compression.**
- Two elastography techniques, **strain technique** and **shear wave technique**, have been developed and clinically used.
- Currently, **only the strain technique** has been available for EUS examinations

Iglesias-Garcia J et al, Gastroenterology 2010
ASGE Report on Emerging Technology, Gastrointest Endosc 2011
Cui XW et al, WJG 2015

What is Elastography?



- Strain elastography (SE) is a **qualitative** method based on tissues response to an externally or internally generated force
- It is based on the fact that **stiffer tissues have lower strains**, meaning that they deform less under compression as **compared to softer tissues** which deform more
- the compression-induced tissues deformations within a region of interest (ROI) are comparatively assessed
- Different colors are used to demonstrate differences between stiffness of the ROI included tissues

Cui XW et al, WJG 2015

What is Elastography?

- The characteristics of the tissues can be further analyzed by using a **semi-quantitative** method based on strain ratios between different tissues included within the selected ROI

- **2 semiquantitative methods:**

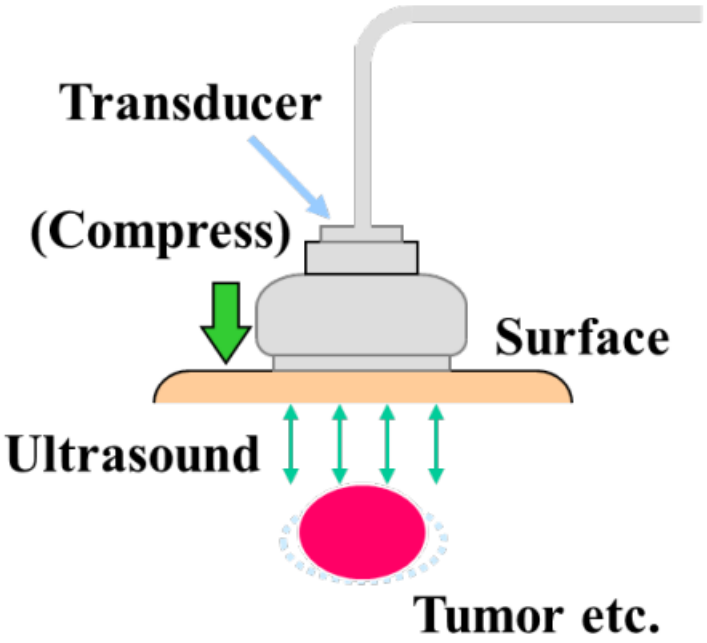
  Strain ratio (SR) and **strain histogram (SH)** were introduced in the second generation EUS elastography systems as reproducible, parametric measurements

  SR measures the relative strain between two selected areas inside a ROI

  SH computes the strain values of elemental areas inside a ROI and produces a graph

Cui XW et al, WJG 2015

What is Elastography?



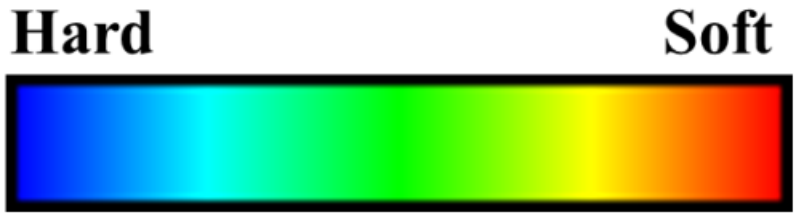
- **The strain (the deformation rate) can be obtained by comparing the echo signal before and after compression**

Bamber J et al, Ultraschall in Med, 2013
Cui XW et al, Endoscopic US 2022

What is Elastography?

- SE with conventional ultrasound systems has been used for the evaluation of lesions:
  - breast
  - cervix
  - prostate gland
  - thyroid gland
  - liver fibrosis

It has been shown that malignant tissues are generally harder than adjacent normal tissues, therefore, it could differentiate benign from malignant lesions based on the stiffness characteristics



Cui XW et al, WJG 2015

EUS background

- Endoscopic ultrasound-guided fine needle aspiration biopsy (**EUS-FNAB**) is performed **when patient management would be affected**
- **EUS has been demonstrated to have significantly changed the diagnosis and/or management of up to 25% to 50% of cases**



Iglesias-Garcia J et al, Endoscopic Ultrasound 2012

EUS background

- **The accuracy of EUS-guided FNAB has been demonstrated to be very high, with sensitivity between 80% and 85%, and specificity approaching 100%**



Iglesias-Garcia J et al, Endoscopic Ultrasound 2012

EUS background

Techniques to improve diagnostic yield (EUSFNA/EUSFNB):

- **Fanning technique**
- **Individualizing use of suction**
- **Wet suction technique**
- **Slow pull technique**
- **ROSE**
- **Minimum number of needle passes in absence of ROSE**



Ang TL et al, Gut Liver 2018

EUS background

Limits



- **Invasive technique**
- **Risk of bleeding**
- **Risk of seeding of malignant cells**
- **Multiple punctures may be necessary to obtain a sufficient amount of tissue**
- **Etc.**

EUS Weapons



- Morphological aspect
- FNA/B
- CH-EUS
- **Elastography**

EUS Elastography

Promising results have been reported for EUS elastography in several studies:

- ✓ **High accuracy in differentiating benign from malignant lesions**
- ✓ **Can show the hardest areas within the lesion, thus being useful for the selection of the most suspicious area to be targeted for EUS-FNAB**
- ✓ **Reduced number of passes**

Iglesias-Garcia J et al, Endoscopic Ultrasound 2012
Cui XW et al, WJG 2015

EUS Elastography

Indications:

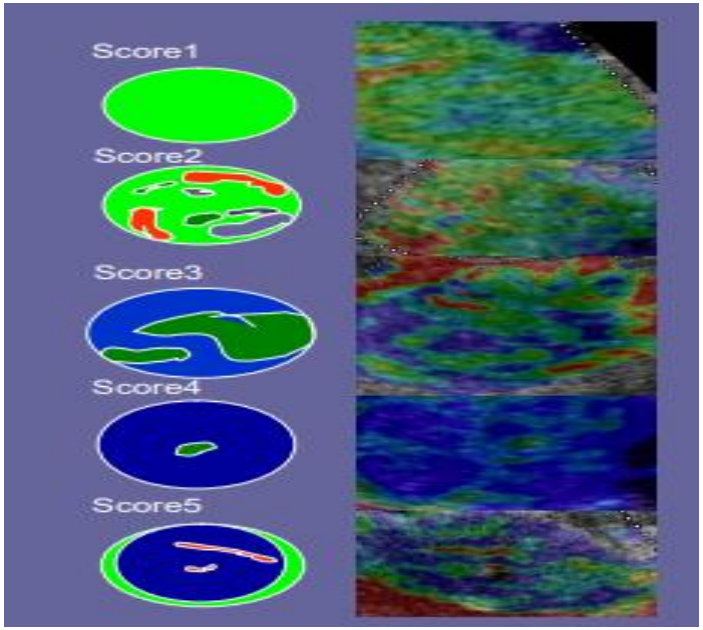
1. **Solid pancreatic lesions**
2. **Chronic pancreatitis**
3. **Lymph nodes**
4. **Subepithelial lesions**
5. **Others**

A lesion that has cystic components should not be evaluated by EUS elastography: cystic lesions are usually shown as an artifact: BGR (blue-green-red) artifact

Cui XW et al, WJG 2015

EUS Elastography, Solid pancreatic lesions

Qualitative elastography



Sensitivity and specificity of sonoelastography in the diagnosis of malignant lesions was 100 and 67%, respectively

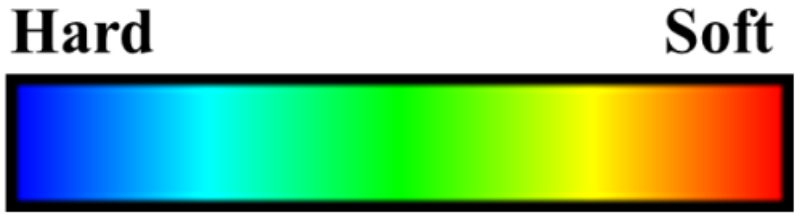


Table 1 Five score classification system for endoscopic ultrasound elastography

Score	Color pattern	Stiffness	Histology
1	Green	Homogeneous soft	Normal pancreatic tissue
2	Green, yellow and red	Soft heterogeneity	Fibrosis
3	Mostly blue with minimal heterogeneity	Hard	Early pancreatic adenocarcinoma
4	Central green hypoechoic region and blue tissue outer layer	Hard	Neuroendocrine tumor, metastasis
5	Blue lesions with heterogeneity due to necrosis	Hard	Advanced pancreatic adenocarcinoma

Giovannini et al, Endoscopy 2006
Cui XW et al, WJG 2015

EUS Elastography, Solid pancreatic lesions

Qualitative elastography

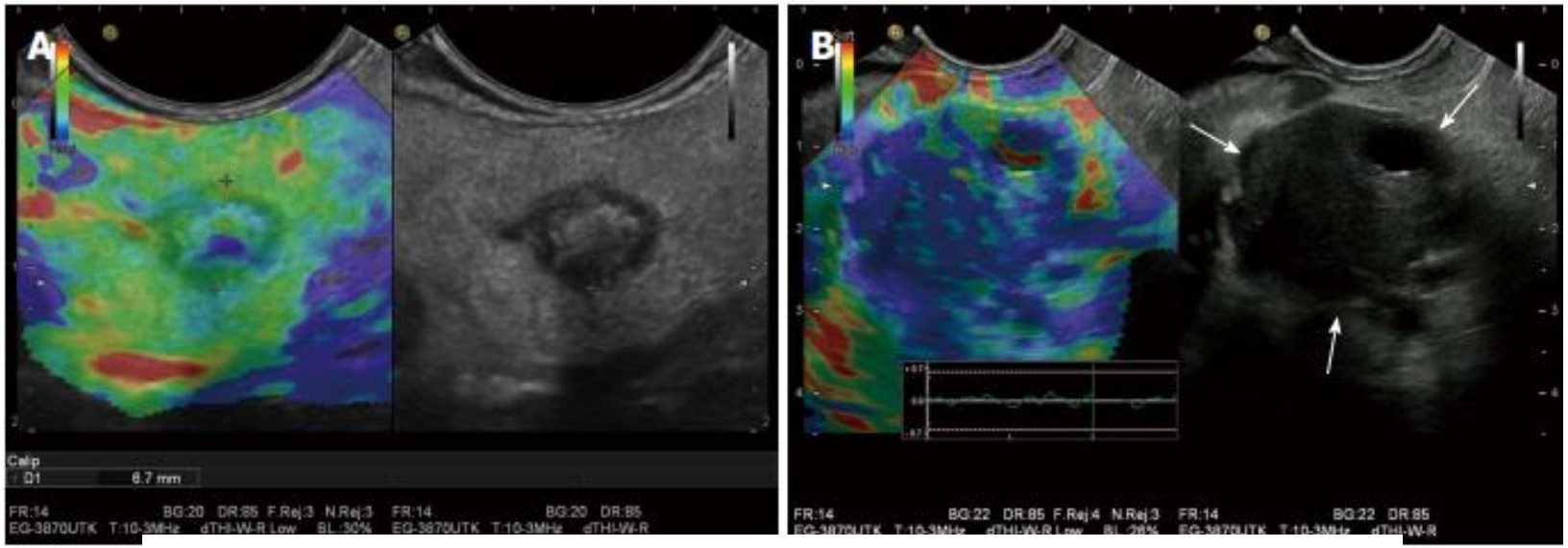


Figure 1 Benign and malignant pancreatic masses on endoscopic ultrasound elastography. A: A pancreatic teratoma is shown as heterogeneous soft (green) pattern (left: EUS elastography image; right: B-mode image); B: A pancreatic ductal adenocarcinoma appears stiffer (blue) than the adjacent normal pancreatic parenchyma, probably due to the presence of fibrosis and marked desmoplasia.

- **On EUS elastography, malignant lesions due to the presence of fibrosis and marked desmoplasia, appears stiffer than the adjacent normal pancreatic parenchyma**
- **Still, no evidence shows that there is a correlation between the tumor stiffness and either the tumor grading, or collagenous content**

Cui XW et al, WJG 2015

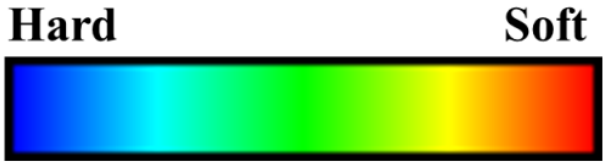
EUS Elastography, Solid pancreatic lesions

Qualitative elastography

Table 2 Four score classification system for endoscopic ultrasound elastography

Score	Color pattern	Stiffness	Histology	Ref.
1	Homogeneous green	Soft	Normal pancreas	[38]
2	Heterogeneous, green-Predominant	Soft	Inflammatory pancreatic masses	[38]
3	heterogeneous, blue-Predominant	Hard	Pancreatic malignant tumors	[38]
4	homogeneous blue	Hard	Pancreatic neuroendocrine malignant lesions	[38]

Diagnostic sensitivity, specificity and overall accuracy of EUS elastography for diagnosing malignancy being of 100%, 85.5% and 94%, respectively based on this score



Iglesias-Garcia J et al, Gastrointest Endosc 2009
Cui XW et al, WJG 2015

EUS Elastography, Technical aspects

Semiquantitative Strain Ratio

- For imaging, the EUS probe is pressed onto the gut wall, with the same pressure needed to generate optimal and stable B-mode image at 7.5 MHz (very little extra compression may be needed)
- The operator positions a round-shaped region of interest (ROI) sized on the target lesion (A) and a smaller ROI (B) above a homogeneous soft reference area either in the surrounding normal parenchyma or in the wall of the gastrointestinal tract
- Lesion covers 25-50% of ROI
- Image stable for at least 5 seconds is required and mean of 3 measurements
- The strain ratio is calculated by dividing the strain data from A by B (A/B), the value of which is displayed automatically by the software of the ultrasound processors

Iglesias-Garcia J et al, Endoscopic Ultrasound 2012
Cui XW et al, WJG 2015
Dietrich CF et al, Endoscopic US 2020

EUS Elastography, Technical aspects

Semiquantitative Strain Histogram (Hue)

- It is a graphical representation of the color distribution (hues) in a selected image field
- The x-axis in the histogram represents the elasticity from 0 to 255
- The y-axis represents the number of pixels in each elasticity level in the ROI
- The mean value of the histogram corresponds to the global hardness or elasticity of the lesion

Iglesias-Garcia J et al, Endoscopic Ultrasound 2012
Cui XW et al, WJG 2015

EUS Elastography, Solid pancreatic lesions

Quantitative Endoscopic Ultrasound Elastography: An Accurate Method for the Differentiation of Solid Pancreatic Masses

JULIO IGLESIAS–GARCIA,[*,§] JOSE LARINO–NOIA,[*,§] IHAB ABDULKADER,[‡] JERONIMO FORTEZA,[‡] and J. ENRIQUE DOMINGUEZ–MUNOZ[*,§]

Department of Gastroenterology, ‡Department of Pathology, §Foundation for Research in Digestive Diseases, University Hospital of Santiago de Compostela, Santiago de Compostela, Spain

Table 2. Accuracy of Qualitative and Quantitative Elastography for the Diagnosis of Malignancy in Solid Pancreatic Masses

	Qualitative elastography	Strain ratio (cut-off level, 6.04)	Elasticity of pancreatic mass (cut-off level, 0.05)
Sensitivity	58/58 (100%; 99.1%–100%)	58/58 (100%; 99.1%–100%)	58/58 (100%; 99.1%–100%)
Specificity	20/28 (71.43%; 52.9%–89.9%)	26/28 (92.9%; 81.5%–100%)	24/28 (85.7%; 71.0%–100%)
PPV	58/66 (87.9%; 79.2%–96.5%)	58/60 (96.7%; 91.3%–100%)	58/62 (93.5%; 86.6%–100%)
NPV	20/20 (100%; 97.5%–100%)	26/26 (100%; 98.1%–100%)	24/24 (100%; 97.9%–100%)
Overall accuracy	78/86 (90.7%; 84.0%–97.4%)	84/86 (97.7%; 93.9%–100%)	82/86 (95.35%; 90.3%–100%)

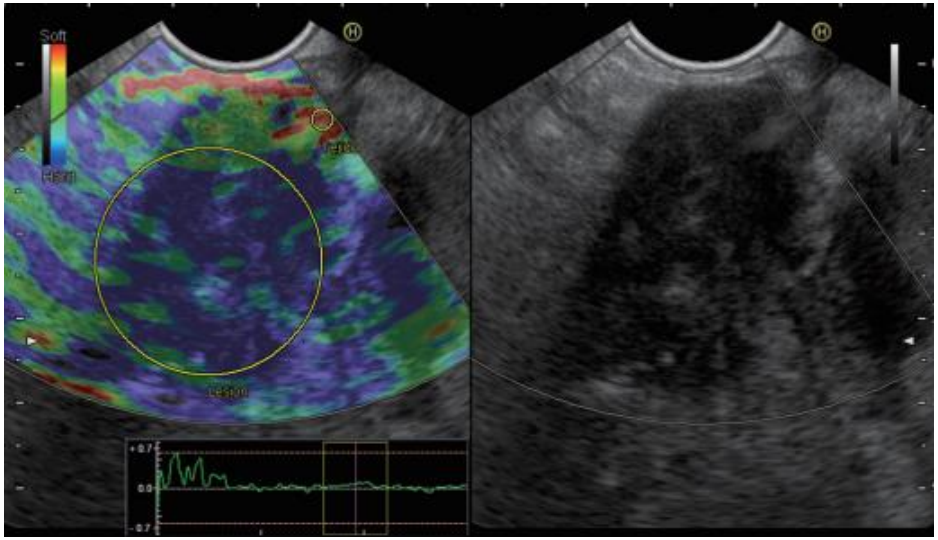
NOTE. Results of 58 malignant masses (adenocarcinoma, 49; metastasis, 2; lymphoma, 1; and malignant neuroendocrine tumor, 6) and 28 benign masses (27 inflammatory masses and 1 pancreatic solid pseudopapillary tumor) are included for analysis. Cut-off points were selected based on receiver operating curve analysis. Percentages and 95% CIs are shown.
NPV, negative predictive value; PPV, positive predictive value.

Gastroenterology 2010

EUS Elastography, Solid pancreatic lesions

(Semi) Quantitative elastography

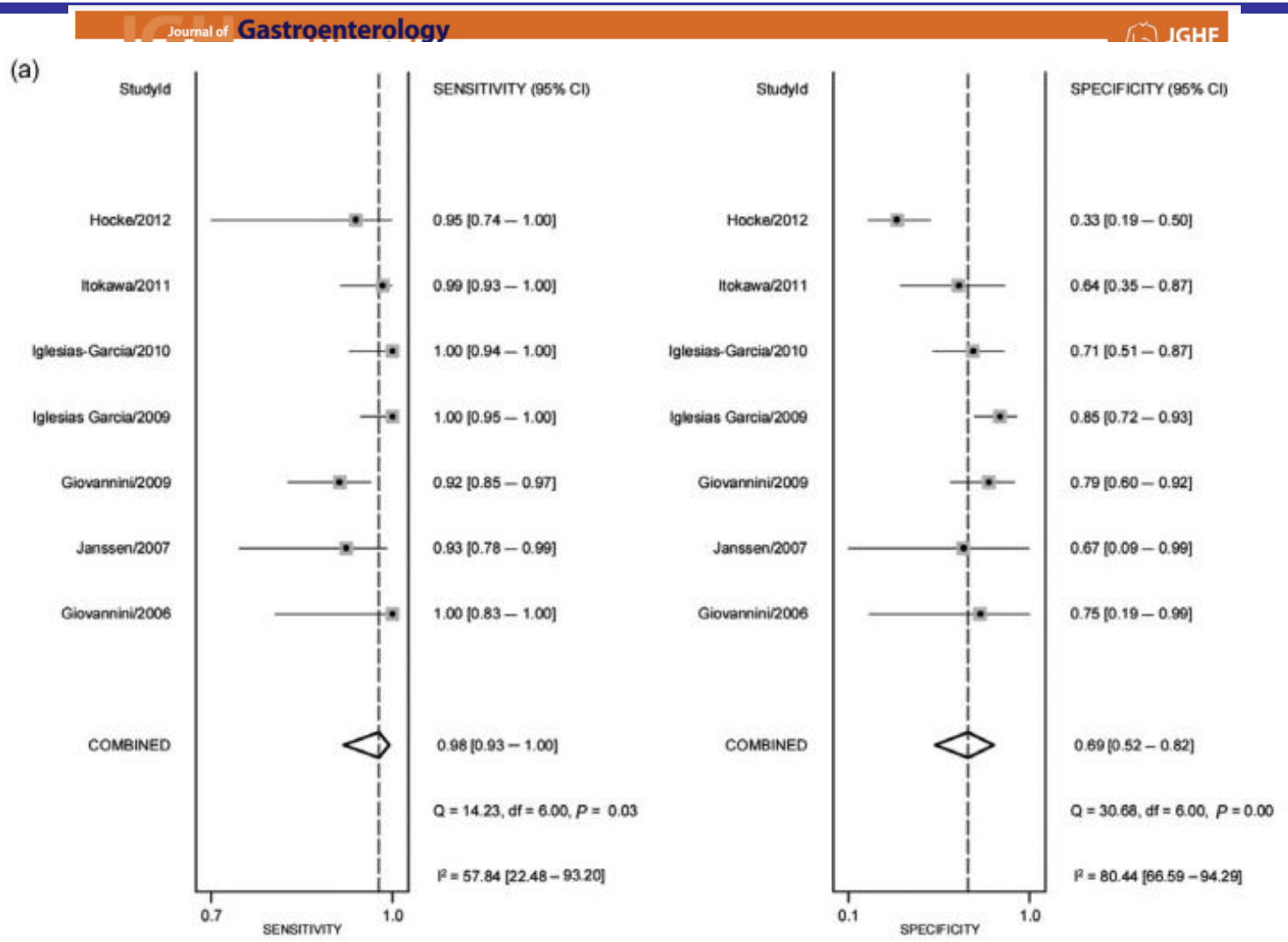
- **Quantitative EUS elastography with strain ratio has higher accuracy (97.7%) and specificity (92.9%) as compared to the qualitative analysis**



neously were considered as malignant. A strain ratio of 15.41 or higher, which was shown by 36 of the 58 malignant tumors, was 100% specific for malignancy.

Iglesias-Garcia J et al, Gastroenterology 2010

EUS Elastography, Solid pancreatic lesions



Qualitative elastography: Sens 0.98 Spec 0.69

Ying L et al, Journal of Gastroenterology and Hepatology 2013

EUS Elastography, Solid pancreatic lesions

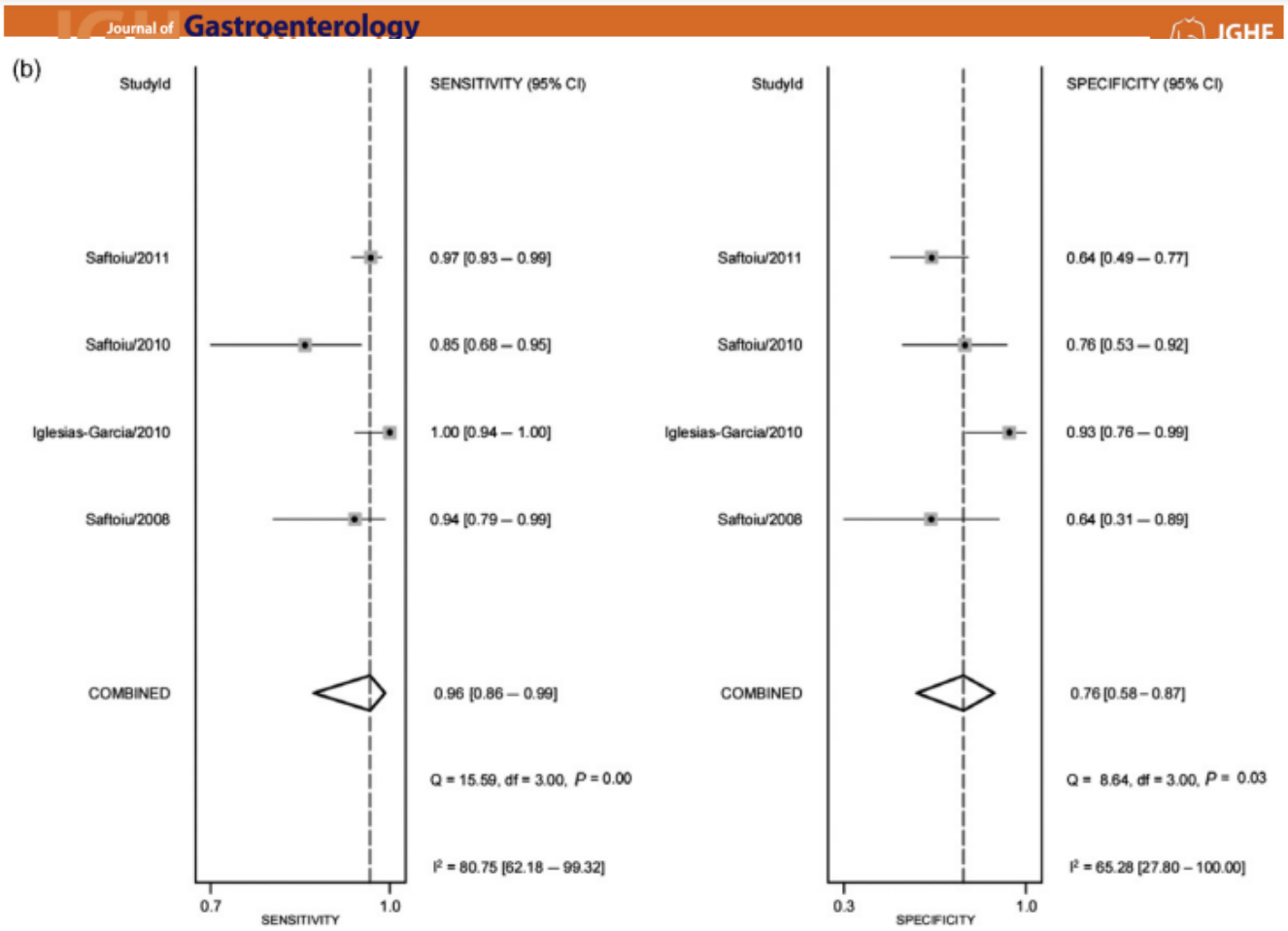
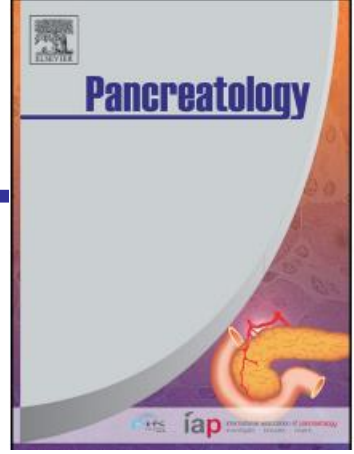


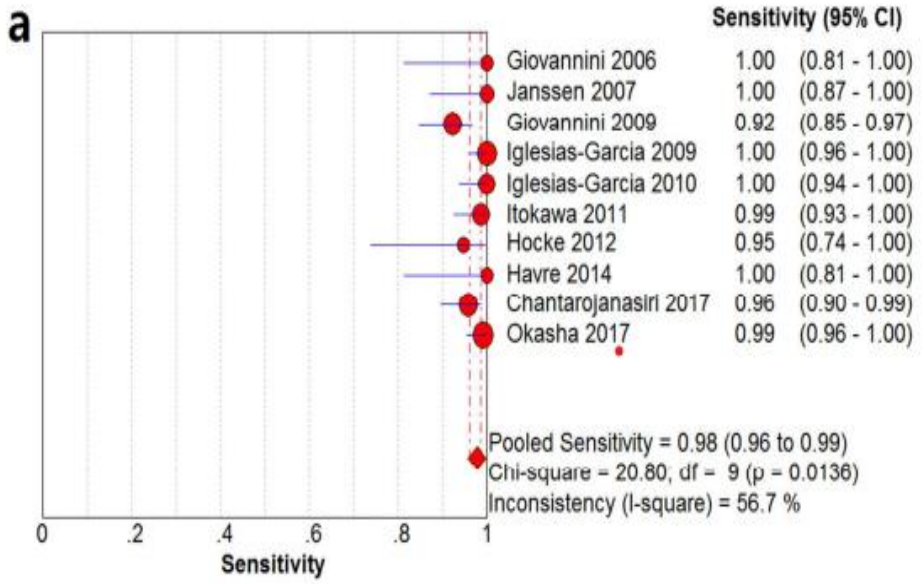
Figure 2 Forest sensitivity and specificity of endoscopic ultrasound (EUS) elastography for differentiation of pancreatic masses. (a) qualitative EUS elastography; (b) quantitative EUS elastography.

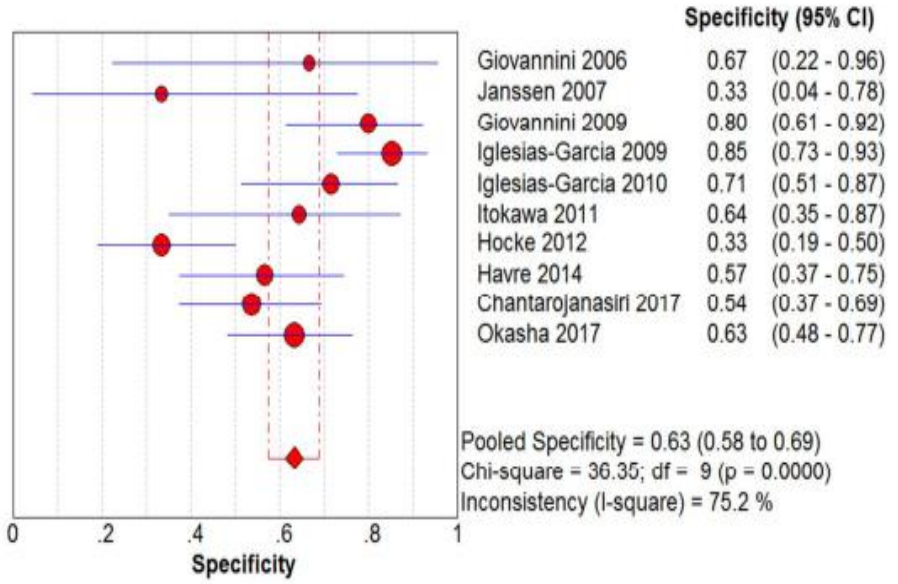
Quantitative elastography: Sens 0.96 Spec 0.76

Ying L et al, Journal of Gastroenterology and Hepatology 2013

EUS Elastography, Solid pancreatic lesions



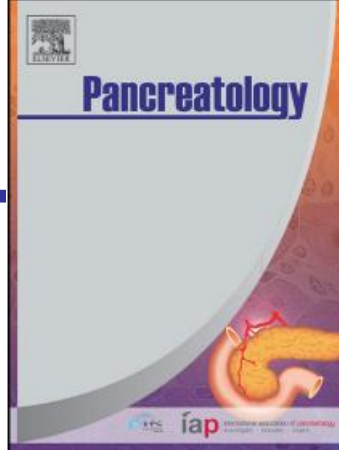


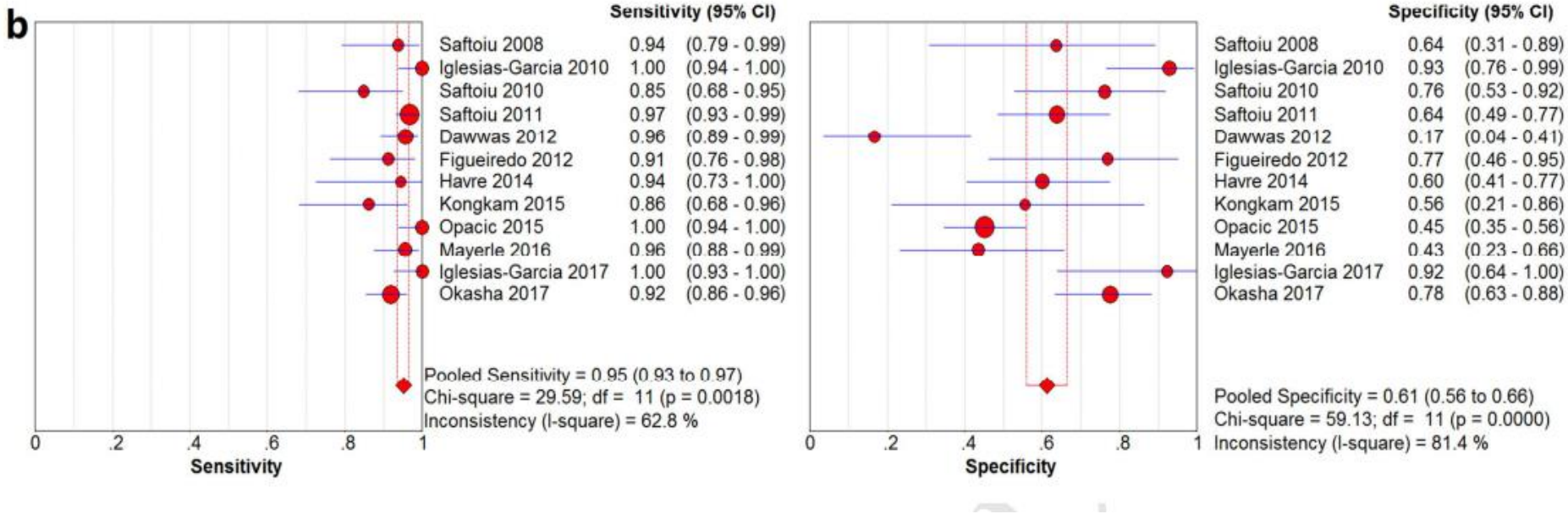


Qualtitative elastography: Sens 0.98 Spec 0.63

Zang et al, Pancreatology 2018

EUS Elastography, Solid pancreatic lesions





Quantitative elastography: Sens 0.95 Spec 0.61

Zang et al, Pancreatology 2018

EUS Elastography, Solid pancreatic lesions

Metanalyses

- Several meta-analyses have evaluated the diagnostic performance of EUS elastography for the characterization of malignant pancreatic tumors
- Overall, their authors showed a high sensitivity (92%–98%) but a low specificity (67%–76%)
- Disappointingly, there was no significant advantage of semi-quantitative strain elastography over qualitative strain elastography

Dietrich CF et al, Endoscopic US 2020

EUS Elastography, Solid pancreatic lesions

Original article

Thieme

Endoscopic ultrasound elastography of small solid pancreatic lesions: a multicenter study

Andre Ignee[1], Christian Jenssen[2], Paolo G. Arcidiacono[3], Michael Hocke[4], Kathleen Möller[5], Adrian Saftoiu[6], Uwe Will[7], Pietro Fusaroli[8], Julio Iglesias-Garcia[9], Ryan Ponnudurai[10], Maria C. Petrone[3], Barbara Braden[11], Eike Burmester[12], Yi Dong[13], Nathan S. Atkinson[11], Christoph F. Dietrich[1,14]

- 218 pts, only small lesions (≤15 mm)
- Lesion stiffness relative to the surrounding pancreatic parenchyma, as **qualitatively** assessed and documented at the time of EUS elastography, was retrospectively compared with the final diagnosis obtained by fine-needle aspiration/biopsy or surgical resection.
- In this study, we were able to show that almost all malignant pancreatic lesions of ≤ 15mm are stiffer than the surrounding pancreatic parenchyma. Only 2/51 patients with PDACs had lesions with soft tissue properties but were proven to be a PDACs over 12 months of follow-up.

Endoscopy 2018

EUS Elastography, Solid pancreatic lesions

Original article

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Endoscopic ultrasound elastography of small solid pancreatic lesions: a multicenter study

Andre Ignee[1], Christian Jenssen[2], Paolo G. Arcidiacono[3], Michael Hocke[4], Kathleen Möller[5], Adrian Saftoiu[6], Uwe Will[7], Pietro Fusaroli[8], Julio Iglesias-Garcia[9], Ryan Ponnudurai[10], Maria C. Petrone[3], Barbara Braden[11], Eike Burmester[12], Yi Dong[13], Nathan S. Atkinson[11], Christoph F. Dietrich[1,14]

- Because of the high **NPV** of elastography for the diagnosis of PDAC **(98 %)**, the finding of a **soft pancreatic lesion of ≤ 15mm** could potentially lead to **deferral of surgical resection**, particularly when contrast-enhanced (endoscopic) ultrasound demonstrates iso- or hyperenhancement relative to surrounding pancreatic parenchyma and no other malignant criteria are present

Endoscopy 2018

EUS Elastography, Chronic Pancreatitis

- **Fibrotic changes in chronic pancreatitis generally result in increased stiffness of the pancreatic parenchyma**
- **Limited NPV in differentiating pancreatic cancer from chronic pancreatitis**
- **In chronic pancreatitis, EUS-elastography semiquantitative measurements correspond to the histological fibrosis score and the probability of exocrine pancreatic insufficiency**
- **Apparent correlation between Rosemont Criteria and different SR values**
- **EUS elastography may help in differentiating Focal-type autoimmune pancreatitis and pancreatic adenocarcinoma by demonstrating a diffuse homogenous increase in the stiffness of the entire organ in autoimmune pancreatitis as opposed to ductal adenocarcinoma, where the increased stiffness is generally seen only within the tumor itself**

Iglesias-Garcia J et al, Gastroenterol Hepatol 2011
Mei M et al, Gastrointest Endosc 2013
Dietrich CF et al, Endoscopic US 2020

EUS Elastography, Lymph nodes

- Differential diagnosis of benign and malignant nodes with EUS remains a challenge

Established criteria on B-mode EUS for the diagnosis of malignant LNs:

- **Hypoechoic structure**
- **No echogenic centre**
- **Round shape**
- **Sharp margins**
- **Size > 1 cm**

Prevalence 25-40%
Accuracy (all criteria): 80%

these features overlap sometimes with benign nodes (the specificity and accuracy with these criteria being rather low)

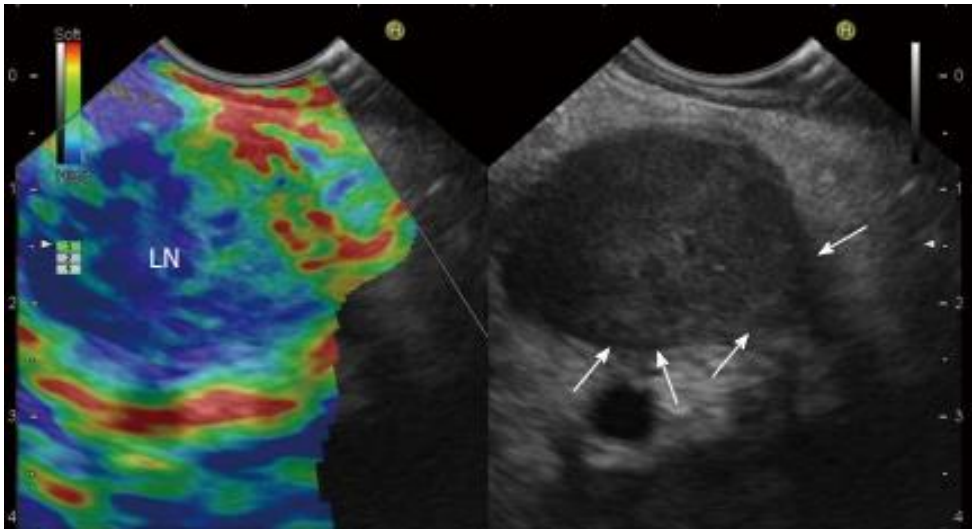
- Malignant nodes at early stages may have less or even none of these typical features

Cui XW et al, WJG 2015

EUS Elastography, Lymph nodes

- **EUS-elastography, as a minimally invasive imaging modality may be helpful for the differential diagnosis of benign and malignant LNs or to single out the more suspicious nodes to be targeted for endosonographic guided tissue sampling**

- **Several publications: similar with pancreatic masses, malignant LNs are considered to be harder than benign ones**



Cui XW et al, WJG 2015

EUS Elastography, Lymph nodes

Endoscopic ultrasound elastography for evaluation of lymph nodes and pancreatic masses: A multicenter study

Marc Giovannini, Thomas Botelberge, Erwan Bories, Christian Pesenti, Fabrice Caillol, Benjamin Esterni, Geneviève Monges, Paolo Arcidiacono, Pierre Deprez, Robert Yeung, Walter Schimdt, Hanz Schrader, Carl Szymanski, Christoph Dietrich, Pierre Eisendrath, Jean-Luc Van Laethem, Jacques Devière, Peter Vilmann, Adrian Saftoiu

	Sensitivity	Specificity	Overall Accuracy
Elastography	91.8%	82.5%	88.1%
B-mode	78.6%	50%	67.3%

World Journal of Gastroenterology 2009

EUS Elastography, Lymph nodes

ORIGINAL ARTICLE: Clinical Endoscopy

EUS elastography for the differentiation of benign and malignant lymph nodes: a meta-analysis (CME)

Wei Xu, MD,[*,1] Jian Shi, MD,[*,1] Xin Zeng, MD,[*,1] Xiang Li, MD,[1] Wei-Fen Xie, MD,[1] Jia Guo, MD,[2] Yong Lin, MD[1]
Shanghai, China

Qualitative elastography

TABLE 3. Subgroup analysis by excluding the outliers

Pooled results	Pooled value	95% CI	*P* value	I^2 value (%)
Sensitivity	85%	79%–90%	.43	0.0
Specificity	91%	85%–95%	.28	21.3
Positive LR	7.99	4.55–14.02	.28	21.3
Negative LR	0.18	0.13–0.25	.63	0.0
Diagnostic OR	53.68	25.89-111.30	.41	0.0

CI, Confidence interval; *LR*, likelihood ratio; *OR*, odds ratio.

GE 2011

EUS Elastography, Lymph nodes



- **Noninvasive elastographic evaluation of suspicious LNs may be particularly valuable if**

  1. **the nodes are not accessible by FNA needle**
  2. **in patients with contraindications to FNA**
  3. **for selecting the best FNA target when multiple nodes are present**

- **Reduce the number of unnecessary FNA**
- **Increase EUS-FNA diagnostic yield**

Dietrich CF et al, Endoscopic US 2020

EUS Elastography, subepithelial lesions (SEL)

- **Preliminary data suggest that EUS elastography could help in characterizing subepithelial lesions (SEL)**
- **In particular, it could be useful in differentiating GIST from other types of SEL. In a pilot study with strain ratio EUS-elastography, GISTs were harder than other types of gastric SEL such as lipoma and ectopic pancreas**
- **However, a subsequent larger study did not show a reliable differentiation between GISTs and leiomyomas using EUS-elastography.**
- **Another study using the strain ratio was able to differentiate between leiomyoma and GIST with a sensitivity and specificity of 100% and 94.1%, respectively**
- **Due to these conflicting data, further studies are needed to evaluate the capability of EUS elastography in differentiating leiomyoma from GIST**

Dietrich CF et al, Endoscopic US 2020

EUS Elastography, Emergent indications



- Fecal incontinence
- Liver
- Biliary tract
- Rectal cancer
- IBD
- Adrenal gland
- Pancreatic exocrine insufficiency
- Prostate cancer

EUS Elastography, Limitations



- **Observer-dependent with operator bias in the selection of ROI and areas for analysis, which could cause intra- and inter-observer variability**
- **Difficult to control the tissue compression by the endosonographer, and excessive pressure applied to the tissues can artificially increase their strain**
- **High-frequency transducer: (the depth of penetration is limited) only the organ or part of the organ near the GI tract can be imaged**

Cui XW et al, WJG 2015

EUS Elastography, Limitations

- **Presence of motion artifacts**
- **The strain value can be impacted by the vessels, cysts and bones in the selected ROI**
- **The strain value may be also impacted if there is insufficient surrounding "normal tissue" as reference in the ROI**
- **EUS elastography needs more training and costs more time in procedure than conventional US elastography**



Cui XW et al, WJG 2015



Grazie