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REVIEW ARTICLE

# JSUM ultrasound elastography practice guidelines: pancreas

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**Abstract** Ultrasound elastography is a relatively new diagnostic technique for measuring the elasticity (hardness) of tissue. Eleven years have passed since the debut of elastography. Various elastography devices are currently being marketed by manufacturers under different names. Pancreatic elastography can be used not only with transabdominal ultrasonography but also with endoscopic ultrasonography, but some types of elastography are difficult to perform for the pancreas. These guidelines aim to classify the various types of elastography into two major categories depending on the differences in the physical quantity (strain, shear wave), and to present the evidence for pancreatic elastography and how to use pancreatic elastography in the present day. But the number of reports on ultrasound elastography for the pancreas is still small, and there are no reports on some elastography devices for the pancreas. Therefore, these guidelines do not recommend methods of imaging and analysis by elastography device.

**Keywords** Pancreas · Strain · Shear wave · Elasticity imaging · Elastography

## Introduction

Ultrasound elastography is a relatively new diagnostic technique for measuring the elasticity (hardness) of tissue by applying dynamic excitation such as manual compression or cardiovascular pulsation to the tissue and thereby measuring the strain or the shear wave generated in this manner [1]. First of all, we will mention its concept and history.

The hardness of a malignant tumor increases as the cell density increases [2–4] The elasticity of tissue had been

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used from ancient times to distinguish between malignancy and benignancy; however, the method for diagnosing hardness consisted of only subjective information on palpation. The development of ultrasound elastography was initiated for the purpose of using the elasticity of tissue as useful information for diagnosis.

In 1987, Ueno et al. [5] used a real-time ultrasound examination to diagnose the deformability of a mammary tumor and to assess the elasticity as a dynamic test, which was the first report of its kind. Later, in 1991, Ophir et al. developed a method for imaging the degree of strain distribution as information on the elasticity of the tissue, and they named the method elastography. In 1996, Shiina et al. published the combined autocorrelation method as a basic principle for the reconstruction of a strain image, with which it became possible to add compression with a free-hand ultrasound probe to display images in real time and, in addition, to overlay them on the B-mode image [6, 7]. On the basis of this principle, the first ultrasound elastography device, called Real-time Tissue Elastography$^{TM}$ (RTE), was put on the market by Hitachi Medical Corporation in 2003, after joint development with Shiina et al. [8, 9].

In the initial stage of its sale, ultrasound elastography was used for distinguishing between the malignancy and benignancy of mammary tumors [10, 11], but later its use was expanded to diagnoses of tumors in other organs [12, 13]. In addition, ultrasound elastography is also used as a noninvasive method of diagnosis for hepatic fibrosis. Elastography will be a substitute for liver biopsy in the future [14].

Elastography is also used to examine the pancreas. In 2005, Hirooka et al. [15] first reported elastography of the pancreas by endoscopic ultrasonography (EUS), and Uchida et al. [16] first reported elastography of the pancreas by transabdominal ultrasonography (US). Since then, various methods of elastography have been reported around the world, such as that for distinguishing between the malignancy and benignancy of pancreatic masses and that for the diagnosis of pancreatic fibrosis.

It is difficult to collect biopsy tissues for the diagnosis of pancreatic fibrosis, and it is also difficult to diagnose pancreatic fibrosis from the pancreatic tissues collected by endoscopic ultrasonography-guided fine needle aspiration (EUS-FNA) [17]. Therefore, elastography and various other methods have been tried for the diagnosis of pancreatic fibrosis. In particular, there are many reports on the usefulness of diagnoses of pancreatic fibrosis by B-mode images of EUS, [18] which are used to grade pancreatic fibrosis [19], and the Japan Pancreas Society (JPS) has proposed a standard for the diagnosis of early chronic pancreatitis [20].

The diagnosis of pancreatic fibrosis based on EUS will be discussed below in the Appendix.

Eleven years have passed since the introduction of RTE. At present, many manufacturers are selling elastography devices. Unlike RTE, there are some devices that use measurement of shear wave speed or the acoustic radiation force impulse (ARFI). Various elastography devices are sold by manufacturers under different names.

Pancreatic elastography can be used not only with US but also with EUS. Moreover, the pancreas itself is deep in the abdominal cavity surrounded by the large vessels and the intestines; therefore, it may be difficult to use some types of elastography.

In these guidelines, various types of elastography are classified and the currently available evidence for pancreatic elastography is presented.

## Classification of pancreatic elastography

A classification of pancreatic elastography devices is presented in the form of a table (Table 1).

This section discusses the classification of elastography [21].

Elastography is broadly divided into two types depending on the physical quantity that is measured. One is strain, which has a negative correlation with tissue elasticity, and the other is shear wave speed, which has a positive correlation with tissue elasticity. As they are based on different principles, the former cannot be used to calculate the elastic modulus (Young's modulus), which is an index to express objective hardness, while the latter can be used to do so.

Elastography to measure strain is classified into strain elastography and ARFI imaging depending on the mechanical energy that causes the strain. The former is a method in which strain is caused in tissue in a mechanical manner from the outside with manual compression or cardiovascular pulsation, while in the latter tissue is deformed using the acoustic radiation force impulse (ARFI). More accurately, ARFI imaging does not express the strain, but rather expresses the displacement.

Elastography to measure shear wave speed is classified into shear wave elastography, which uses ARFI as the method to excite shear waves, and transient elastography, in which shear waves are excited in a mechanical manner. However, Fibroscan$^{TM}$, the only transient elastography device available on the market, is not capable of acquiring B-mode images and, therefore, it is technically difficult to perform an accurate examination of the pancreas. In addition, there are no reports of its use for the pancreas. For these reasons, it is understood that the use of Fibroscan$^{TM}$

**Table 1** Elastography classification (except mechanical vibration type)

| Excitation methods | Measurement | |
|---|---|---|
| | Strain (displacement) | Shear wave speed |
| Cardiovascular pulsation (manual compression)[a] | **Strain elastography**<br>US Real-time Tissue Elastography™: RTE (Hitachi Aloka)<br>Elastography (GE, Toshiba, Philips)<br>eSieTouch™ Elasticity Imaging (Siemens)<br>EUS Real-time Tissue Elastography™: RTE (Hitachi Aloka)<br>ELST™ (Olympus) | |
| ARFI (acoustic radiation force impulse) | **ARFI imaging**<br>Virtual Touch ™ Imaging: VTI (Siemens) | **Shear wave elastography**<br>Virtual Touch™ Quantification: VTQ (Siemens)<br>ElastPQ ™ (Philips)<br>Virtual Touch ™ IQ:VTIQ (Siemens)<br>Shear Wave ™ Elastography: SWE (SSI) |

[a] Unlike superficial organs, manual compression of the pancreas is difficult as the excitation method of generating strain. Therefore, cardiovascular pulsation (manual compression) is used

for the pancreas is difficult at present, and so it is omitted from the classification table.

There are two types of methods for evaluating shear wave speed: a method in which the number obtained as the average speed within a small region (target ROI) is displayed, and a method in which an image is produced based on the distribution of the speeds in the ROI.

Two major types of probes are available for strain elastography: US and EUS. However, US is the only type on the market for other kinds of elastography.

Each classification and each device will be discussed in the sections below.

## Strain elastography

US (transabdominal ultrasonography)

(a) Method of examination (procedure, precautions, etc.)

Strain elastography is a method in which the tissue hardness is estimated based on the strain from the cardiovascular pulsation of the aorta [21]. The larger the strain, the softer the tissue is diagnosed; the smaller the strain, the harder the tissue is diagnosed. Strain is expressed with colors overlain on a B-mode image (color map), and reference B-mode images are also displayed.

If the B-mode images, which are the fundamental information on ultrasound waves, are not generated very clearly, it is not possible to obtain excellent elastograms [11]. Therefore, the first step is to generate B-mode images with as few artifacts as possible.

Observation should be made from the epigastric fossa in a dorsal position, (semi) sitting position, or left lateral decubitus position. To obtain the pancreas strain using the cardiovascular pulsation of the aorta, no vibration should be caused by the probe, and the probe should lightly touch the abdominal wall for observation.

Imaging of the pancreas may be easily affected by the influence of respiration; therefore, an instruction should be given to temporarily stop breathing.

Regarding setting the ROI, there are reports on two types of methods [14]: a method in which the ROI is set only within the target area, and a method involving both the target area and the surrounding tissue. The former is mainly used for the diagnoses of hepatic fibrosis and other diffuse diseases, while the latter is mainly used for the diagnoses of neoplastic diseases.

The colors in an elastogram minutely vary with the passage of time according to cardiovascular pulsation. It is desirable that elastograms with good reproducibility are taken at every pulsation by recording the images of elastograms in a range of 5–10 pulsations.

(b) Method of evaluation

*Quality evaluation (color pattern diagnosis)*

Color pattern diagnosis is a visual evaluation of the color tone of an elastogram. In general, evaluation of the color pattern is based on what major color tones are present and whether the color tone is homogenous or heterogeneous (Fig. 1a) [22–26] As color pattern diagnosis is judged individually, it may vary depending on the examiner.

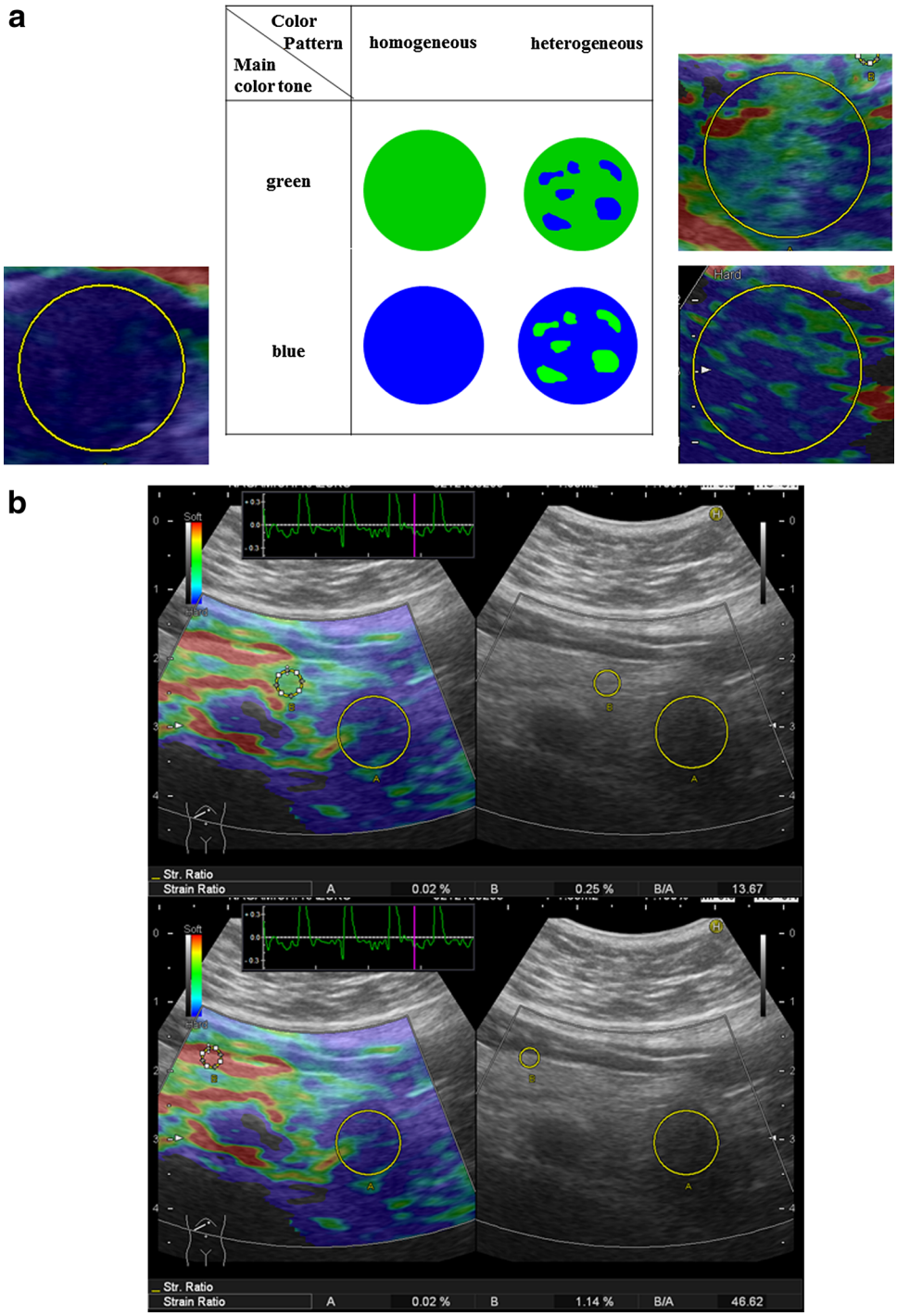



**Fig. 1** Qualitative evaluation schema (color pattern diagnosis). **a** The evaluation is made based on whether there is a major color tone and whether the color tone is homogeneous or heterogeneous. **b** The strain ratio in a case in which a different comparison area is defined for the same pancreatic tumor. In the *upper view*, the comparison area is defined in a part of the pancreas not included in the tumor. In the *lower view*, the comparison area is defined in the *red area* around the pancreas in the elastogram

*Quantitative evaluation (measurement of strain ratio)*

Whereas color pattern diagnosis is subjective, more objective quantitative evaluation (e.g., strain ratio) involves comparing the strain in a target with the strain in a comparator to quantify the elasticity of tissue [23, 24, 26, 27]. In the case of the mammary glands, the fat lesion ratio (FLR) method has been established, in which a fat area is used as a comparator [28]. In the case of the pancreas, however, there is no gold standard of a tissue that may be a target of comparison. There is a report on use of the red area around the pancreas as a comparator [26, 27], and there is another report on the non-tumor part of the pancreas as a comparator [23, 24] (Fig. 1b). In the former method, the red area around the pancreas is estimated to be a fat area because there is a fat area around the pancreas. However, there is no evidence for the fact that the red area truly reflects a fat area. In the latter method, there are

problems such as the case of a pancreatic head tumor where it may be difficult to identify a non-tumor part that is not influenced by obstructive pancreatitis. Recently, a technique has been developed for GE elastography in which the strain index (%) is calculated using a predefined scale, and the selection of a comparator is not required (described below).

In addition to the strain ratio, there are some reports on other quantitative evaluation methods (e.g., histograms) [29–31]. For details, see the section about EUS.

(c) Clinical benefits

Reports on pancreatic elastography have mainly focused on EUS. In recent years, there have been many reports on multicenter studies and meta-analyses, most of which are discussions of identification of the malignancy/benignancy of pancreatic tumors [29–35] On the other hand, there have been few reports on strain elastography with US [22, 23, 36]. When EUS is used, elastography is performed close to the pancreas, which can be advantageous because the pancreas is imaged more clearly, with little influence of intragastric gas in comparison to US. However, EUS places more of a burden on patients, because EUS is more invasive than US. Consequently, at present, there is no consensus regarding which of these devices should be used for different purposes, such as close examination of the pancreas and pancreatic tumor screening.

(d) Control of diagnostic accuracy and its limits

In strain elastography of the pancreas, the pulsation of the aorta is used to acquire elastograms. Accordingly, excellent elastograms may be easily acquired in cases where the pancreatic body is located between the aorta and the probe. The depth should be approximately 6 cm or less from the body surface to acquire an excellent elastogram, as in the case of acquiring clear B-mode images.

*Real-time Tissue Elastography™: RTE (Hitachi Aloka)*

This is a technique in which the imaging of the tissue strain is processed using the combined autocorrelation method [37]. Elastography with EUS is only possible with RTE. As this is the first strain elastography and this is the only elastography device with which evaluations by EUS are possible, RTE with EUS is the most advanced in the field of pancreatic elastography [22–27, 29–36]

The RTE application program can be installed on the ARIETTA 70/60, HI VISION Ascendus, HI VISION Preirus, HI VISION Avius, Noblus, HI VISION 900, EUB-8500, EUB-7500, EUB-7000HV (Apron EUB-7000HV), ProSound F75, and ProSound α7. A linear probe (EUP-L52, 7–3 MHz) or micro-convex probe (EUP-C532) can be implemented.

RTE displays the hardness of the tissue in the ROI as relative color tones. More specifically, in the ROI, relatively hard tissue is shown in blue, tissue of an average hardness is shown in green, and relatively soft tissue is shown in red. In total, 256 color tones are used for coloration (Fig. 2a). In a large number of reports on quality evaluation (color pattern diagnosis), malignancy is determined if the major color tone is blue, and benignancy is determined if the major color tone is green [22–26] In addition, there are a large number of reports in which the color tones are not even in cases of pancreatitis and the color tones are even in cases of pancreatic endocrine tumors. Elastograms are not acquired in regions where reliable elastograms are not imaged, such as areas without excellent strain and areas where the influence of an artifact is strong.

In one of the quantitative evaluation methods, the ratio of the strain values (strain ratio) between a target region and a comparison region is calculated as an index of the objective hardness of the target region. A target ROI (A) is defined in the target region in an ROI and a target ROI (B) is defined for a comparison region to automatically calculate the strain ratio in the lower part of the screen (Fig. 2b).

A strain graph is displayed on the screen in synchronization with the vibration transmitted to the probe, which is informative to know if excellent strain is generated. If patterned waves are observed in synchronization with the pulsation of the aorta, it is assumed that excellent strain is generated. For analysis, an elastogram at the time of maximum deformation of the pancreas should be selected.

The number of reports on strain elastography with US is extremely small in comparison with EUS. According to their reports, Uchida et al. used strain elastography with US to evaluate the color patterns of the normal pancreas, pancreatic cancers, pancreatic endocrine tumors, and chronic pancreatitis. They recognized characteristic observations in each of these, added the observations of the color patterns from the elastography to the B-mode observations, and improved the diagnosis sensitivity [22]. There is a report on an attempt to distinguish between malignancy and benignancy of pancreatic solid tumors from the strain ratio using US [23]. However, the cutoff values of the strain ratio used to distinguish between malignancy and benignancy differ from report to report [25, 27], and at present there is no consensus. There is a report on a comparison between changes in the strain ratio before and after preoperative chemoradiation of pancreatic cancer and histological judgment of the curative effects [36]. Strain elastography with US may be helpful for the estimation of curative effects. However, each of these reports examines a small number of cases, and thus further research is needed.

*Elastography (GE)*

This technique employs the revised direct strain method, in which the size of a strain is calculated directly from the compressibility of the waveform in each region by

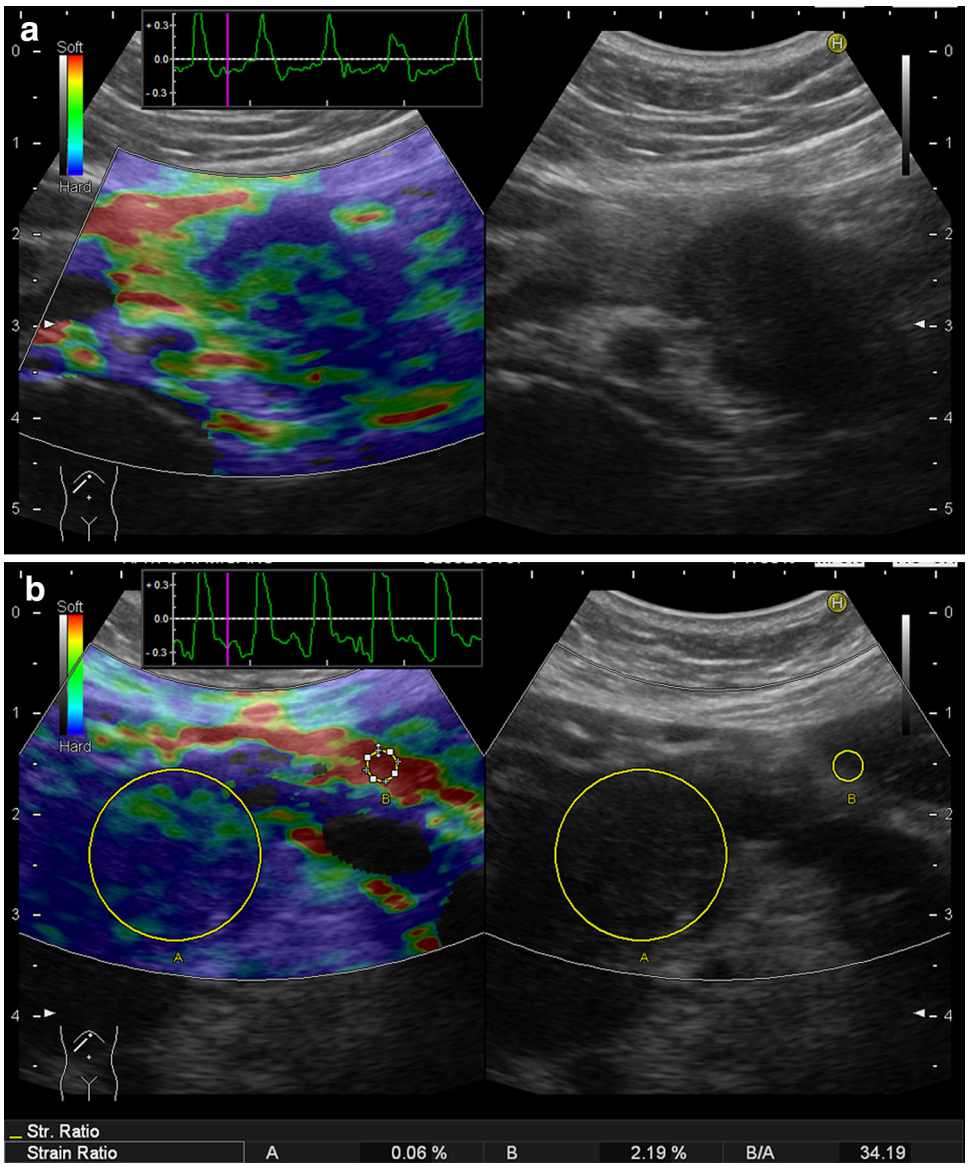



**Fig. 2** Real-time Tissue Elastography (qualitative evaluation) manufactured by Hitachi Aloka. **a** The case of pancreatic body cancer: in the tumor, the main color tone is a heterogeneous blue. On the *upper left* of the screen, a strain graph is displayed. **b** The case of pancreatic head cancer: the ROI (*A*) is defined in the tumor and the ROI (*B*) is defined in the red area around the pancreas as a comparison area. The strain ratio is calculated to be 34.91, as shown on the *lower right* of the screen

separating the signals collected before and after a strain into micro areas. The conventional convex probes used in the B-mode can be used.

A quality bar is displayed in the upper left of the screen as an index of whether an excellent strain has been captured (Fig. 3a). The strain is expressed on the quality bar in three levels with green, yellow, and red as the color codes, among which green indicates the most excellent strain when it reaches the upper part of the bar. In addition, a quality graph is displayed in the lower right of the screen, indicating the capture timing of the most excellent strain at the timing of the top of the graph waveform.

For the qualitative evaluation method, the distribution of the strain in the ROI is relatively evaluated and displayed on a color map. For the quantitative evaluation method, a target ROI can be defined in any part of the ROI to calculate the elasticity index. The elasticity index refers to a value quantifying the average strain values in the ROI as 1.0, strain values larger than the average as 0 to less than 1.0, and strain values smaller than the average as 1.0 to less than 6.0. Furthermore, it is possible to calculate the elasticity index (*E*) in multiple different target areas, i.e., the ratio *E*2/*E*1 of *E*1 and *E*2 as the *E* ratio.

In 2013, a function was added to the LOGIQ E9 and S8 to render the strain value in a prescribed scale as an absolute value in the form of color mapping, rather than rendering the strain distribution in the ROI into relative images. In this method, a target ROI is defined in the ROI to display the strain index (%) corresponding to the colors displayed on the screen (Fig. 3b). In this case, the maximum strain in a specified scale is defined as 100 %. It will be necessary to define preferable scales for each organ on the basis of examination of a large number of cases. Reports on this technique are needed.

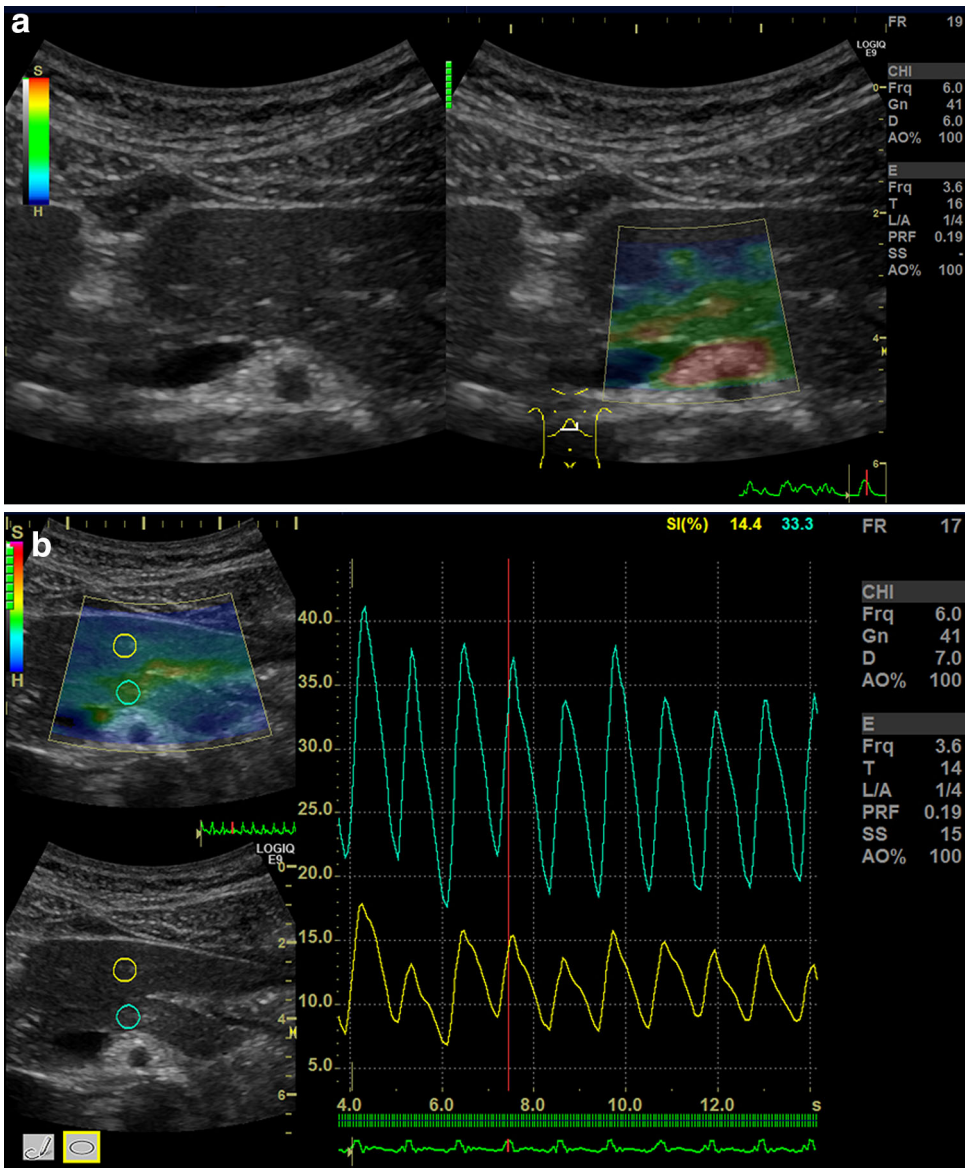



**Fig. 3** Elastography (qualitative evaluation) manufactured by GE. **a** Elastography used for a normal pancreas: *green* indicates the normal pancreas, *blue* indicates the liver, and the *reddish color tone* indicates the tissue between the liver and the pancreas. The quality *bar* on the *upper left* of the elastogram is *green* to the top layer, indicating an excellent elastogram. **b** Elastography used for a normal pancreas: the elastogram is on the *left side*, and the changes over time (10-pulse period) of the strain index are on the *right side*. The strain index shows periodic waveforms synchronous with pulsation

To define an elasticity index and strain index specific to each case, it is necessary to adopt reproducible values. GE's elastography has a function to plot time-dependent changes. It is recommended that 5–10 waveforms be recorded to confirm the pattern of the waveforms, and to adopt the values at the point in time when representative waveforms are recognized (Fig. 3b).

Thus far, there have been no reports using GE's elastography, but it has been confirmed that the difference in a phantom with different hardness between the target region and other regions was acquired as the ratio of the indices.

*Elastography (Toshiba)*

This technique uses the tissue Doppler method to detect tissue strain; i.e., the strain value of the ultrasound beam is measured. The devices that are capable of real-time elastography processing are the Aplio 500, 400, and 300, and the Xario 200 and 100; the latter two support the use of a convex probe. A velocity graph is shown in the lower left of the screen, which is informative about whether waveform patterns with sufficient amplitude are being observed to select images capturing excellent strain.

For the qualitative evaluation method, the distribution of the strain values in the ROI is evaluated and displayed in the form of a color map. In the latest version, a function has been added whereby the graphs are sectionalized each time the zero point of the velocity graph is exceeded, and when a section is selected, an elastogram (color map) is displayed for the time phase when the graph returns to the zero point in that section (Fig. 4a). Thanks to this function, if a section that includes a wave with large amplitude in

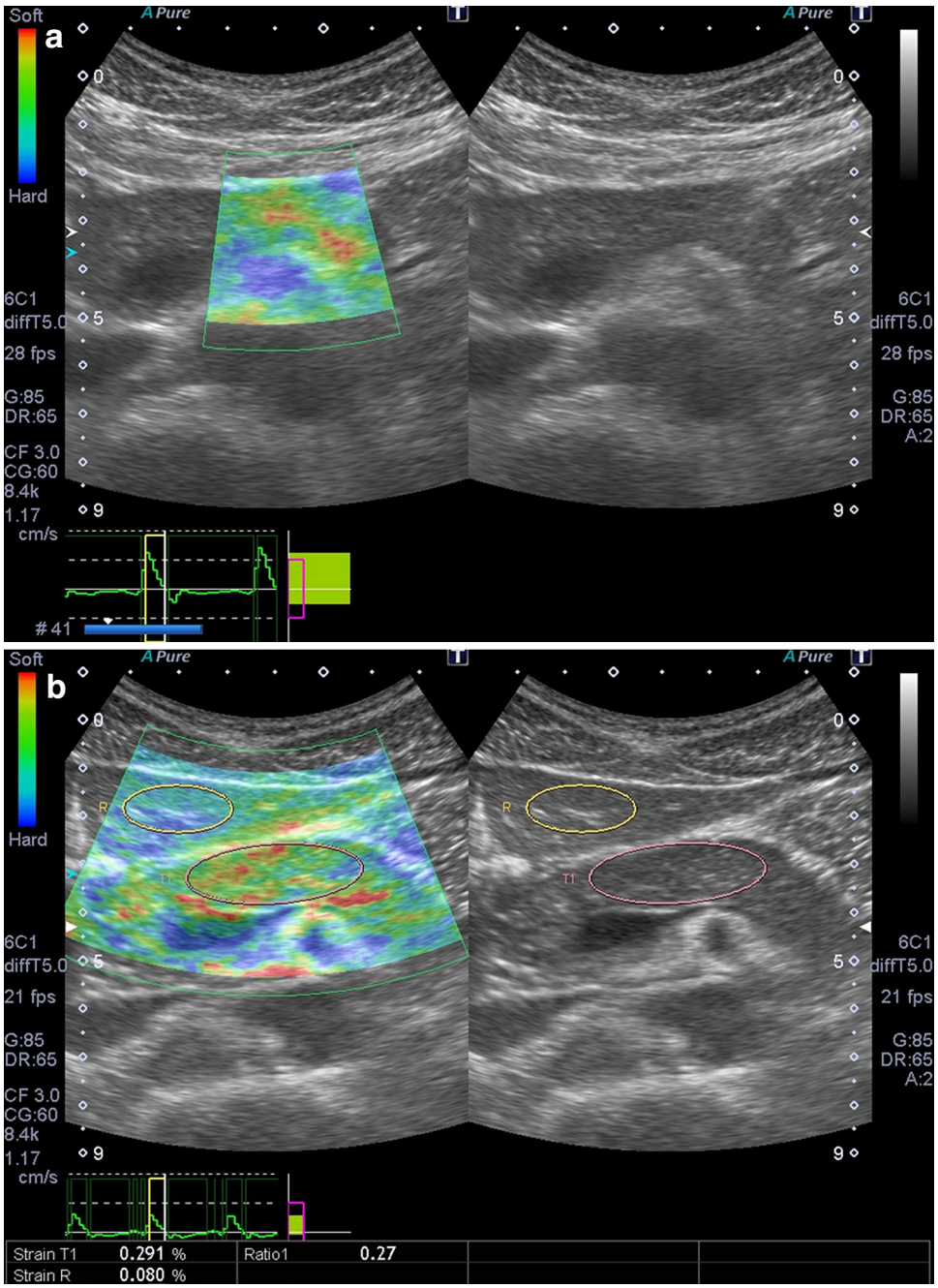



**Fig. 4** Elastography (qualitative evaluation) manufactured by Toshiba. **a** Elastography used for a normal pancreas: a velocity graph is displayed in the *lower left* of the screen. Every time the graph exceeds the zero point, a square section is formed. In this example, the pancreas shows *color tones* from *red* to *green*. **b** Elastography used for a normal pancreas: when a target ROI is defined, the strain ratio is automatically calculated and displayed in the lower part of the screen. For the shape of the ROI, a *circle* or a freeform curve can be selected as well as an ellipse

synchronization with pulsation is selected, an elastogram obtained under preferable conditions is automatically adopted; therefore, stable analysis with little dependence on the practitioner can be expected.

For the quantitative evaluation method, measurement of the strain ratio is possible. When a target ROI is defined in any position in the ROI, the average of the strain values in the target ROI is displayed. As the target ROI shape, a circle or an ellipse can be selected, or a freeform curve can be drawn. When the target ROIs are selected for both the target area and the comparator area, the strain ratio is automatically calculated and displayed in the lower part of the screen (Fig. 4b).

### *eSie Touch$^{TM}$ Elasticity Imaging (Siemens)*

This is a strain elastography technique that uses the spatial correlation method to detect the strain in tissue generated due to a micro movement. The calculation to generate an image is always executed covering the whole B-mode image; therefore, it is possible to change the size of the ROI, and alter its location, after freezing.

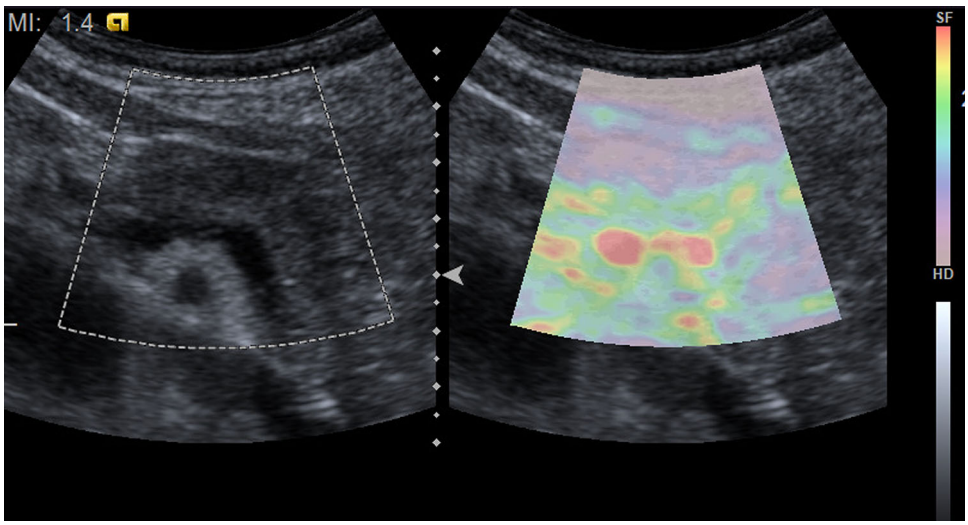



**Fig. 5** eSie Touch Elasticity Imaging manufactured by Siemens. eSie Touch Elasticity Imaging manufactured by Siemens used for normal pancreas

The type of image display in the ROI can be selected from color-scale and gray-scale images (Fig. 5). The default color setting for the color scale is the opposite of that with RTE. The gray scale is displayed independent of, and in parallel with, the B-mode image, and is not overlain on the B-mode image. In a mammary gland area, the diameter of a tumor ($E$) measured in the elastography and the diameter of the tumor measured in the B-mode image are compared. If $E > B$, this is one of the indices that the tumor is malignancy ($E/B$ ratio diagnosis). The $E/B$ ratio diagnosis based on the gray scale is widely used.

Mateen et al. [38] reported that eSie Touch was useful for evaluation of the expansion of a lesion in cases of acute pancreatitis and for judgment of the curative effect of pancreatitis treatment.

*Elastography (Philips)*

This technique is a type of strain elastography that employs a method similar to RTE. This technique adopts a technique called nanometer tissue strain tracking technology. The depth for producing an excellent elastogram is the same as that for producing a clear B-mode image; i.e., generally within the 5-cm range from the body surface. The devices that can use this technique are the iU22, EPIQ, and linear probe (L12-5, L17-5). A compression bar is used as the index to see if an excellent strain has been generated. This compression bar indicates two parameters, i.e., the amount of collected strain data and the scattering; the color represents the amount of strain data and the height represents the scattering. To obtain images that can be used for evaluation, it is necessary to keep the height of the compression bar at a certain level within the range where the compression bar is colored green (Fig. 6).

At present, there are no reports on the pancreas, and future reports are hoped for.

Endoscopic ultrasonography (EUS)

*Real-time Tissue Elastography$^{TM}$: RTE (Hitachi Aloka)/ ELST (Olympus)*

EUS uses a high-frequency (5–12 MHz) ultrasound system, with which it is possible to observe the pancreatic parenchyma from a close distance. This is an image diagnosis technique that can produce high-accuracy images of the pancreatic parenchyma. In addition, gas in the alimentary tract, which interferes with the ultrasound waves, is eliminated with observation made from the inside of the stomach or duodenum. Consequently, the pancreas from the head to tail can be evaluated by EUS. Elastography that is performed by EUS (EUS elastography) has the ability to evaluate the elasticity of the pancreatic parenchyma in the entire area of the pancreas with high precision; therefore, this elastography is expected to be a new and precise diagnosis technique for pancreatic diseases.

(a) Method of examination (procedure, precautions, etc.)

In Japan, EUS elastography can be implemented using four types of ultrasound systems manufactured by Hitachi Aloka (HI VISION Ascendus, HI VISION Preirus, HI VISION Avius, Noblus) and six types of ultrasonic endoscopes manufactured by Hoya-Pentax (EG-3270UK, EG-3630U, EG-3630UR, EG-3830UT, EG-3670URK, EG-3870UTK), or using ultrasound system EU-ME2 (PREMIER PLUS) manufactured by Olympus and the five types of ultrasonic endoscopes manufactured by Olympus (GF-UCT260, TGF-UC260 J, GF-UCT240-AL5, GF-UC240P-AL5, GF-UE260-AL5). The elastography developed by the two manufacturers has, respectively, different brand names: RTE (Hitachi Aloka) and ELST (Olympus). Olympus, however, has been provided with the technology

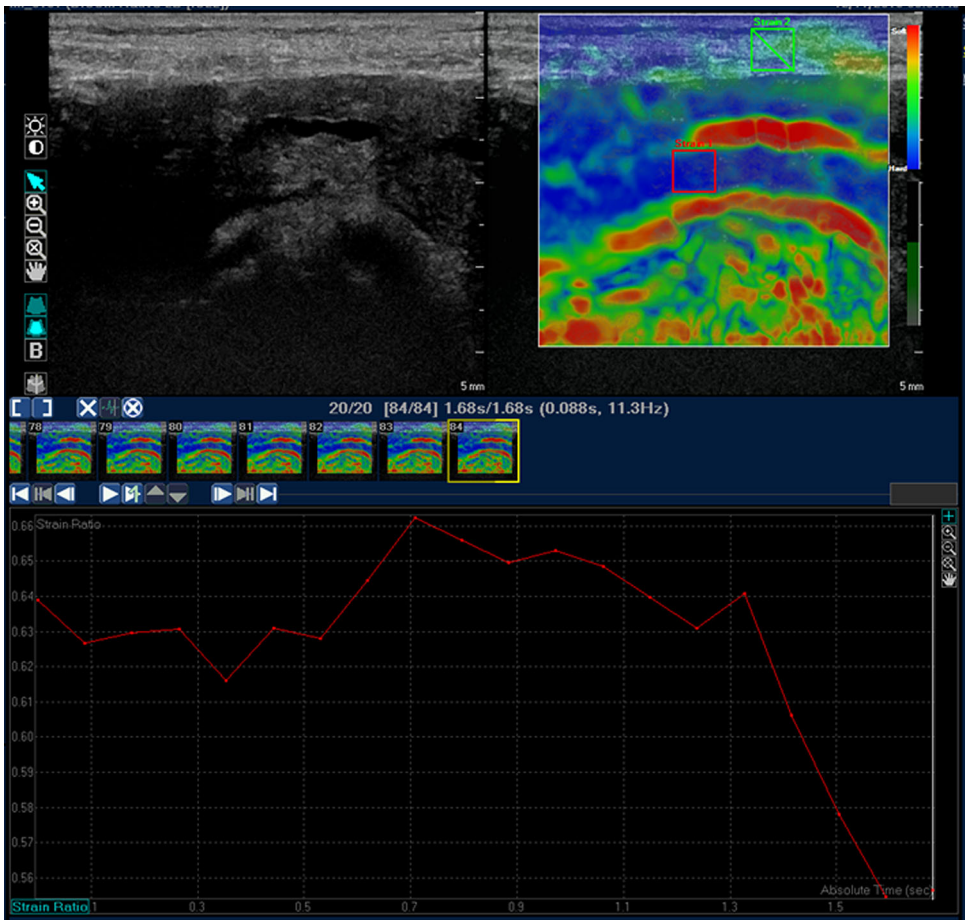



**Fig. 6** Elastography manufactured by Philips. Elastography manufactured by Philips used for autoimmune pancreatitis: a swollen pancreas is generally depicted in *blue*. The view in the *lower part* shows the graph showing changes over time

from Hitachi Aloka; therefore, it should be understood that their principles are generally equivalent. As the principles and the characteristics are the same as those of US, also see "Real-time Tissue Elastography$^{TM}$: RTE (Hitachi Aloka)", Real-time Tissue Elastography.

Next, actual scanning procedures will be described.

Firstly, the points regarding imaging a lesion are as follows. In the same way as with US, first, the probe should be placed so that it lightly touches the wall of the stomach or the duodenum, and second, you should select an imaging point that is not affected by an artifact such as multipath reflection, and pay attention to orienting the ultrasonic beam toward the aorta, and set the probe so that strain is generated in the depth direction. In this state of observation, it is possible to obtain a good-quality B-mode image (the image particles are clear, the contrast resolution is highly shown) suitable for the RTE image. If the B-mode is not imaged clearly, excellent RTE images cannot be obtained either. Therefore, it is important to be sure to produce an excellent B-mode image and to switch it to an RTE image.

There are two types of methods for setting the ROI: one method is to set the ROI only within a lesion, and the other method is to set the ROI at both a lesion and the peripheral area. The former is mainly used in examinations for hepatic fibrosis and other diffuse liver diseases, and the latter is mainly used in examinations for neoplastic diseases. However, in comparison with the liver, the pancreas is a small organ, and it may be possible to assess the hardness of a lesion's tissue with reference to the peripheral tissue in the case of the pancreas (in particular, the adipose tissue). Consequently, it is recommended that the ROI be set so as to include peripancreatic tissue. There are many reports emphasizing that, rather than being limited to a certain uniform size, the range displayed within the ROI is so wide that a lesion is on the order of half its size or less, with the range of the ROI sufficiently including the peripancreatic soft tissue [29, 39]. However, usually with such a large-sized ROI, it is difficult to avoid large blood vessels, and so it needs to be noted that the splenic vein and other branches of the portal vein will be included in the ROI.

Next, we describe the selection standards for RTE images. It is understood that the conditions for excellent RTE images are frames in which strain is generated in the depth direction, the RTE image is generated in the entire ROI, the RTE image is stably generated for a certain period

(5 s or longer in normal cases), and appropriate vibration energy is captured. For the evaluation of vibration energy, it would be preferable to refer to a strain indicator, which indicates the intensity of compression on the tissue on a 7-point scale, or a strain graph, which uses waveforms to indicate changes in the tissue with time, and these are equipped on each respective device. If the strain indicator shows that the intensity of compression is 3–5, or if the strain graph shows that the time phase of a relaxation of the pancreas under compression by the aorta is at the maximum in the downward direction, then such a frame is a frame in which preferable vibration energy has been captured.

Furthermore, even when an excellent B-mode image is obtained, it may be difficult to obtain excellent RTE images in some cases, including observation of a part that is a long distance from the aorta, and observation in a case of advanced arteriosclerosis. This is because sufficient vibration energy is not captured, in which case the following ideas may be effective and are worth attempting.

1. Change the direction of the observation if the lesion looks like it is both transgastric and transduodenal.
2. Change the posture from the left lateral decubitus position to the prone position or the dorsal position to find a posture in which the lesion comes between the probe and the ventral aorta.
3. Increase the RTE frame rate. Elastograms generated from smaller vibration energy may be captured. (However, the distance resolution may be degraded.)
4. Change the size of the EUS balloon and sufficiently suction the air in the alimentary tract so as to further stabilize the endoscope.

(b) Method of evaluation

There are two types of evaluation methods. One method (qualitative evaluation) is to evaluate the pattern of an elastogram such as the major color tone or the homogeneity/heterogeneity of color tones, etc. Another method (quantitative evaluation) is image analysis techniques that are used to evaluate the characteristics of a lesion in a quantitative manner. The former method may introduce some bias depending on the subjectivity and experience of the examiner. The latter is a more objective method, but the analytical procedure is complicated.

*Qualitative evaluation (color pattern diagnosis)*

There are many reports on color pattern diagnoses by EUS, among which the most representative is the elastic score advocated by Giovannini et al. [40]. This is a diagnosis method in which observation of the color tone of RTE images in and around the target tumor (the balance between green and blue) and observation of their homogeneity/heterogeneity are used for classification on a 5-point scale (score 1–5), as shown in Fig. 7, where the malignancy of a pancreatic tumor is higher as the score becomes higher. This visual classification is easy to understand, but judgment may be subjective and the decision making is influenced by the area ratio between the tumor and the peripheral area. Consequently, one of its shortcomings is that this evaluation is not usable for a massive tumor and/or a tumor of a large size with an irregular shape.

*Quantitative evaluation (image analysis diagnosis)*

The image analysis diagnoses that have been reported thus far include those using strain ratio (Fig. 8), [24, 27, 41] using strain histogram (Fig. 9), [42, 43] and using neural network [29, 44, 45]. With these methods, (semi) quantification of tissue elasticity is possible, but a comparison between different analysis methods has not been conducted, so there is no consensus about which of these methods is the best.

1. Strain ratio (Fig. 8)

Strain ratio is a quantitative evaluation method that analyzes the difference in hardness between the peripheral tissue and the lesion.

$$\text{Strain ratio} = \text{Peripheral tissue strain value}/\text{lesion strain value}$$

The above equation is used for the calculation. The numerator is peripheral tissue strain value, mainly consisting of adipose tissue; therefore, the harder the tissue, the higher is the value. The background of this theory is the assumption that the adipose tissues of different individuals are of the same hardness, based on which the (semi) quantification of tissue hardness becomes possible. The hardness of a pancreatic tumor is expressed as an approximation but is quantified. Consequently, the application of this diagnosis method is so easy that there have been many reports on prospective studies in which it was used [24, 27, 41].

2. Strain histogram (Fig. 9)

The color tone (hardness) of an RTE image is converted into a gray scale (value) of 256 tones from 0 (blue) to 255 (red). Thus, it becomes possible to reproduce a gray-scale image and a gray-scale histogram to express its distribution. In addition, if a threshold is defined on the gray scale, it is possible to convert it into a binary indication of harder tissue (0) and softer tissue (1) on either side of the threshold, and thus to reproduce an RTE image in the form of a binary image. When these images and histograms are statistically analyzed, parameters called feature values can

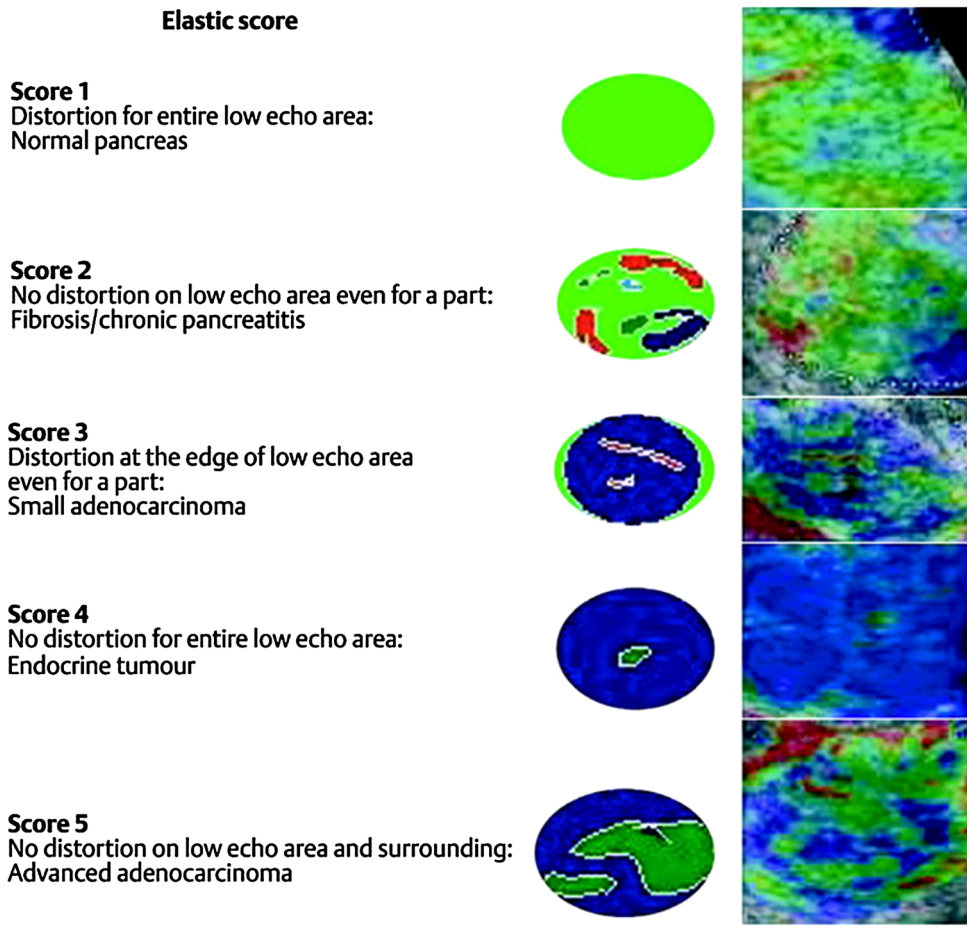



**Fig. 7** The elastic score. The elastic score by Giovannini et al. Classification into 5 scores is made based on the main color tone and the homogeneity of the colors. (Redrawn from Fig. 5 in reference No. 40. With the kind permission of Thieme Medical Publishers.)

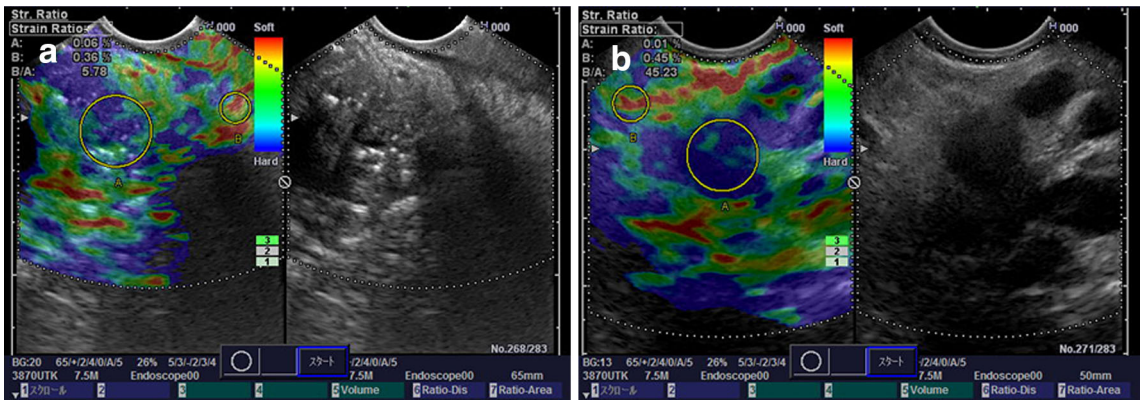



**Fig. 8** Measurement of the strain ratio based on EUS. **a** An example of chronic pancreatitis: the color tone in the target area is an heterogeneous *green*, and the strain ratio is 5.78. **b** An example of a pancreatic cancer: the color tone in the target area is an heterogeneous *blue*, and the strain ratio is 45.23

be calculated. These consist of 11 items: the average of the relative strain (MEAN), the standard deviation of the relative strain (SD), the ratio of the area of low strain (%AREA), the complexity (COMP), the kurtosis of the histogram (KURT), the skew of the histogram (SKEW), the contrast (CONT), the entropy (ENT), the inverse difference moment (IDM), the angular second moment (ASM), and the correlation (CORR). Their meanings are as shown in Table 2. In addition to the tissue elasticity, the homogeneity/heterogeneity of the elasticity can be quantified. Consequently, this function is applied mainly to the diagnosis of chronic hepatitis and cirrhosis in the liver area. In

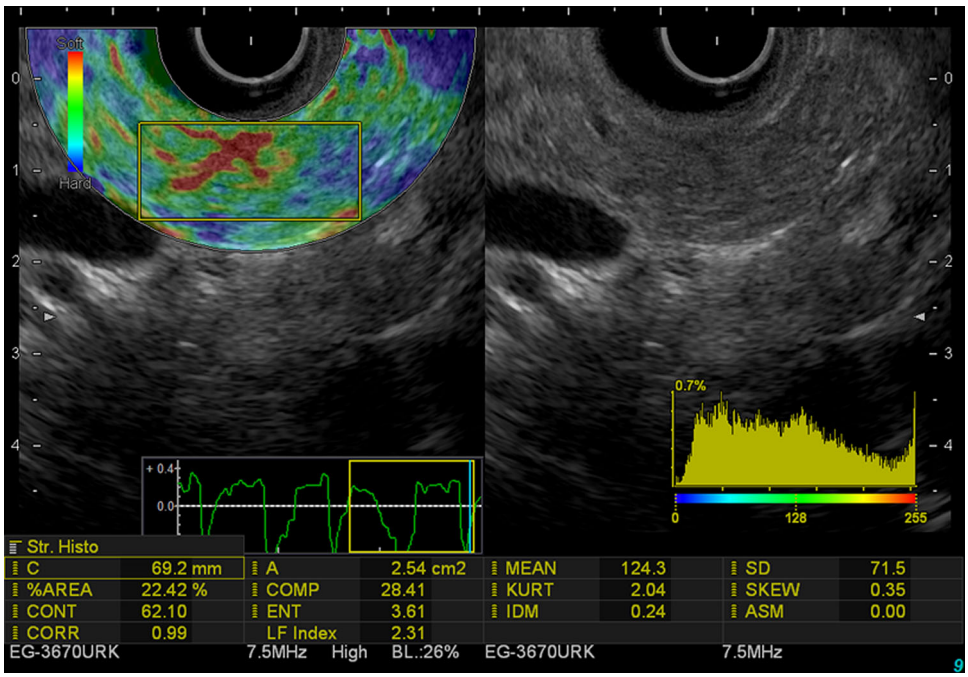



**Fig. 9** Measurement of the strain histogram based on EUS. The B-mode image of the pancreatic parenchyma is on the *right*, and the RTE image is on the *left*. In the example image, the pancreatic parenchyma is depicted in a relatively even *green* (soft). The image analysis is conducted based on the pancreatic parenchyma in the RTE image (the *yellow-sided square* in the ROI), and its result is displayed in the lower part

**Table 2** Feature values of the 11 items calculated using the strain histogram measurement function

| Image | Parameters | Information |
|---|---|---|
| Gray scale image | Mean | Mean of the gray levels |
| | Standard deviation | Standard deviation of the gray levels |
| | ASM | Measure of the homogeneity on the gray scale image |
| | Contrast | Measure of local gray level variation on the gray scale image |
| | Correlation | Measure of gray level linear dependence on the gray scale image |
| | Entropy | Measure of the randomness of gray level distribution |
| | IDM | Measure of the homogeneity on the gray scale image |
| | Skewness | Measure of the asymmetry of the gray level distribution |
| | Kurtosis | Measure of the "peakedness" of the gray level distribution |
| Black and white image | %Area | Percentage of the white area (≒ hard area) |
| | Mean of Complexity | Complex ratio of the shape of the white area (≒ hard area) and is calculated as periphery$^2$/area of the white area |

the pancreas area, it can be applied to the diagnosis of chronic pancreatitis and pancreatic fibrosis [42, 43]. A strain histogram measurement function is available with HI VISION Ascendus, HI VISION Preirus, and HI VISION Avius.

3. Neural network

This is a technique for automatic analysis using a computer, as reported by Saftoiu et al. [29, 44, 45]. This is a means for quantifying the color tone of an RTE image for histogram analysis in the same manner as the function of strain histogram measurement. As the selection of images, etc., is automatically analyzed by a computer, this is an analysis method in which artificial bias is not easily applied.

Note: With the histogram analysis in a report by Saftoiu et al. [44], diagnosis of pancreatic tumor benignancy/malignancy was possible with a sensitivity of 91.4 %, a specificity of 87.4 %, and a proper diagnosis rate of 89.7 %. After this automatic analysis system was introduced, the proper diagnosis rate was improved to 95 %. In addition, further training increased the rate to 97 % on average [44].

(c) Clinical benefits

Differential diagnosis of the pancreas (particularly the discrimination of malignancy/benignancy) and evaluation of chronic pancreatitis and pancreatic fibrosis are indications for this technique. In addition, future expectations include the possibility of improvement in the ability to detect pancreatic tumors in the same manner as reports on the mammary glands [39, 46], enhancement of EUS-FNA visibility, potential enhancement of diagnosis ability [39, 46], and forecasting of the recurrence of autoimmune pancreatitis [47].

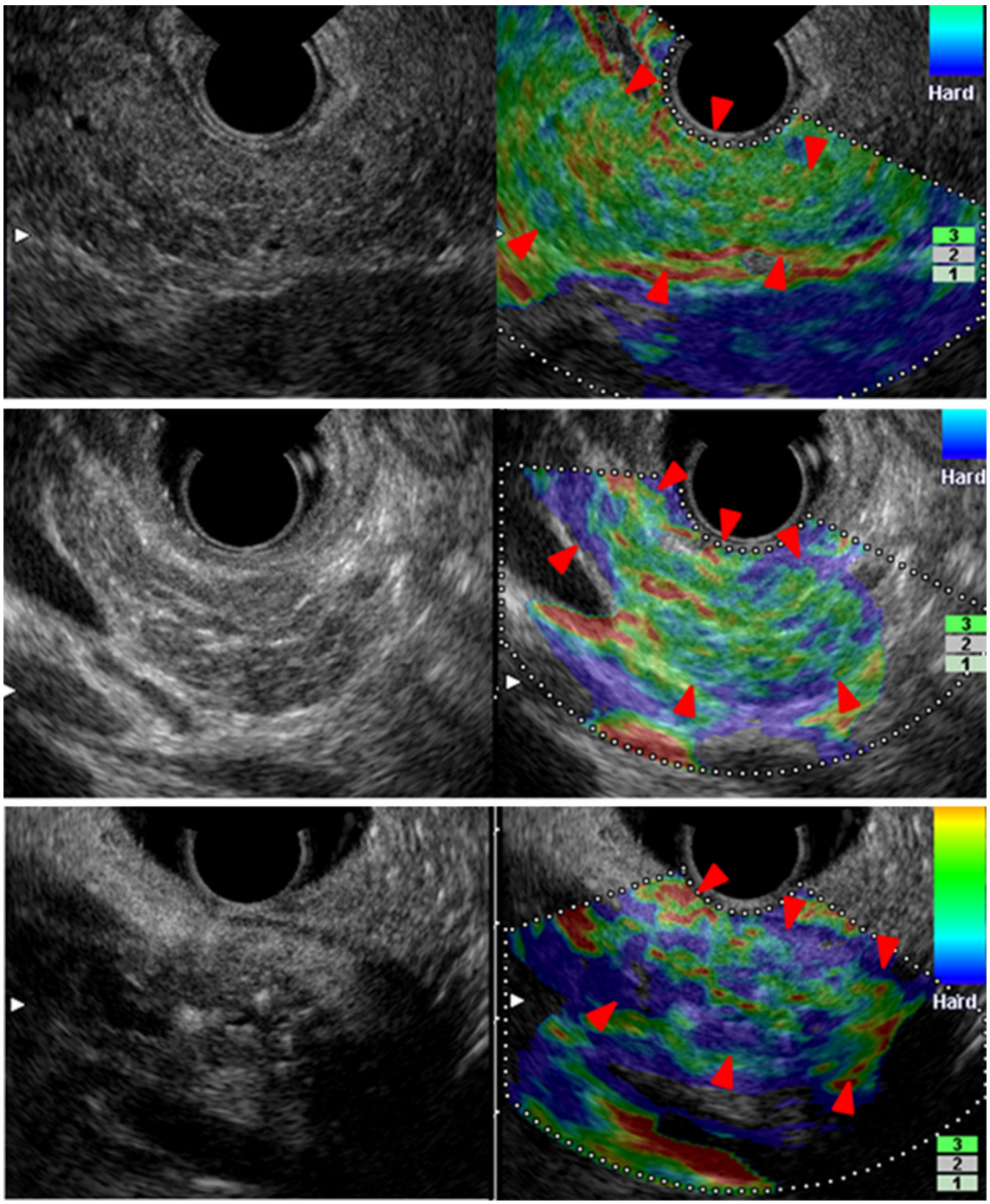



**Fig. 10** The EUS-EG images. *Upper* The EUS-EG used for a normal pancreas: the EUS-EG image shows homogeneous color tone and is depicted in a *greenish color*. *Middle* The EUS-EG used for an early chronic pancreatitis: the EUS-EG image shows a *blue color tone* in comparison with the example of a normal pancreas, but the color tone is depicted in a relatively homogeneous color. *Lower* The EUS-EG used for a chronic pancreatitis: the EUS-EG image shows a *blue color tone*, which is heterogeneous depicted in comparison with a normal pancreas and early chronic pancreatitis

1. Diagnosis of pancreatic tumors

According to Giovannini et al. [40], the color pattern analysis of malignancy/benignancy was reported to have a sensitivity of 100 % and a specificity of 67 %. Furthermore, according to an examination of various facilities where this classification was simplified, the sensitivity was 92.3 % and the specificity was 80.0 % [48].

According to a recent meta-analysis, discrimination of pancreatic tumor benignancy/malignancy using EUS

elastography had a sensitivity of 95 % (95 % CI 93–96 %) and a sensitivity of 69 % (95 % CI 63–75 %) [35] in 13 articles involving 1,042 cases, and a sensitivity of 95 % (95 % CI 94–97 %), a specificity of 67 % (95 % CI 61–73 %), and an odds ratio of 42.28 (95 % CI 26.90–66.46) in an examination of 1,044 cases [33].

2. Diagnosis of chronic pancreatitis and pancreatic fibrosis (Fig. 10)

It has been reported that the MEAN and SD calculated using the strain histogram measurement function in the case of obstructive pancreatitis have a negative correlation with pancreatic fibrosis, and that the correlation with pancreatic fibrosis is positive for KURT and SKEW [42]. Among these, the MEAN is particularly useful for the diagnosis of pancreatic fibrosis. The diagnosability is high regardless of the rate of pancreatic fibrosis progression (proper diagnosis rate of about 80 %) [42]. In addition, there have been reports on examinations using the MEAN and strain ratio in the diagnosis of chronic pancreatitis. According to these reports, it is possible to diagnose chronic pancreatitis with high accuracy [43, 49]. In the same manner as with the liver, RTE can potentially be used in the evaluation of fibrosis and chronic pancreatitis; however, the number of such reports is extremely small, and thus, at the present time, it is understood that further examination is necessary.

3. Other diagnoses

This technique may be useful for the identification of a target for taking a sample of tissue from a pancreatic cancer by EUS, and it has been pointed out that this may reduce the number of FNA [34, 46].

(d) Control of diagnostic accuracy and its limits

To maintain high diagnostic accuracy, it is important to produce excellent B-mode images and RTE images. However, when EUS elastography is employed in practice, there are cases in which excellent reproducibility is not attained due to factors such as the strength of the pressure on the tissue and the size of the ROI, even if a lesion is clearly depicted in the B-mode image. At present, for maintaining the accuracy of diagnosis, it is also important to obtain at least three to five excellent RTE images for the evaluation of the tissue elastic image, rather than evaluation with only one frame [27, 49], and to make an evaluation from moving images that last for a certain duration (at least 5 s) [24, 29, 44, 45]. It has been reported that it is difficult to evaluate a 35-mm or larger lesion and a lesion that is distant from the transducer [50], and a relatively longer time should be taken for the observation.

To eliminate subjectivity due to the examiner (to enhance the objectivity of RTE images), various types of image analysis diagnoses may be possible, but it is recommended that evaluation be made based on multiple frames, not only one frame [27, 42, 49], or video clips [24, 29, 44, 45]. In particular, some extreme differences have been pointed out regarding strain ratio cutoff values, and multicenter prospective studies with management of accuracy are necessary in the future to determine a cutoff value that is to be finally recommended. It has been reported that the sensitivity of pancreatic tumor malignancy/benignancy diagnosis is high but the specificity is low [33, 35]. It has been reported that differential diagnosis only by RTE images may be difficult in a case of pancreatic cancer in chronic pancreatitis [39, 51]. For the diagnosis of pancreatic cancers in cases of chronic pancreatitis, it is necessary to make an evaluation from the position of a comprehensive evaluation based on various types of image diagnoses including the usual B-mode images as well as CT, MRI, and PET examinations. In addition, further improvement is required in the diagnosis of chronic pancreatitis. In the case of chronic pancreatitis, in addition to pancreatic fibrosis, the amount of cell migration (the amount of inflammatory cell infiltration) and calcification may have an influence on the increase in the hardness of the pancreas, and diagnosis of their rate of progression can be considered to be a future issue.

To spread EUS elastography in the future and to maintain its sufficient accuracy, it is necessary to develop unified methods of imaging and analysis and to construct a training system for imaging.

## Appendix: Regarding the diagnosis of pancreatic fibrosis based on EUS elastography—in comparison with the estimation of B-mode EUS findings

Since around 2000, EUS diagnosis has been actively used for chronic pancreatitis. In the "Japanese Clinical Diagnostic Criteria for Chronic Pancreatitis 2009," examinations of pancreatic parenchyma and the pancreatic duct by means of EUS were mentioned along with a discussion of images characteristic of early chronic pancreatitis [20]. Hyperechoic foci and stranding, lobularity, and hyperechoic MPD margin can be cited as examples of diagnoses with EUS (B-mode observations) that indicate fibrosis of the pancreatic parenchyma or pancreatic duct, but the interpretation of these diagnoses depends in part on the examiner, and so there has been a demand for objectivity. Under this backdrop, examinations of the significance of EUS elastography with respect to pancreatic fibrosis have begun in recent years.

There have been several reports on diagnoses of fibrosis of the pancreas based on EUS elastography in which qualitative and quantitative evaluation of images was performed. Itoh et al. [42] and Iglesias-Garcia et al. [49]

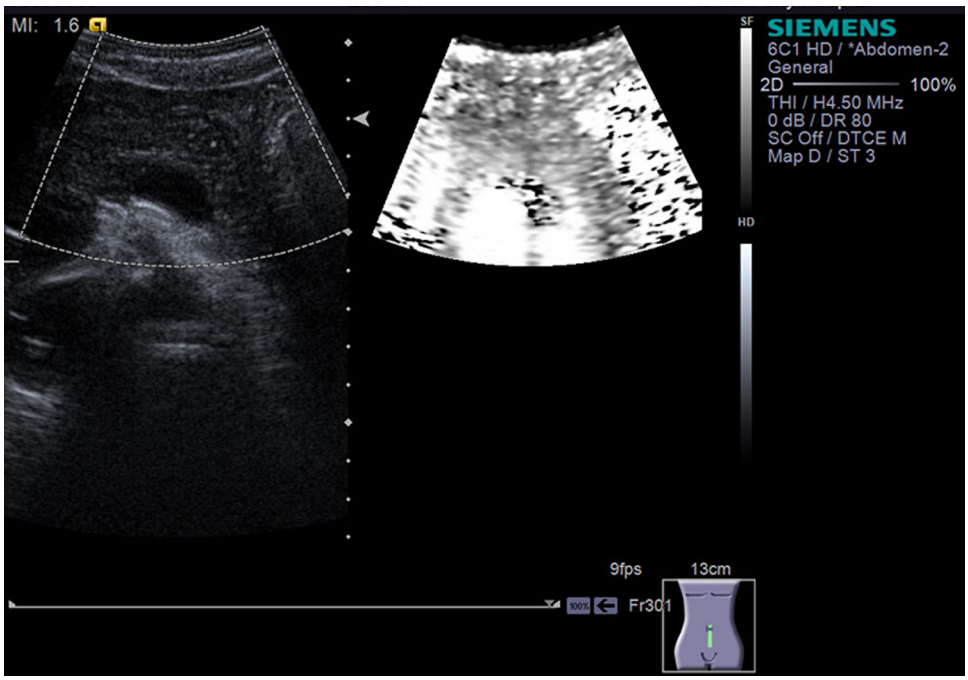



**Fig. 11** Virtual Touch Imaging (VTI) manufactured by Siemens. Virtual Touch Imaging (VTI) manufactured by Siemens used for a normal pancreas. Regions with a small change are depicted in *black*, while regions with a large change are depicted in *white*. (Courtesy of Dr. Yoshihiko Tachi, Dr. Tadashi Iida, and Dr. Katsumi Nakano, Komaki Municipal Hospital.)

quantified images obtained from EUS elastography in an attempt to evaluate pancreatic fibrosis. Itoh et al. [42] performed a comparative examination of the level of progress of pathological fibrosis in resected specimens and noted the potential for quantitative evaluation of pancreatic fibrosis based on EUS elastography. Furthermore, Iglesias-Garcia et al. [49] noted a significant correlation between EUS elastography and the conventionally used criteria for EUS diagnosis of chronic pancreatitis. In addition to these, there is a report on uneven pancreatic parenchyma in elastography even in cases in which there is a finding of a slight suspicion of early chronic pancreatitis in a B-mode image [52]. Furthermore, there is a report on the contribution of EUS elastography to the discrimination of chronic pancreatitis and fibrotic changes due to aging [43]. It is understood that the employment of EUS elastography in the diagnosis of pancreatic fibrosis is highly significant from the point of view of the objectivity of a diagnosis of pancreatic fibrosis based on B-mode EUS.

## ARFI imaging

*Virtual Touch™ Imaging: VTI (Siemens)*

(a) Method of examination (procedure, precautions, etc.)

ARFI imaging is elastography that uses the acoustic radiation force impulse (ARFI) method of excitation to create images of tissue strain (more precisely, of displacement). Unlike strain elastography, manual compression is not necessary, and ARFI imaging is said to be barely dependent on the examiner. Only Virtual Touch Imaging (VTI) manufactured by Siemens is commercially available on the market. For the measurement of displacement, VTI uses the spatial correlation method. VTI has two types of image display functions: one that displays gray-scale images without overlaying them on the B-mode images, and another in which images are displayed in color by overlaying them on the B-mode images. The maximum depth of the displayed ROI is 6 cm. A linear probe (9L4) and a convex probe (6C1) are used. To take images, the target lesion is captured in the B-mode image, so that the ROI can be defined. After this, the examinee is asked to hold his or her breath for about 1 s, and the examiner pushes the trigger button to take images. Real-time display is not possible, so only still images are captured (Fig. 11). Future studies and results with this method are anticipated.

(b) Method of evaluation

There are no reports on procedures carried out for the pancreas, and the method of evaluation of the pancreas is unknown.

(c) Clinical benefits

There are no reports on procedures carried out for the pancreas, and the clinical benefits for the pancreas are unknown.

(d) Control of diagnostic accuracy and its limits

There are no reports on procedures carried out for the pancreas, and the control of diagnostic accuracy and its limitations regarding the pancreas are unknown.

**Shear wave elastography**

(a) Method of examination (procedure, precautions, etc.)

Shear wave elastography is a method for estimating the hardness of a target tissue in which the ROI is set in the target area in a B-mode image, focused ultrasound is emitted in the ROI so as to apply acoustic radiation force impulse, and the shear wave speed is measured. In this method, the higher the shear wave speed, the harder is the target tissue, and the lower the shear wave speed, the softer is the target tissue. Tracking of the shear waves, which are transverse waves, is performed with the outgoing/incoming transmission of the ultrasonic pulses (search pulse) for the regular B-mode.

To generate shear waves with an amplitude sufficient for measurement, it is important to remove factors that attenuate the ultrasonic waves on the route from the probe to the ROI. For stable measurement, a clear imaging of the pancreas in the B-mode image is important.

(b) Method of evaluation

*Quantitative evaluation (measurement of shear wave speed)*

As the shear wave speed is expressed as an absolute value, it is not necessary to define a comparison area. The shear wave speed is expressed in m/s (VTQ, VTIQ, and ElastPQ) or kPa (ElastPQ, shear wave elastography). If the shear wave speed is expressed in kPa, it is assumed that there are no changes in the volume due to deformation of the object (Poisson's ratio $\gamma = 0.5$) and that the density is equal to the density of water (density $\rho = 1$ g/cm [3]).

*Qualitative evaluation (diagnosis of color pattern)*

The hardness of the tissue in the ROI is expressed in the form of a color map depending on the shear wave speed at each point. At the present time, however, this is possible only with Virtual Touch IQ (Siemens) or shear wave elastography (super sonic imaging).

(c) Clinical benefits

Unlike strain elastography, the pulsation of the aorta is not used; therefore, stable measurement is possible even in cases other than the pancreas body, such as the head or tail. On the other hand, as the shear wave speed is expressed as an absolute value, the issue of the selection of a comparison area does not arise. This is why there are expectations for the clinical application of shear wave elastography for the pancreas.

(d) Control of diagnostic accuracy and its limits

There is a limit to the acoustic radiation force impulse that is certainly safe within the body. Accordingly, if the tissue in the ROI is hard, it is not possible to generate sufficient shear waves, and so measurement error tends to occur. In the case of a tumor that causes measurement error, it is recommended that the ROI be defined on a tip of the tumor if it is in a mammary gland area [11]. This information should also be referenced in the case of the pancreas. Furthermore, it has been reported that if the target area is far from the probe, the shear wave speed tends to be low [53]. This is thought to be because the attenuation of the focused ultrasound reduces the acoustic radiation force impulse, which in turn reduces the amplitude of the shear waves, making it difficult to perform detection with the diminished search pulse.

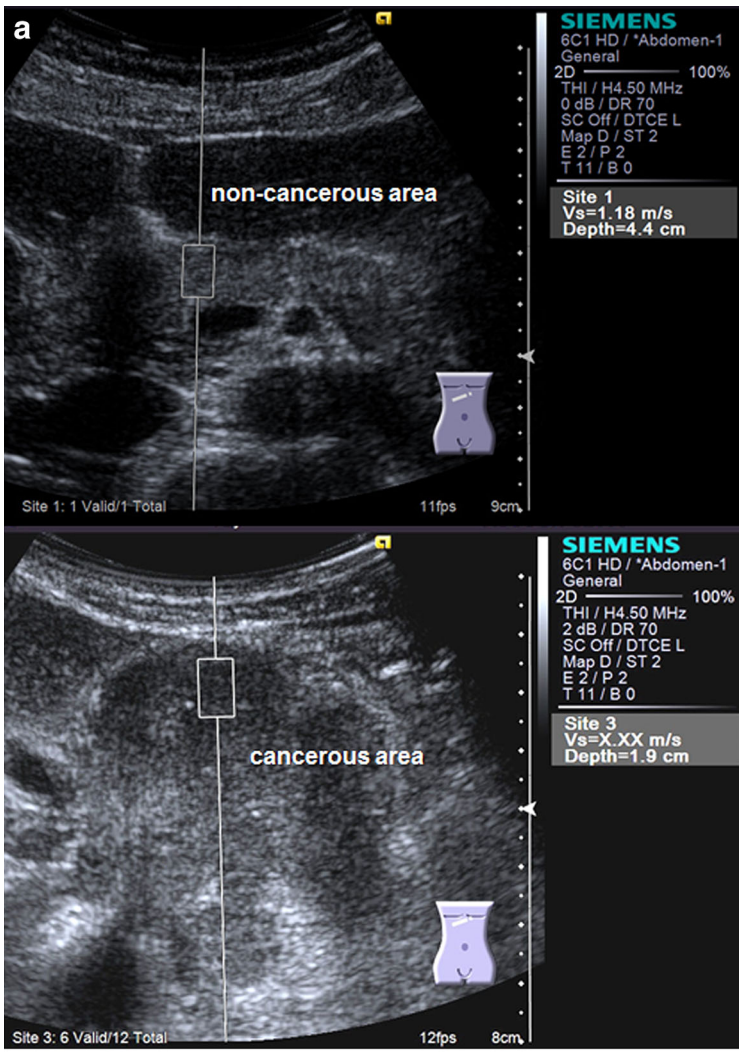
The focused ultrasound used in this technique satisfies current safety standards. However, the transmission waveform and wave length are different from those of ultrasonic pulses. Therefore, it is difficult to assess its influence on the body, and a possible increase in temperature may be a safety issue [54]. In particular, its safety in simultaneous use with contrast media has yet to be confirmed [55, 56], and the Ultrasound Equipment and Safety Committee of the Japan Society of Ultrasonics in Medicine recommends that this technique should be sufficiently employed after a sufficient time has passed for microbubbles to disappear from within the body [57].

*Virtual Touch™ Quantification: VTQ (Siemens)*

Reports on shear wave elastography of the pancreas have increased in number [53, 58–61] This technique can only be used with US, and not with EUS. The VTQ devices ACUSON S3000 and S2000 are compatible with this technique. The regular convex probes that are used in the B-mode can be used.

A 10 mm × 6 mm ROI can be set in any target area in a B-mode image. After the button for emitting focused ultrasound is pushed, the measurement is completed within 1 s. The measured shear wave speed is displayed on the right side of the screen in m/s. If the confidence of the measured value is low, a measurement error occurs with an indication of X.XX m/s (Fig. 12a).

VTQ has a report function, in which the values of a plurality of measurements for the same site are automatically averaged, and the mean, the median, the standard deviation, and the IQR are displayed (Fig. 12b). In the same lesion, three locations can be selected, from Site 1 to Site 3. To confirm the reproducibility of a measured value, it is recommended that the same measurement is repeated for the same site about three times if the reproducibility is high, or 10 times if it is not, and to use the median. In the lower part of the B-mode screen, the total measurement time for each site (Total) and the total number of successful measurements (Valid) are displayed (Fig. 12a).




**b**

Abdomen Shear Velocity Measurements

| Site 1 Vs (m/s) | Depth (cm) | Site 2 Vs (m/s) | Depth (cm) | Site 3 Vs (m/s) | Depth (cm) |
|---|---|---|---|---|---|
| 1.23 | 4.6 | 1.05 | 3.8 | 0.90 | 4.4 |
| 0.89 | 4.4 | 2.64 | 3.6 | 1.07 | 4.5 |
| 0.87 | 4.4 | 0.93 | 3.6 | 0.92 | 4.4 |
| 1.29 | 4.3 | 1.18 | 3.2 | 1.12 | 4.3 |
| 0.96 | 4.3 | 1.20 | 3.2 | 0.94 | 4.3 |
| 1.21 | 4.2 | 1.10 | 3.1 | 0.97 | 4.3 |
| 1.37 | 4.2 | 1.21 | 3.0 | 1.06 | 4.6 |
| 0.96 | 4.2 | 0.94 | 3.3 | 0.98 | 4.6 |
| 1.42 | 4.2 | 1.01 | 3.3 | 1.09 | 4.6 |
| 1.21 | 4.4 | 0.94 | 3.2 | 1.04 | 4.6 |
| 1.02 | 4.0 | 0.92 | 3.2 | | |
| 0.85 | 4.0 | 1.01 | 3.2 | | |
| 0.78 | 4.0 | 1.09 | 3.2 | | |
| 1.11 | 4.1 | | | | |
| 1.14 | 3.7 | | | | |
| 1.15 | 3.7 | | | | |
| 1.14 | 3.7 | | | | |
| 0.84 | 3.7 | | | | |
| Median | 1.13 | | 1.03 | | 1.01 |
| Mean | 1.08 | | 1.05 | | 1.01 |
| Std Dev | 0.19 | | 0.11 | | 0.08 |
| IQR | 0.32 | | 0.20 | | 0.13 |

**Fig. 12** Virtual Touch Quantification (VTQ) manufactured by Siemens. **a** Virtual Touch Quantification (VTQ) manufactured by Siemens for a pancreatic body cancer. *Upper* The ROI is defined in a non-cancer region. The shear wave speed in the ROI (Vs = 1.18 m/s) and the depth of the ROI (depth 4.4 cm) are displayed on the right side of the screen. *Lower* The ROI is defined on the cancer. The shear wave speed is displayed as X.XX m/s, which indicates a measurement error. **b** The report on shear wave speed measured with VTQ: the shear wave speed is displayed for each part. In the lower part of the screen, the median, the mean, the standard deviation, and the IQR are displayed for each part, which are updated with every measurement. **c** VTQ used for each of the head, body, and tail parts of a pancreas: if the pancreas is clearly depicted in a B-mode image, the shear wave speed can be measured in every part of the pancreas

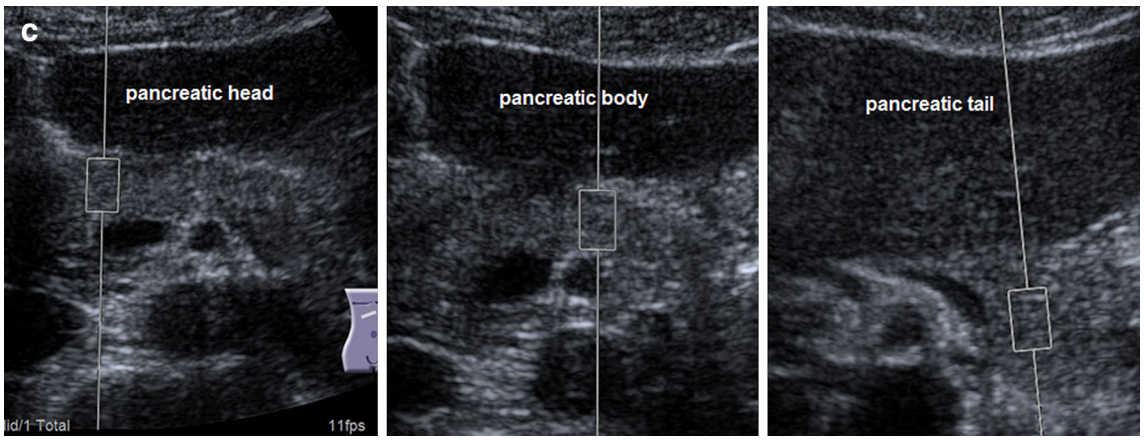



**Fig. 12** continued

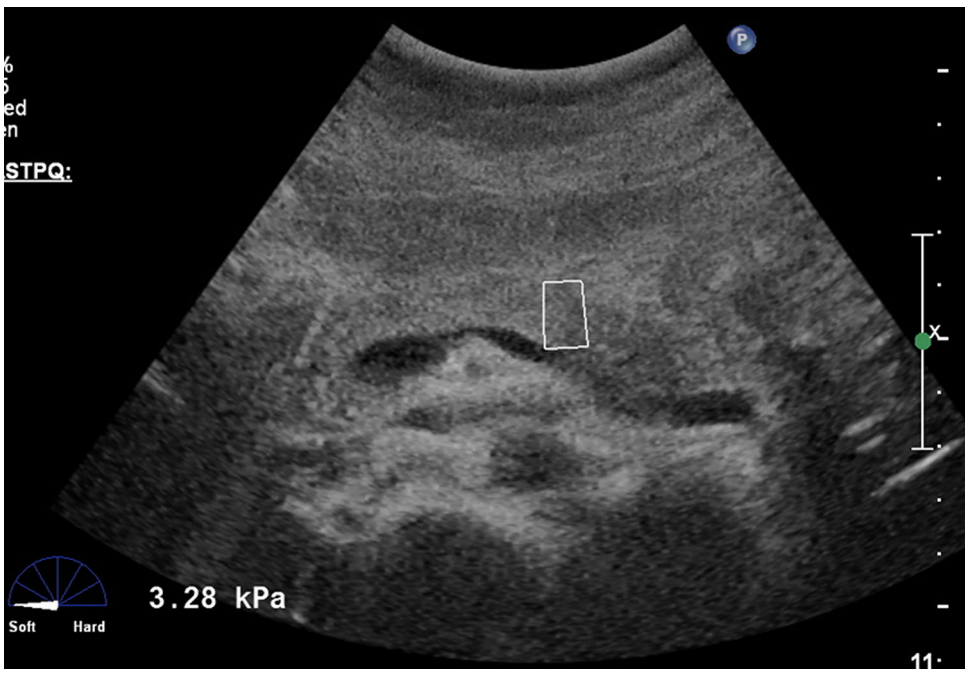



**Fig. 13** ElastPQ manufactured by Philips. ElastPQ manufactured by Philips used for a normal pancreas. The elastic modulus is displayed in the *lower right* of the screen

There have been experiences in which the difference between measured values becomes large even in the case of measurements for the same site. There is a report regarding the liver in which cases of IQR >30 % are excluded [62]. As the pancreas is a small organ deep in the body cavity, it can be understood that fluctuation may occur more frequently than in the case of the liver, and there is also a report that excludes IQR >40 % [53].

Kawada et al. [53] reported that a measurement success rate of 100 % was attained in the head, body, and tail of the pancreas with rates of 80, 83, and 68 %, respectively, and a measurement success rate of 80 % or higher was attained with rates of 100, 100, and 96 %, respectively, if the measurement success rate was defined as the rate with which a measurement was taken without an error (X.XX m/s) in 10 trials made with respect to each of the head, body, and tail parts that were depicted in the B-mode image. If the B-mode image is clearly depicted, the shear wave speed can be stably measured in each of the head, body, and tail parts (Fig. 12c).

Yashima et al. [58] reported that chronic pancreatitis was diagnosed with a sensitivity of 75 % in a comparison of 46 cases of chronic pancreatitis and 52 cases of normal pancreases if the cutoff value of the shear wave propagation velocity was set to 1.40 m/s. Kawada et al. [53] reported that pancreatic cancer patients showed a high hardness tendency in a comparison of pancreatic hardness in parts other than tumors in 18 patients with pancreatic

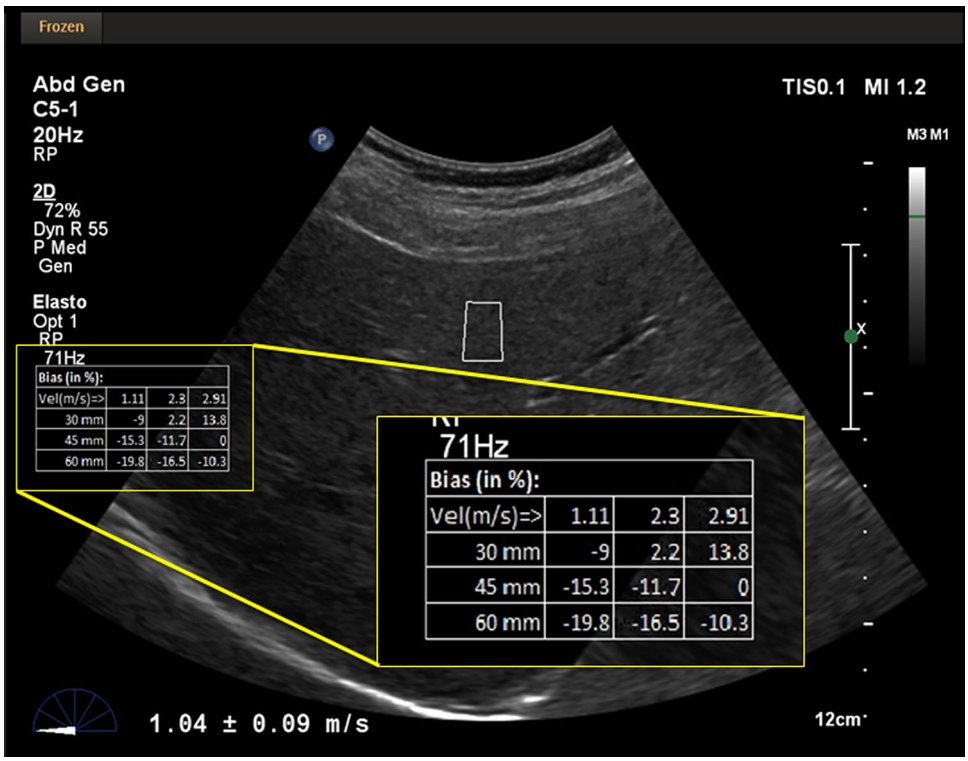



**Fig. 14** Bias of shear wave speed at different depths. A table of the bias of shear wave speed at different depths is displayed in an ElastPQ image

cancer before the start of treatment and 42 people who were not pancreatic cancer patients for the purpose of selecting a high-risk group for pancreatic cancer. A recent report noted that pancreatic cancer patients showed a high frequency of inflammatory changes such as fibrosis in a histological comparison between parts of the pancreas other than cancer parts in pancreatic cancer patients and the pancreases of people who were not pancreatic cancer patients [63]. Some reports say that there is a positive correlation between shear wave speed and the amount of (past) drinking [53, 58]. Another report says the technique is useful for the differential diagnosis of whether a pancreatic cystic tumor is mucous or serous [60].

### *ElastPQ™ (Philips)*

ElastPQ is a type of shear wave elastography that uses a method close to that of SWE and VTQ. The devices that can use ElastPQ are the iU22 and EPIQ, and the probe used in this technique is a convex probe (C5-1). The imaging method is generally equivalent to that of VTQ; i.e., a 10 mm × 6 mm ROI can be set in any target area in a B-mode image, and just by pushing a button, focused ultrasound is emitted. The average and the standard deviation for the ROI are calculated, and the elastic modulus (kPa) or shear wave velocity (m/s) is displayed in the lower part of the screen (Fig. 13). If the confidence of the measured value is low, a measurement error occurs with an indication of 0.00 kPa (m/s).

ElastPQ has a report function in which a plurality of measurement values for the same part is automatically averaged, and the mean, the median, and the standard deviation can be displayed.

The possible maximum depth of the ROI is 8 cm, but it should be noted that the values are calculated lower by a maximum of about 20 % as the measurement depth becomes deeper (Fig. 14).

With ElastPQ, the frequency of acoustic radiation force impulse can be changed in two steps, and thus it is possible to make an excellent measurement of shear wave speed even at a deep site.

There are no reports on the use of ElastPQ with respect to the pancreas, and the results of future research are hoped for.

### *Virtual Touch™ IQ: VTIQ (Siemens)*

VTIQ was put on the Japanese market in May 2012 as a version that adopted VTQ. VTIQ presents a color mapping of the shear wave speed at each point in the ROI. In addition, unlike VTQ, in which the shear wave speed in the ROI is averaged and displayed as a single value, in VTIQ an optional 2-mm square target ROI can be placed in any location in the ROI to display the shear wave speed in each target ROI (upper part of Fig. 15).

VTIQ is equipped with a quality mode that shows a color map to indicate whether an elastogram is of sufficient confidence (lower part of Fig. 15).

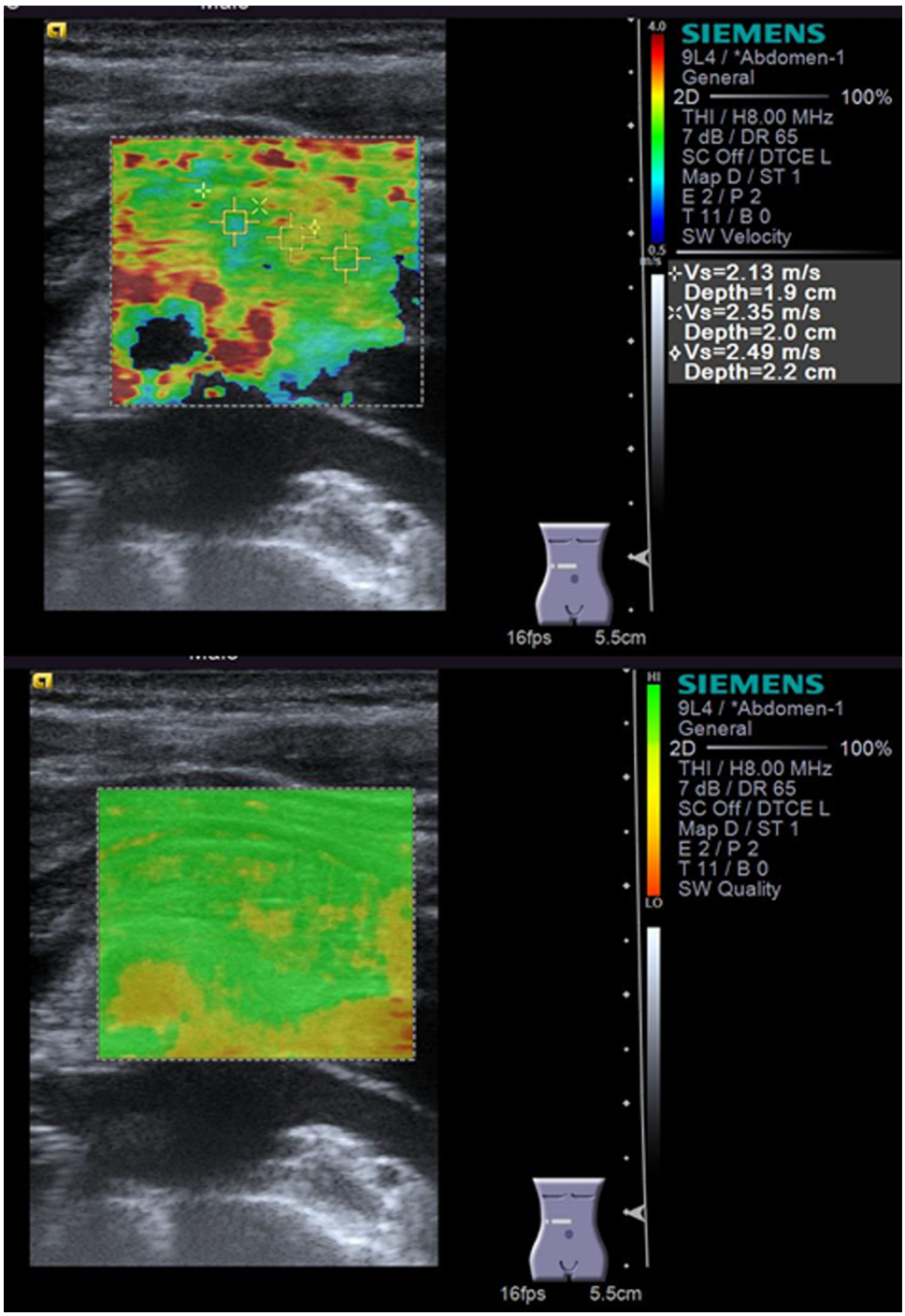



**Fig. 15** Virtual Touch IQ manufactured by Siemens used for normal pancreatitis. *Upper* The target ROI is as small as a 2-mm$^2$. The shear wave speed is displayed for any region in the ROI. *Lower*. The confidence of the elastogram in each region in the ROI is displayed in color. The closer to *green* in the color map, the higher is the confidence of the data; the closer to *red* in the color map, the lower is the confidence

At the present time, only the linear probes can be used. Future development is desired so that this technique may be used with a convex probe, which can be easily used for general-purpose observation of the pancreas.

There are no reports on cases where VTIQ was used for the pancreas, and the results of future studies are hoped for.

*Shear Wave$^{TM}$ Elastography: SWE (Super Sonic Imaging)*

In SWE, ultrasonic beams are continuously emitted to different depths in the tissue, and thus a conically shaped wave surface of shear waves is formed. The shear wave speed is measured by an ultrafast imaging method, in which all transducers are used to repeat outgoing/incoming

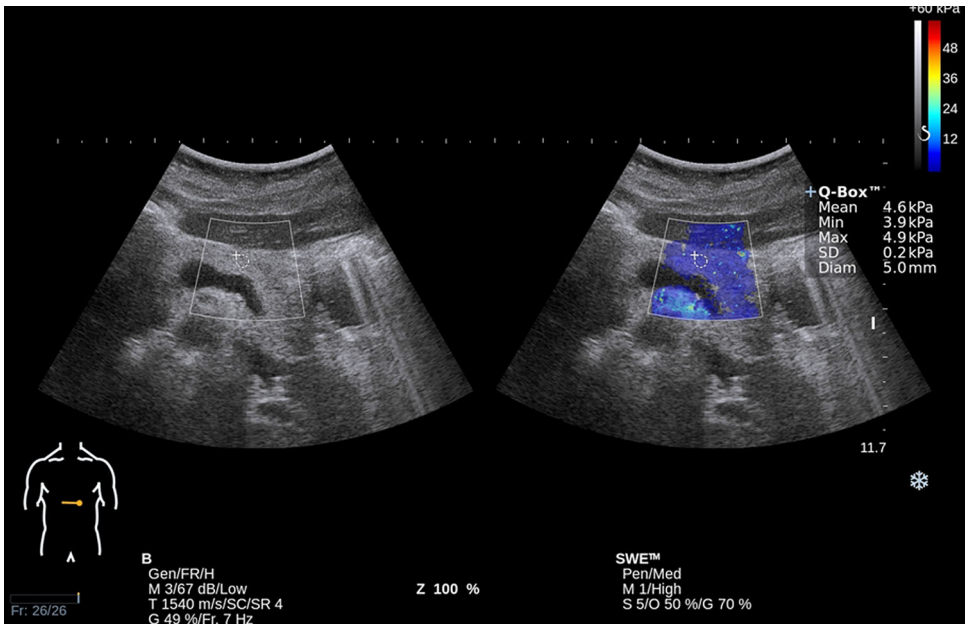



**Fig. 16** Shear Wave Elastography manufactured by Super Sonic Imaging. Shear Wave Elastography manufactured by Super Sonic Imaging used for a normal pancreas. (Courtesy of Dr. Takashi Kumada and Dr. Katsuhiko Otobe, Ogaki Municipal Hospital.)

transmissions of ultrasonic waves. The ROI is rendered to a color map according to the shear wave speed.

An ROI can be defined in any location. The mean ± SD, the minimum value, the maximum value of the shear wave speed in the ROI are displayed. It is possible to display a ratio when comparing two ROIs in different locations.

Arda et al. [64] carried out SWE centering on soft tissue for various organs in healthy volunteers; the results of their measurement of normal pancreases showed 11.1 ± 3.2 kPa for males and 10.8 ± 3.1 kPa for females.

The potential future clinical application of this technique for the pancreas is expected (Fig. 16).

## Conclusion

These guidelines presented the classifications and how to use ultrasound elastography for the pancreas and the currently available evidence as of early 2014. As described in these guidelines, the number of reports on ultrasound elastography for the pancreas is still small. No reports have been made on some devices; therefore, these guidelines did not present the methods of imaging and analysis that are recommended for each of those devices. Strain elastography with EUS has been shown to be excellent for diagnosis of the malignancy/benignancy of pancreatic tumors. Ultrasound elastography is considered to be a device that is suitable for clinical applications for the pancreas.

We expect that methods of imaging and analysis for ultrasound elastography for the pancreas will be established as the number of future reports increases and as devices are improved, and thus it will develop into an essential method for the diagnosis of pancreatic diseases.

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**Conflict of interest** None.

**Ethical standard** Human rights statements and informed consent: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from all patients for being included in the study.

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