Endoscopic Ultrasound Elastography – a New Imaging Technique for the Visualization of Tissue Elasticity Distribution

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Abstract

Endoscopic ultrasound (EUS) elastography is an imaging procedure used for the visualization of tissue elasticity during usual EUS examinations. EUS elastography can be accomplished real-time with state-of-the-art ultrasound systems, with the images being represented in transparent color superimposed on the conventional gray-scale B-mode scans. The aim of this review was to introduce the potential range of applications of EUS elastography.

EUS elastography might be useful for the differentiation of benign and malignant lymph nodes, with a qualitative pattern analysis and a quantitative histogram analysis of the color images being used to adequately classify the lesions. Mapping of the tissue elasticity distribution might be useful for the differential diagnosis of focal pancreatic masses, especially in the setting of chronic pancreatitis where the accuracy of EUS-guided fine needle aspiration is also low. EUS elastography might also enhance the detection and differentiation of various solid tumors (adrenal tumors, submucosal tumors, etc.) situated nearby the gastrointestinal tract.

Routine use of EUS elastography thus offers supplemental information that enhances conventional EUS imaging, with a possible decrease in the number of unnecessary EUS-FNA procedures used for tissue confirmation. However, future enhancements of the EUS elastography technology, as well as prospective, randomized studies will probably establish the clinical impact of dynamic elasticity imaging.

Key words

Elastography - endoscopic ultrasound - lymph nodes - pancreatic diseases

Rezumat

Elastografia ecoendoscopică reprezintă o tehnică imagistică folosită pentru vizualizarea elasticității tisulare în timpul examinărilor ecoendoscopice uzuale. Poate fi efectuată în timp real folosind sisteme ultrasonografice noi, care permit reprezentarea imaginilor elastografice în mod color transparent, suprapus pe imaginile convenționale în scară gri. Scopul acestui articol este de a prezenta aplicațiile posibile ale elastografiei ecoendoscopice.

Elastografia ecoendoscopică poate fi utilă pentru diferențierea ganglionilor benigni şi maligni, iar pentru clasificarea corectă a leziunilor pot fi folosite atât o analiză calitativă (a pattern-urilor), cât şi analiză cantitativă (bazată pe histograme) a imaginilor color. Determinarea distribuției elasticității tisulare ar putea fi folosită pentru diagnosticul diferențial al maselor focale pancreatice, în special în contextul pancreatitei cronice, în care acuratețea puncției fine aspirative ghidate ecoendoscopic este de asemenea redusă. Elastografia ecoendoscopică ar putea să amelioreze detecția şi diagnosticul diferitelor tumori solide situate în vecinătatea tubului digestiv (tumori suprarenaliene, tumori submucoase).

Utilizarea de rutină a elastografiei ecoendoscopice oferă informații suplimentare complementare examinărilor ecoendoscopice, cu o posibilă scădere a numărului de puncții fine aspirative necesare pentru confirmarea diagnosticului tisular. Cu toate acestea, impactul clar al evaluărilor dinamice ale elasticității va fi stabilit după ameliorarea tehnologiei elastografice ecoendoscopice şi după efectuarea unor studii prospective, randomizate.

Introduction

Endoscopic ultrasound (EUS) elastography is a recent imaging procedure used for the calculation and visualization of tissue elasticity during usual EUS examinations (1). The method allows the assessment of elasticity distribution and shows differences in hardness between diseased tissue and normal tissue (12). EUS elastography can be accomplished real-time with state-of-the-art ultrasound

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systems, with the images being represented in transparent color superimposed on the conventional gray-scale B-mode scans (1-3).

Elasticity measurements have been reported to be useful for the diagnosis and differentiation of many tumors, which are usually stiffer than normal soft tissues (4). Different methods to visualize the elasticity of the tissues have been developed during the past years (5, 6), but clinical applications were described only for the diagnosis and imaging of breast lesions (6-9) and prostate cancer (10-12). Recent applications of elastography emerged in the cases where conventional ultrasound imaging is not useful, such as the visualization of thermal lesions after radio frequency ablation (RFA) of liver lesions (14,15) or high intensity focused ultrasound (HIFU) of prostate lesions (16). Based on the intrinsic deformation of tissues during cardiac movement and respiration, intravascular (17-19) and cardiac (20) applications of ultrasound elastography have also been developed. Transient elastography was recently used for the evaluation of fibrosis in chronic liver diseases by measurement of the liver stiffness (21-25).

Ultrasound elastography was recently introduced in clinical practice for the differentiation of breast tumors, with real-time images of the elasticity of the targeted structure represented in transparent color superimposed on the conventional ultrasound image (26). In this setting, elastography complements conventional ultrasound, while future improvements in the technology might further enhance its value for clinical applications. By using the same ultrasound technology, EUS elastography allows the visualization of lymph nodes and pancreatic masses. Furthermore, different solid tumors situated near the gastrointestinal tract might be also visualized and potentially characterized by this technique.

The aim of our review was to introduce the potential range of applications of EUS elastography, in view of our recent experience with the method.

Technical details

The principle of elastography is that tissue compression produces strain (displacement) within the tissue and that the strain is smaller in harder tissue as compared to softer tissue (26). Consequently, by measuring the tissue strain induced by compression, it is possible to estimate the tissue hardness, which may be useful in diagnosing and differentiating malignant tumors. Ultrasound elastography thus estimates the axial strain of the tissues along the direction of insonification / compression. This is done by analyzing backscattered ultrasound signals returned if the tissue is slightly compressed and decompressed during the procedure, and can be recently obtained in real-time with standard ultrasound systems (1-3). The free movement of the endoscope tip, as well as sporadic motion of the tissues induced by respiratory or heart movements, determines probably lateral slippage of the target structure in respect to the gastrointestinal wall and the transducer. Moreover, compression of harder tissue structures is often followed by a lateral displacement of these structures. It is reported to be difficult to represent the volume of the sideslip with conventional 2D methods (1). To minimize artifacts, a new technique has been previously introduced and described in detail, which allows the 3D reconstruction of the tissue elasticity and enables the compensation of sideslips (Combined Autocorrelation Method) (1, 26). The method was previously tested in vitro on tissue phantoms showing that lesions can be detected and represented with higher accuracy as compared with conventional methods based on the 2D Model. Moreover, lesions invisible on conventional B-mode ultrasound images can be detected by the new technique (1).

EUS elastography equipment includes a Hitachi 8500 ultrasound system with an embedded Sono-Elastography module (Hitachi Medical Systems Europe Holding AG, Zug, Switzerland), coupled with the EG 3830 linear endoscope or the EG 3630 radial endoscope (Pentax, Hamburg, Germany). Real-time EUS elastography can be thus performed with the conventional EUS probes, without any need for additional equipment that induces vibration or pressure. Due to its similarity with color Doppler examinations, EUS elastography is performed by using a two panel image with the usual conventional gray-scale B-mode EUS image on the right side and with the elastography image on the left side (Figs.1-6). A region of interest (ROI) for the elastography calculations is manually selected and should include the targeted lesion, as well as the soft surrounding tissues. The ROI needs to be set to include sufficient surrounding tissue because elasticity values are displayed relative to the average strain inside the ROI. The system also displays a compression threshold which has to be set up between 3 and 4. To visualize tissue elasticity patterns, different elasticity values are marked with different colors (on a scale of 1 to 255) and the sono-elastography information is shown superimposed on the conventional gray-scale image. The system is set-up to use a hue color map (red-green-blue), where hard tissue areas are marked with dark blue, medium hard tissue areas with cyan, intermediate tissue areas with green, medium soft tissue areas with yellow and soft tissue areas with red.

Discussion

Malignant tumors are generally harder than the surrounding tissue. Consequently, palpation has always been used for the localization and characterization of different tumors. The utility of palpation techniques is based on the hypothesis that the range of hardness and elastic moduli varies between normal and pathological human tissues (3). Because the mechanical properties of normal and diseased tissues are of pathological relevance, the development of a direct measure of tissue elasticity would be of great help for the characterization of lesions, by supplementing the information already obtained by conventional ultrasound imaging methods based on acoustic tissue scattering (2).

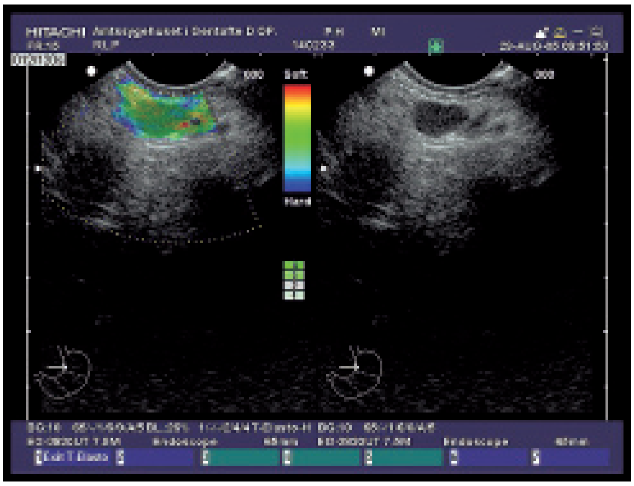

Fig. 1 EUS elastography image showing a 10 mm, benign lymph node in the mediastinum, visualized as a homogenous, intermediate hardness area (green) on the left panel.

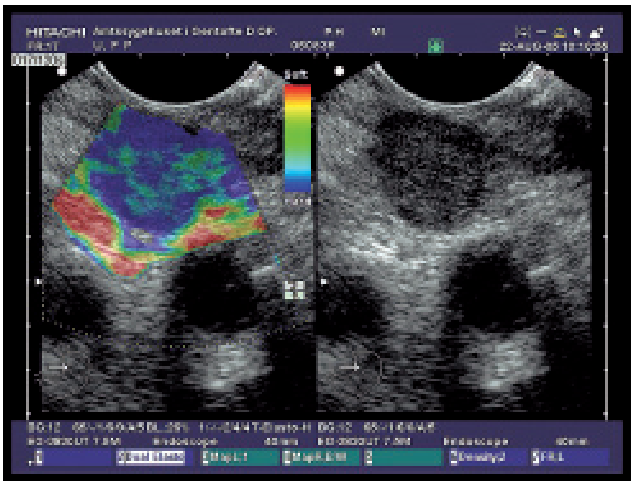

Fig. 2 EUS elastography image showing a 15 mm, malignant lymph node in the mediastinum, visualized as an inhomogeneous hard area (cyan-blue) on the left panel.

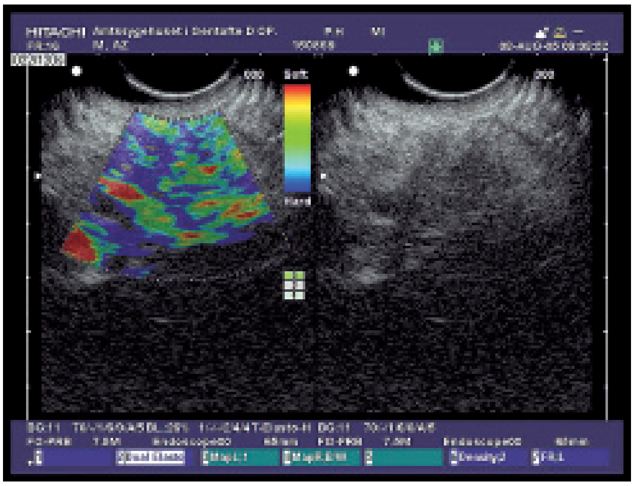

Fig. 3 Inmnlk homogeneous pancreatic head, with hyperechoic foci and bands depicted by conventional EUS, suggestive of chronic pancreatitis. Areas of different hardness are visible on the left EUS elastography panel as a mixture of colors (red, yellow, green, cyan, blue).

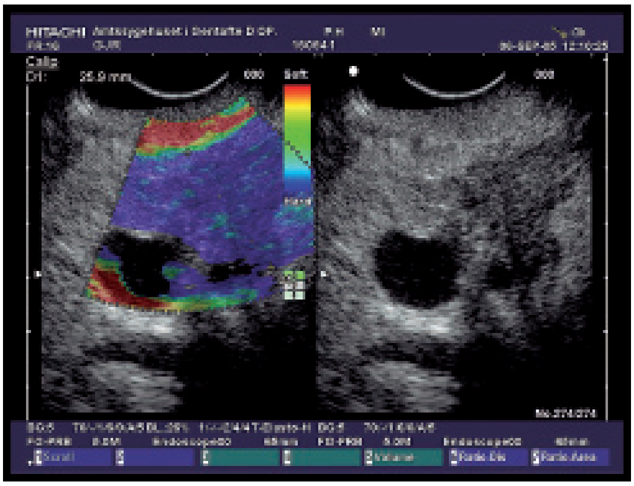

Fig. 4 Large pancreatic tumor of the pancreatic head depicted by conventional EUS as a hypoechoic mass, with irregular borders and invasion of the portal vein. EUS elastography image shows the tumor as a hard structure (blue) on the left panel.

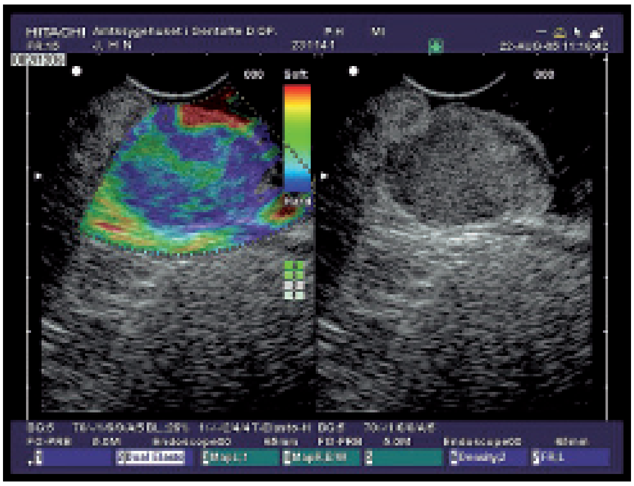

Fig. 5 EUS elastography appearance of a 3 cm, benign gastrointestinal tumor (GIST), with inhomogeneous hardness (blue-green).

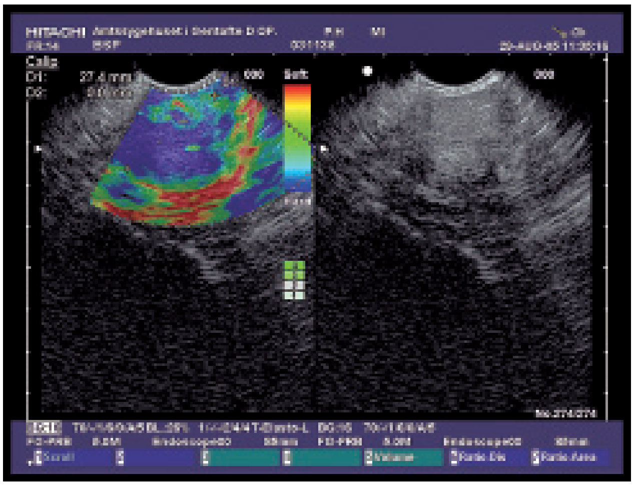

Fig. 6 Left adrenal metastasis confirmed on EUS-FNA, originating from a non-small cell lung carcinoma. Better visualization and definition of the tumor margins can be observed on the left EUS elastography panel that depicts a hard structure (blue) at the level of the left adrenal.

The development of 3D ultrasound elastography could add even more, conferring the capability to haptically explore regions of the body normally inaccessible to direct palpation (27, 28). The validation of ultrasound elastography might probably represent the initial step toward tactile imaging, with the visualization and reconstruction of tissue elasticity distribution on haptically explorable surfaces.

Elasticity imaging currently comprises a series of techniques that depict a mechanical response or property of tissues, offering complementary information to ultrasonic imaging (2). The most used approach is static compression elastography, where data is recorded before and after controlled compression of the tissues (up to 2% applied strain) (5). Quasi-static (dynamic) compression elastography is a variant where the probe is still moving, while cross correlation analysis is used to track tissue displacements and consequently to measure the strain field (3, 4). Transient elastography uses a shear elasticity probe, a device based on one-dimensional collection of data, being very useful for the collection of data in moving organs like the liver (21-25). One other option is the use of sono-elastography, which refers to motion detection when the tissue is excited by a vibrating actuator (29, 30). Various improvements and adjustments of these techniques are currently under development, with growing literature on theoretical, but also clinical applications of elastography.

Our previous experience with EUS elastography showed that it might be useful for the differentiation of benign and malignant lymph nodes (31). Both a qualitative subjective pattern analysis and a quantitative histogram analysis of the color images recorded during EUS elastography can be used to adequately classify the lesions (Figs.1, 2). The differential diagnosis between benign and malignant lymph nodes based on the EUS appearance is difficult and frequently requires EUS-guided fine needle aspiration biopsy (EUS-FNA) for confirmation of malignancy (32, 33). Thus, an improvement of the EUS elastography methodology through adequate quantification of tissue elasticity would be very useful for a minimally invasive staging of cancers. Although studies on the utility of EUS elastography are currently ongoing, mapping of the tissue elasticity distribution might be useful for the differential diagnosis of focal pancreatic masses (Figs.3,4), especially in the setting of chronic pancreatitis where the accuracy of EUS-FNA is also low (34, 35). Other applications of EUS elastography might consist in the detection and differentiation of left adrenal masses (Fig.5) or submucosal tumors (Fig.6), as well as any other solid masses situated nearby the gastrointestinal tract.

The ability to differentiate lymph nodes or pancreatic masses has to be looked upon as an adjunct to the imaging techniques and not as a replacement of tissue confirmation. Currently, there is no imaging method that can reliably differentiate malignancy in patients with lymph nodes or pancreatic masses. Nevertheless, categorizing the risk of malignancy is very important to decide subsequent invasive staging procedures. As established by EUS elastography imaging, the most probable masses to harbor malignancy could be targeted preferentially by EUS-FNA, while some masses that are considered most probably benign might be spared of EUS-FNA (31). Moreover, EUS elastography offers an alternative for the differential diagnosis in case of negative EUS-FNA, as well as in situations where EUS-FNA is not possible due to technical problems, interposed malignant tissue and vascular structures, or absence of a definitive clinical impact.

Pitfalls

The main pitfall of EUS elastography is represented by the impossibility to control tissue compression by the EUS transducer. This was also proven to be extremely difficult even by external ultrasound elastography, where images obtained with the application of strong pressure lead to misdiagnosis (26). Light pressure has to be applied, while this is not possible to be controlled through the endoscope. Development of a pressure gauge is certainly necessary, but the dynamic monitoring of the EUS elastography real-time sequences can be used to obtain still images that are appropriate for elasticity analysis.

The use of EUS elastography is also hampered by the induction of motion artifacts determined by respiratory or heart movements, which can not be adequately eliminated or quantified. The presence of nearby structures with very low or very high density and stiffness, such as the heart, major vessels or spine, is also difficult to be excluded from the ROI analyzed. Selection of the ROI has to carefully include only surrounding soft tissues, since the methodology of elastography assumes computations relative to the average strain inside the ROI. However, the presence of different nearby structures that might influence elastography calculations cannot be eliminated in all the cases.

Since the examiner has to choose the best images from a dynamic sequence, a high examiner bias is certainly favored. This will have to be excluded in further studies by blinding of the examiners from the clinical and pathological information. The qualitative pattern analysis of the EUS elastography still images might be also associated with significant intra- and inter-observer variability. A semiquantitative approach by means of histograms of color images might be more helpful, but it is still hampered by the selection of the images by the examiners (31). Nevertheless, computer analysis models based on dynamic histogram analysis might better characterize the mixture of tissue hardnesses depicted by EUS elastography images.

Conclusions

In conclusion, EUS-guided elastography is a promising technique that might improve the characterization and differentiation between benign and malignant masses visualized during EUS, with an excellent sensitivity, specificity and accuracy. Routine use of EUS elastography imaging thus offers supplemental information that enhances conventional EUS imaging, with a possible decrease in the number of unnecessary EUS-FNA procedures used for tissue confirmation. Further enhancements of the EUS elastography technology, as well as prospective studies with blinded examiners and adequate statistical power, will probably establish more clearly the clinical impact of dynamic elasticity imaging.

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