EUS elastography (strain ratio) and fractal-based quantitative analysis for the diagnosis of solid pancreatic lesions

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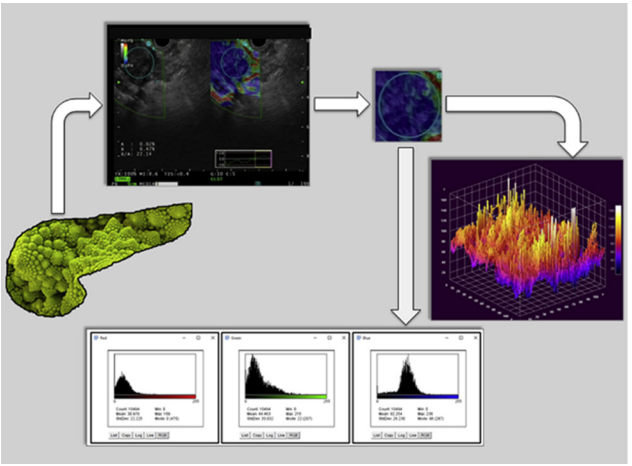
GRAPHICAL ABSTRACT



Background and Aims: EUS elastography is useful in characterizing solid pancreatic lesions (SPLs), and fractal analysis–based technology has been used to evaluate geometric complexity in oncology. The aim of this study was to evaluate EUS elastography (strain ratio) and fractal analysis for the characterization of SPLs.

Methods: Consecutive patients with SPLs were prospectively enrolled between December 2015 and February 2017. Elastographic evaluation included parenchymal strain ratio (pSR) and wall strain ratio (wSR) and was performed with a new compact US processor. Elastographic images were analyzed using a computer program to determine the 3-dimensional histogram fractal dimension. A composite cytology/histology/clinical reference standard was used to assess sensitivity, specificity, positive predictive value, negative predictive value, and area under the receiver operating curve.

Results: Overall, 102 SPLs from 100 patients were studied. At final diagnosis, 69 (68%) were malignant and 33 benign. At elastography, both pSR and wSR appeared to be significantly higher in malignant as compared with benign SPLs (pSR, 24.5 vs 6.4 [$P < .001$]; wSR, 56.6 vs 15.3 [$P < .001$]). When the best cut-off levels of pSR and wSR at 9.10 and 16.2, respectively, were used, sensitivity, specificity, positive predictive value, negative predictive value, and area under the receiver operating curve were 88.4%, 78.8%, 89.7%, 76.9%, and 86.7% and 91.3%, 69.7%, 86.5%, 80%, and 85.7%, respectively. Fractal analysis showed a significant statistical difference ($P = .0087$) between the mean surface fractal dimension of malignant lesions ($D = 2.66 \pm .01$) versus neuroendocrine tumor ($D = 2.73 \pm .03$) and a statistical difference for all 3 channels red, green, and blue ($P < .0001$).

Conclusions: EUS elastography with pSR and fractal-based analysis are useful in characterizing SPLs. (Clinical trial registration number: NCT02855151.) (Gastrointest Endosc 2018;87:1464-73.)

(footnotes appear on last page of article)

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EUS is one of the most accurate techniques for the diagnosis of solid pancreatic lesions (SPLs). Although EUS-guided sampling shows sensitivity rates for malignancy ranging from 84% to 95%,[1,2] the diagnosis of SPLs can still be a challenge in some cases, such as in a background of chronic pancreatitis or negative or inconclusive sampling. SPLs that are negative for malignancy after EUS-guided sampling cannot be definitively considered benign if there is a high degree of clinical suspicion of malignancy. In this case, close follow-up, a second EUS biopsy sample, or surgery is mandatory.[3]

Pancreatic cancer is one of the most heterogeneous neoplastic diseases because of different causes, such as a mixture of normal and malignant cell subpopulations within tissue, dense fibroblastic stroma, variations in blood flow, and genetic landscape determined by a variable number of mutations and therefore molecular subtypes of pancreatic cancer.[4] Because pancreatic cancer heterogeneity can be characterized by spatial and temporal variations identifiable using imaging techniques, a number of different qualitative, semiquantitative, and quantitative methodologies have been proposed.

EUS elastography (EUS-E) is a US technique that measures the hardness of tissues. The level of hardness of SPLs can be evaluated using qualitative scores and/or quantitative methods (strain ratio [SR]).[5] A meta-analysis analyzed 13 high-quality studies using EUS-E for the diagnosis of SPLs, identifying that the sensitivity and specificity rates of EUS-E were 95% and 67%, respectively.[6] Most studies on EUS-E have been carried out using the Hitachi US machine (Hitachi Medical Systems Europe, Zug, Switzerland), and a cut-off value of 6.04 has been used to describe malignant SPLs.[7] Recently, a new compact US processor (EU-ME2; Olympus Europa SE & Co KG, Hamburg, Germany) has been developed that incorporates a specific software that allows real-time elastography.

The concepts of "fractal" and "fractal geometry" were introduced in the second half of the 20th century as a mathematical tool for describing the roughness of natural objects.[8,9] Natural, including anatomic, fractals are characterized by 4 attributes: (1) the irregularity of their shape, (2) the statistical self-similarity of their structure (the schemas defining them are not equal but are continuously repeated at decreasing orders of magnitude), (3) their noninteger or fractal dimension, and (4) scaling, which means the properties measured depend on the scale at which they are measured. An object can be defined by a topologic or Euclidean dimension, which assigns an integer to every point or set of points in Euclidean space: 0 to a point (defined as that which has no part), 1 to a straight line (defined as a length without thickness), 2 to a plane surface (defined as having length and thickness but no depth), and 3 to 3-dimensional figures (a volume defined by length, thickness, and depth). Because no anatomic structure corresponds to a regular Euclidean figure, its dimension is always expressed by a noninteger number falling between 2 integer topological dimensions. It has been demonstrated that fractal geometry can be used to evaluate the geometric complexity of anatomic and imaging patterns observed in benign and malignant masses. In the field of medicine, fractal geometry has been applied to pathology, anatomy, and radiologic imaging.[10-15]

The primary aim of this study was to evaluate the role of EUS-E (SR) for the differential diagnosis of SPLs. The secondary aim was to preliminarily explore a computer-aided fractal-based analysis of EUS-E images in the differentiation of SPLs.

METHODS

Patients

Consecutive patients with SPLs detected by CT or magnetic resonance imaging and confirmed at EUS were enrolled in the study between December 2015 and February 2017. The inclusion criteria were patients with identified SPLs and patients > 18 years old. The exclusion criteria were patients who declined to participate in the study and patients with contraindications to the procedure. Informed consent was obtained from all patients before the procedure. This study was designed as a prospective, observational, single-center study.

EUS elastography

EUS was performed with the patient under deep sedation using linear array GF-UCT-180 series echoendoscopes (Olympus Europa SE & Co KG) in combination with the echoprocessor EU-ME2 (Olympus Europa SE & Co KG). Endosonographic and elastosonographic images of SPLs were obtained and recorded.

The quantitative score of elastography was expressed by the SR, which was calculated as follows: a larger round-shaped region of interest (ROI) was positioned in the lesion (A) and a smaller ROI (B) was positioned in a homogeneously soft area in the surrounding healthy parenchyma (parenchymal SR [pSR]) or in the closest healthy GI tract wall (wall SR [wSR]). Both areas were manually selected by a single expert operator. Elastosonographic SRs (B/A) were calculated and displayed automatically by software embedded in the EU-ME2 echoprocessor (Fig. 1).

EUS-E with SR was performed 6 times on each patient: 3 SR measurements comparing the lesion with the healthy