Review Article:
ULTRASOUND ELASTOGRAPHY: DEVELOPMENT OF THE IMAGING TECHNIQUE FOR TISSUE ELASTICITY ASSESSMENT

Elysanti Dwi Martadiani
Department of Radiology
Udayana School of Medicine/Sanglah General Hospital, Denpasar, Indonesia

ABSTRACT

Difficulty in differentiate a malignant from benign tumor based on tumor stiffness or elasticity drives the founding of more advanced imaging modality. Elastography is a non-invasive method in which stiffness or strain images of soft tissue are used to detect or classify tumors. Elastography relies on imaging the strains induced in the tissue as a result of a small external mechanical compression. An important field that has emerged as complementary to ultrasonic imaging is that of ultrasound elastography. Ultrasound elastography is very helpful to differentiate cancers from benign lesions in breast, prostate, thyroid, pancreas and lymph nodes, to evaluate local strain of the arterial wall and plaques, and to measure the stiffness of the liver in vivo. It also shows good sensitivity, specificity and accuracy for evaluate malignant tumor for breast, thyroid, pancreas, lymph node and prostate.

Keywords: *ultrasound, elastography, tumor, elasticity*

Correspondence: Elysanti Dwi Martadiani, Department of Radiology, Udayana School of Medicine, Sanglah General Hospital, Denpasar, Indonesia

INTRODUCTION

Many imaging modalities for detecting tumor currently have been highly developed, such as doppler ultrasound and endoscopic ultrasound, multislice CT scanner, positron emission tomography (PET) and also various sequences of conventional magnetic resonance imaging (MRI) and functional MRI. As compared with CT scan and PET, ultrasound has the advantage that this modality does not have radiation hazard. Ultrasound is also less expensive comparing with MRI. Other benefit of ultrasound that it could display a real time imaging appearance and widely available. From several imaging modalities, ultrasound still become a first choice for assessing tumor of the specific organs such as thyroid, breast, pancreas or prostate.

In fact, occasionally some tumor gave similar appearance on conventional ultrasound (one of these is thyroid nodule), so that in this condition ultrasound could not differentiate malignant from benign tumor. In the assessment of several tumor (thyroid, prostate and breast), clinical evaluation like palpation is very important because in particular, a firm or hard consistency tumor is associated with an increased risk of malignancy. However, this clinical parameter is highly subjective and dependent on the experience of the examiner. An ambiguity also often arised when clinician and radiologist evaluate breast nodule especially for BIRADS category 3. Fine needle aspiration (FNA) biopsy is the best single test for differentiating malignant from benign lesions. But this procedure is invasive and needs time to give information about the examined tissue.

One of the clue to consider about a malignant lesion is that lesion giving harder consistency or stiffer than normal tissue or than a benign lesion. Unfortunately, no conventional imaging modality, including ultrasound, MRI or CT, can directly provide information about tissue hardness or elasticity (Emelianov et al, 2004). Founded on those conditions, many investigators seek a medical imaging technology that can estimate or assess the mechanical properties of tissues, in order to differentiate a benign tumor from a malignant one which is based on the tumor tissue elasticity.

WHAT IS AN ELASTOGRAPHY ?

In 1991, Ophir et al. used external compression methods to form strain images under static conditions and called the method elastography (Jaros) Elastography is a non invasive method in which stiffness or strain images of soft tissue are used to detect or classify tumors. When a mechanical compression or vibration is applied, the tumor deforms less than the surrounding tissue because of the strain in the tumor is less than the surrounding tissue (Wikipedia, 2008). Elastography has been applied in several imaging modalities, such as ultrasound,

magnetic resonance elastography (MRE) and computed tomography. Work over the last several years has shown that ultrasound and MRI are the preferred imaging modalities since both can exploit signal phase to sensitively track internal tissue motion. Ultrasonic imaging is the most common medical imaging technique for producing elastograms because of using ultrasound has the advantage of being cheaper and faster than MRI techniques (Emelianov et al, 2004; Wikipedia, 2008)

Elastography that has been applied in ultrasound is called ultrasound elastography (UE). Although ultrasound elastography is not yet used in routine clinical practice, it has been shown to be useful in the differential diagnosis of several cancers, especially breast and thyroid cancer (Lyshchik et al,2005) Recently, UE also has been used to differentiate cancers from benign lesions in prostate, pancreas and lymph nodes (Rago et al, 2007). UE also applied in some researches to evaluate local strain of the arterial wall and plaques (intravascular ultrasound elastography).(Jaros) The other application is transient elastography which is used to measure the stiffness of the liver in vivo (i.e., FibroScan, Echosens, France) (Wikipedia, 2008)

PRINCIPLE OF ULTRASOUND ELASTOGRAPHY

It is well known that some diseases, such as cancer, lead to a change of tissue hardness (so-called elasticity modulus) (Frey H, 2003). Changes in tissue mechanical properties that caused by exudation of fluids from the vascular system into the extra- and intracellular space or by loss of lymphatic system, as in the case of cancer, can increase the stiffness or elastic modulus of the tissue. A tumor or a suspicious cancerous growth is normally 5-28 times stiffer than the background of normal soft tissue (Wikipedia,2008).

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. 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. UE thus estimates the axial strain of the tissues along the direction of insonification/compression by tracking the tissue motion. 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 (Adrian Săftoi et al, 2006)

In practical terms, radio frequency RF ultrasonic data before and after the applied compression are acquired, and speckle tracking techniques (e.g., cross correlation methods) are employed in order to calculate the resulting strain. The resulting strain image is called elastogram, on which hard areas appear dark and soft areas appear bright (Lyshchik et al,2005; Jaros). Elasticity imaging, therefore, consists of three main components: 1) evaluation of externally induced internal tissue motion using imaging devices, 2) measurement of strain tensor components and, finally, 3) reconstruction of the spatial distribution of the elastic modulus using displacement and strain images (Emelianov et al, 2004)

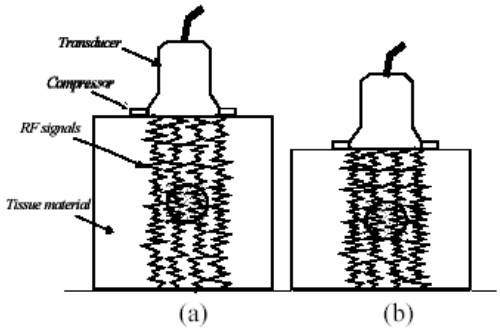

Fig. 1: The principle of Elastography: The tissue is insonified a) before and b) after a small uniform compression. In the harder tissues (e.g. the circular lesion depicted) the echoes will be less distorted than in the surrounding tissues, denoting thus smaller strain (Konofagou et al, 2003)

Hardness is directly related to the value of the shear or Young's elastic modulus. The contrast in elasticity imaging is determined by variations of Young's (or shear) modulus. The Young's moduli in biological tissues span a huge dynamic range. The differences between various soft tissues are about 5-6 orders of magnitude.(Emelianov et al, 2004) In the harder tissues (e.g. the circular lesion depicted) the echoes will be less distorted than in the surrounding tissues, denoting thus smaller strain. If one or more of the tissue elements has a different stiffness parameter than the others, the level of strain in that element will generally be higher or lower; a stiffer tissue element will generally experience less strain than a softer one (Jaros)

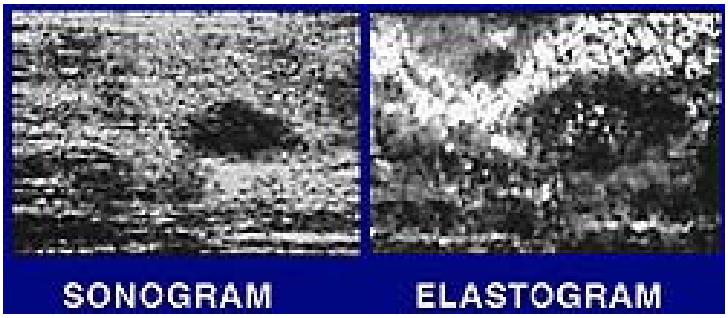

Fig. 2: These cross-sectional images were taken from a cranio-caudal scan of a breast of a volunteer patient using a modified Diasonics Spectra™ ultrasound scanner operating with a 5 MHz transducer array. The sonogram and the corresponding elastogram were taken simultaneously from the identical anatomical site. The sonogram shows the presence of a solitary hypoechoic (echo-free, or dark) lesion. The elastogram displays the hard tissues as dark, and the soft tissues as light. It shows the same lesion as being hard (typical of most breast cancers) and larger, most likely due to desmoplasia that causes hardening only around cancerous lesions. It also shows a soft core, suggestive of a necrotic center. Additionally, a second small (~6mm) lesion is detected on the elastogram at 10 o'clock relative to the main lesion. The elastogram ability to display the smaller lesion demonstrates its capability of detecting tumors in earlier stages of development (Ophir,1998)

ULTRASOUND ELASTOGRAPHY OF THE BREAST LESION

The primary goal of UE was the identification and characterization of breast lesions (Rago et al, 2007) It can provide the investigator with another characteristic, stiffness, of the lesion. Through lightly compressing of the target lesion, UE can non-invasively determine strain and elasticity distributions inside objects scanned and map the elasticity of the lesion by using a standardized color scale (Zhi et al,2007). Itoh et al first used UE to detect breast lesions and proposed the 5-point scoring system. They had higher sensitivity of UE than that of conventional sonography (Itoh et al, 2006) Thomas et al evaluated this new modality in 108 patients and found that specificity was improved from 78% for conventional sonography to 91.5% for UE (Thomas et al,2006)

Zhi et al explain that UE was performed at the same time as the sonographic examination. Because the ultrasound scanner was equipped with an elastography unit, the elasticity of a lesion could be measured by a different color. On the B-mode image, they displayed the target lesion. Then they moved the region of interest (ROI) around the lesion, making sure that the target tissue occupied no more than one third of the total area of the ROI. The probe was moved inferior and superior to obtain the elasticity images. Importantly, to obtain images that were appropriate for analysis, they applied the probe with only light pressure, with the pressure indicator bar displayed as only 2 to 3. The target lesion was scored as 1 to 5, using the scoring system proposed by Itoh et al. If a lesion was scored as 1 to 3, it would be benign; if a lesion was scored as 4 to 5, it would be malignant (Zhi et al, 2007). Itoh et al evaluated the color pattern both in the hypoechoic lesion (ie, the area that was hypoechoic or isoechoic relative to the subcutaneous fat [except for echogenic halo] on B-mode images) and in the surrounding breast tissue. On the basis of the overall pattern, they assigned each image an elasticity score on a five-point scale (Fig 3) (Itoh et al, 2006).

There is an overlap of the elasticity between benign and malignant lesions in the breast, which limits the use of UE (Hiltawsky et al, 2001) Most false-negative findings on UE were found in early stages of invasive ductal carcinoma, which were all in stages 1 and 2, and in noninvasive carcinoma, and some invasive soft tissue carcinomas such as cystosarcoma phylloides that had large central necrosis (the lesions with large central necrosis all had false-negative findings) (Stavros et al, 1995; Zhi et al, 2007) Consequently, large-scale necrosis may impair the diagnostic assessment in UE. Zhi et al reported that 9 of 209 benign lesions were misdiagnosed by UE. That rate was much lower than those for mammography and sonography, which would decrease unnecessary biopsies considerably. Among the false-positive diagnoses, 3 had calcifications, which might affect the diagnosis on UE, and 1 had a dotted remote hemorrhage that had already been organized, which may have increased the hardness of the lesion.

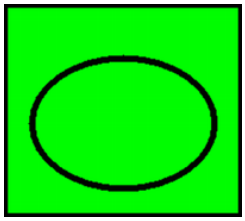

Figure 3a: Images present general appearance of lesions for elasticity score **1**. Black circle indicates outline of hypoechoic lesion (ie, border between lesion and surrounding breast tissue) on B-mode images. A score of 1 indicated even strain for the entire hypoechoic lesion (ie, the entire lesion was evenly shaded in green/bright).

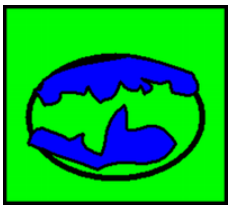

Figure 3b: Images present general appearance of lesions for elasticity score **2**. Black circle indicates outline of hypoechoic lesion (ie, border between lesion and surrounding breast tissue) on B-mode images. A score of 2 indicated strain in most of the hypoechoic lesion with some areas of no strain (ie, the hypoechoic lesion had a mosaic pattern of green/bright and blue/dark).

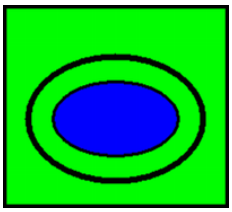

Figure 3c: Images present general appearance of lesions for elasticity score **3**. Black circle indicates outline of hypoechoic lesion (ie, border between lesion and surrounding breast tissue) on B-mode images. A score of 3 indicated strain at the periphery of the hypoechoic lesion, with sparing of the center of the lesion (ie, the peripheral part of lesion was green/bright, and the central part was blue/dark).

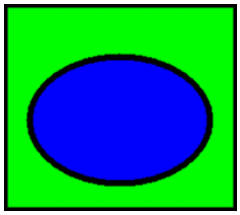

Figure 3d: Images present general appearance of lesions for elasticity score **4.** Black circle indicates outline of hypoechoic lesion (ie, border between lesion and surrounding breast tissue) on B-mode images. A score of 4 indicated no strain in the entire hypoechoic lesion (ie, the entire lesion was blue/dark, but its surrounding area was not included).

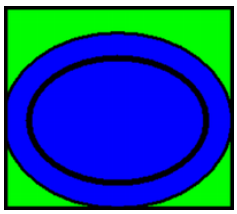

Figure 3e: Images present general appearance of lesions for elasticity score **5**. Black circle indicates outline of hypoechoic lesion (ie, border between lesion and surrounding breast tissue) on B-mode images. A score of 5 indicated no strain in the entire hypoechoic lesion or in the surrounding area (ie, both the entire hypoechoic lesion and its surrounding area were blue/dark).

Therefore, when using UE, one should pay attention to all the factors that would affect the stiffness of lesions and cause misleading results. The sensitivity, specificity, accuracy, and positive predictive value of UE improved to 89.7%, 95.7%, 93.9%, and 89.7%, respectively, which were much higher than those of mammography and sonography. In addition, the negative predictive value improved to 95.7%, which was higher than that of sonography, and the false-negative rate dropped to 8 of 87 cancers, which was much lower than those of mammography and sonography. This combination includes detection of 2 features of a lesion, morphologic characteristics and hardness, which reflect the properties of the lesion. Shape, margin, internal echogenicity, echo texture distribution, posterior echo, and a bilateral reflection sign have been shown to be valuable in the differential diagnosis of benign and malignant breast tumors (Zhi et al,2007)

When using UE to screen a lesion, there are many things to pay attention to. The first is that the area of the target lesion occupied in the ROI should be less than one third. The echo signals acquired with the ultrasound scanner are captured on an external computer and used to calculate the tissue strain with the combined autocorrelation method (Frey, 2003) This is a qualitative elasticity measurement that is relative to the average strain inside the ROI. To compare the target lesion elasticity with that of normal breast tissue, both tissue

types should be present in the ROI (Kallel et al, 1998) The second thing is that light pressure on the target lesion should be applied with the probe by hand. There is a pressure indicator on the machine, and the pressure scale should be between 2 and 3. If the pressure scale is greater than 3, it means that the pressure is too high, which causes nonlinear properties of tissue elasticity and leads to misdiagnosis (Itoh et al, 2006; Zhi et al, 2007)

ULTRASOUND ELASTOGRAPHY OF THE THYROID LESION

US examination is a very accurate and highly sensitive method for detecting thyroid gland lesions; however, its usefulness in differentiating between benign and malignant thyroid gland tumors is relatively low. For patients with thyroid gland nodules, fine-needle aspiration biopsy has proved to be an efficient tool for thyroid cancer diagnosis. Despite the advantages of fine-needle aspiration biopsy, it is an invasive procedure and subject to sampling and analysis uncertainties. Thus, improved, more reliable criteria for determining which nodules should be followed up and which should be aspirated are needed (Ross et al, 2002)

The thyroid gland is well positioned for elastographic examination because it is easily assessable and can be efficiently compressed against underlying anatomic structures by using a US probe. A report on thyroid nodules concluded that off-line processed US elastograms may predict malignancy with 96% specificity and 82% sensitivity (Lyshchik et al, 2005). US elastographic measurement was performed during the US examination, using the same real-time instrument and the same probe. The probe was placed on the neck with light pressure, and a box was highlighted by the operator that included the nodule to be evaluated. The principle of US elastography is to acquire two ultrasonic images (before and after tissue compression by the probe) and track tissue displacement by assessing the propagation of the imaging beam (Rago et al, 2007)

There are two different methods of thyroid strain imaging: (i) real-time elastography implemented on a US scanner and (ii) off-line processing of strain images reconstructed from RF data stored during US examination. Real-time strain imaging has some advantages over off-line elastography: First, it is easy to perform and requires no more than 3–5 minutes of additional examination time. Real-time elastography can be implemented on commercial US systems and used during routine US examinations. In addition, this examination allows the dynamic visualization of tumors during compression. Off-line processing of strain images involves the use of more sophisticated image-processing algorithms that increase image quality and spatial resolution. In addition, only with off-line processing was it possible to quantitatively measure the stiffness of tissue, compare the stiffness of benign and malignant tumors with the stiffness of the surrounding normal parenchyma, and use the results of these measurements for the differential diagnosis of thyroid cancer. However, this method is more labor intensive and time consuming (Lyshchik et al, 2005)

In the real-time (elasticity imaging mode) elastography (fig.4), image quality often was compromised by decorrelation artifacts caused by carotid artery pulsation and the nonaxial and out-of-plane movements of the thyroid gland under compression. Subcutaneous fat appeared as a very bright (soft) band in the upper part of the elastogram and was markedly different from the underlying muscles, which were much darker (harder). The anterior, posterior, and medial surfaces of the thyroid gland were easily distinguishable from the surrounding structures in most cases. However, the tissue along the lateral margin of the thyroid gland was almost always obscured by motion artifacts caused by pulsation of the carotid artery. The lower 10–15 mm of the elastogram was not clearly seen because of a substantial amount of noise due to the low signal amplitude at this depth.

The off-line processed elastograms of the normal thyroid gland were characterized by higher contrast resolution and somewhat lower spatial resolution. This was because the correlation window used to process the off-line-mode elastograms was larger than that used to process the real-time elastograms. Consequently, subcutaneous fat and the upper layers of the anterior neck muscles were not visualized on the off-line processed elastograms. Like the real-time images, the off-line processed images also had substantial amounts of decorrelation noise near the carotid artery and in deeper parts of the image (Lyshchik et al, 2005). Study by Rago et al classified the elasticity of the thyroid tissue using elasticity score (Table 1). The highest elasticity scores, indicative of a greater nodular consistency, were invariably associated with malignancy with minimal loss of sensitivity (specificity 100%, sensitivity 97%) (Rago et al, 2007)

Table 1. Elasticity score

1: Elasticity in the whole nodule
2: Elasticity in a large part of the nodule
3: Elasticity only at the peripheral part of the nodule
4: No elasticity in the nodule
5: No elasticity in the nodule and in the posterior shadowing

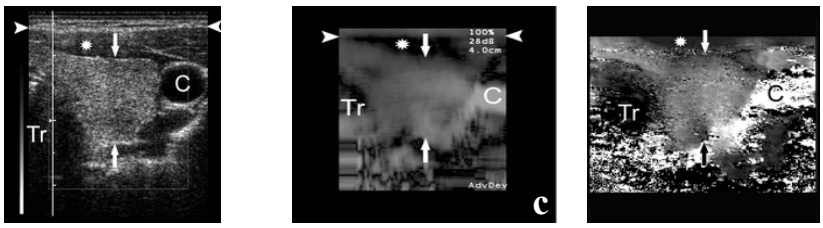

Fig 4: (a) Transverse B-mode sonogram, **(b)** real-time elastogram, and **(c)** off-line processed elastogram obtained in 31-year-old man show a normal left thyroid gland lobe without lesions. Anterior and posterior borders (arrows) of thyroid gland, subcutaneous fat (arrowheads in **a** and **b**), anterior neck muscles (*), carotid artery *(C),* and trachea *(Tr)* are seen (Lyshchik et al,2005)

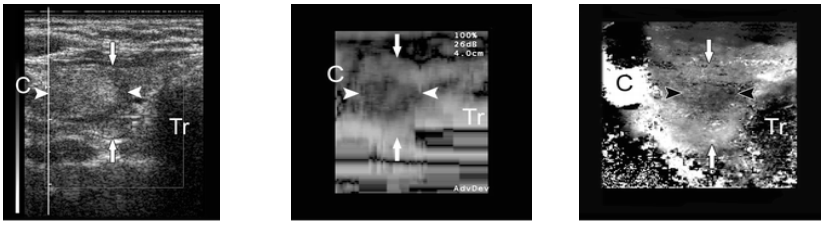

Fig. 5: (a) Transverse B-mode sonogram, **(b)** real-time elastogram, and **(c)** off-line processed elastogram obtained in 54-year-old woman with a solid benign isoechoic thyroid gland tumor (arrowheads) in the lateral segment of the right thyroid gland lobe. In **b**, the tumor is partially visible; it is markedly darker than the surrounding normal thyroid gland tissue and has an irregular, barely distinct margin. In **c**, the tumor is somewhat visible; it is slightly darker than the surrounding normal thyroid gland tissue and has a very irregular, almost indistinct margin (Lyshchik et al,2005).

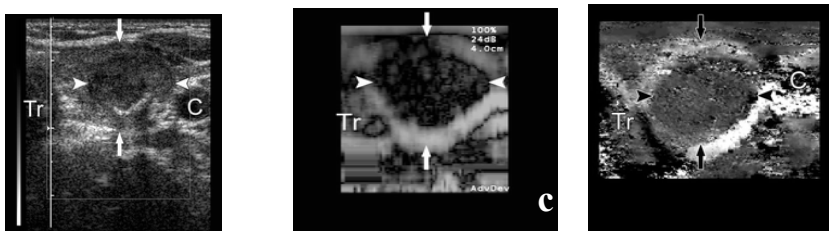

Fig. 6: (a) Transverse B-mode sonogram, **(b)** real-time elastogram, and **(c)** off-line processed elastogram obtained in 48-year-old woman with papillary thyroid carcinoma (arrowheads) in the central part of the left thyroid gland lobe. In **b** and **c**, the tumor is highly visible; it is very dark compared with the surrounding normal tissue and has a regular and distinct margin.

Conventional US maintains a pivotal importance to define which nodules are suitable for the US elastographic characterization. Indeed, nodules in which US reveals the presence of calcified shell have to be excluded from the US elastographic evaluation because the US beam does not cross the calcification, and the probe compression does not result in tissue strain deformation. Similarly, in cystic nodules, US elastography cannot give useful information, the main determinant of nodule stiffness being the fluid content, and not the solid wall. Further studies will be necessary to understand whether US elastographic measurements can give reliable results in nodules that are greater than 20% cystic. One other limitation of this technique is that the nodule to be examined must be clearly distinguishable from other nodules present in the thyroid, to select it for the US elastography measurement. Thus, multinodular goiters with

coalescent nodules in most cases are not suitable for this analysis (Rago et al, 2007)

Diagnostic performance of US elastography will greatly depend on the quality of the freehand compression data acquired and on the specifications of the image reconstruction algorithm used. In thyroid gland elastography, two main sources of noise can be pinpointed: (i) Pulsation of the carotid artery: a substantial decrease in decorrelation noise on the elastograms are seen in patients who had big thyroid gland nodules and in whom the carotid artery was not in direct contact with the thyroid gland, so that the thyroid are not easily affected by carotid artery pulsation; (ii) out-of-plane motion of the examined lesion under compression: the anatomy surrounding the thyroid gland consists of numerous movable structures like the trachea and the jugular vein, so it is difficult to restrict the movement of the thyroid gland to the imaging plane (Lyshchik et al, 2005)

ULTRASOUND ELASTOGRAPHY OF THE PROSTATE

Elastography can detect prostate cancer foci within the prostate with good accuracy and has potential to increase ultrasound-based prostatic cancer detection. For prostatic UE, the patient was scanned in the dorsosacral position and the prostate was manually compressed with a transrectal ultrasonic probe. The echo signals from inside the tissue were measured before and after the tissue compression and an elastogram was generated by spatially differentiation of the displacement distribution (Miyanaga et al, 2006). Salomon et al reported that sensitivity and specificity for detecting prostatic cancer were 75.4% and 76.6%, respectively. A total of 439 suspicious areas in elastography were recorded, and 451 cancerous areas were found in the radical prostatectomy specimens. Positive predictive value, negative predictive value, and accuracy for elastography were 87.8%, 59%, and 76%, respectively (Salomon et al, 2008) The other study has shown that elastography successfully detected 93% of the untreated prostate cancer lesions. Detection of cancer lesions using elastography was significantly higher than by digital rectal examination (59%) and transrectal ultrasonography (55%) (Miyanaga et al, 2006)

ENDOSCOPIC ULTRASOUND (EUS) ELASTOGRAPHY

Endoscopic ultrasound (EUS) represented a major advance in the diagnosis and staging of gastrointestinal malignancies. In addition to providing imaging of tumours and enhancing TNM staging, EUS also provides guidance for fine needle aspiration (FNA) and biopsies of undiagnosed masses and lymph nodes suspicious for malignant invasion, providing further diagnostic and staging information. However, FNA is technically demanding and multiple punctures of lymph nodes or masses are sometimes required to obtain sufficient tissue for histologic assessment. In addition, when several lymph nodes appear suspicious, the choice of which to puncture is not always clear. The ability to more accurately evaluate masses and lymph nodes prior to their puncture in an effort to aid in targeting lesions for FNA and possibly reduce complications would be welcomed by echo-endoscopists. At least two strategies have been developed with these goals in mind, contrast enhanced endosonography and elastography (Giovannini, 2007)

Endoscopic ultrasound (EUS) elastography is an imaging procedure used for the visualization of tissue elasticity during usual EUS examinations. 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. Routine use of EUS elastography offers supplemental information that enhances conventional EUS imaging, with a possible decrease in the number of unnecessary EUS-FNA procedures used for tissue confirmation (Săftoiu et al, 2006; Uomo, 2008). 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 (Săftoiu et al, 2006).

Săftoiu et al were able to differentiate between benign and malignant lymph nodes with a high sensitivity, specificity and accuracy (91.7 %, 94.4 % and 92.86 %, respectively), based on five pre-defined patterns obtained on EUS elastography (Săftoiu et al, 2006). Uomo concluded that EUS elastography represents a promising method which allows characterization and differentiation of a normal pancreas, Positive predictive value, negative predictive value, and accuracy for elastography were 87.8%, 59%, and 76%, respectively The positive and negative predictive values were 88.9% and 90.6%, respectively (Uomo, 2008).

The main pitfall of EUS elastography is represented by the impossibility to control tissue compression by the

EUS transducer. 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 (Săftoiu et al,2006). 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 (Săftoiu et al,2006)

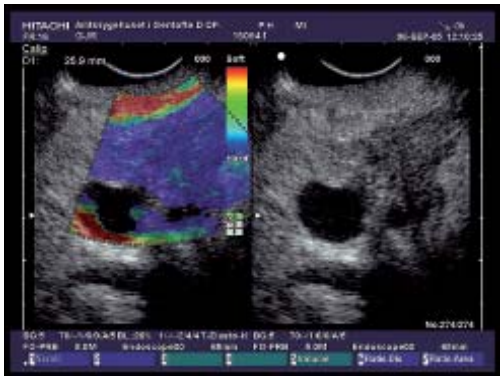

Fig. 7: Large pancreatic tumor of the pancreatic head depicted by conventional EUS as a hypoechoic mass, with irregular borders and invasion of the portal vein. EUS elastography image shows the tumor as a hard structure (blue) on the left panel (Săftoiu et al,2006)

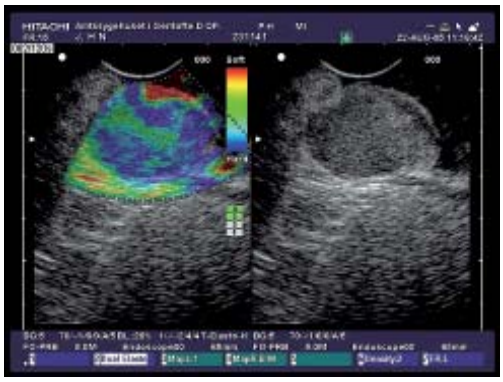

Fig.8: EUS elastography appearance of a 3 cm, benign gastrointestinal tumor (GIST), with inhomogeneous hardness (blue-green) (Săftoiu et al,2006)

TRANSIENT ELASTOGRAPHY FOR EVALUATING LIVER FIBROSIS

Liver fibrosis is characterized by the accumulation of an extracellular matrix, which distorts the hepatic architecture. The major etiologies of liver fibrosis are viral-associated hepatitis, alcohol abuse, non-alcoholic steatohepatitis and autoimmune disease. The progression of liver fibrosis increases the stiffness of liver and the resistance of liver blood flow. An insufficiency of liver blood flow results in liver failure and eventual liver cirrhosis (Kawamoto et al, 2006). Liver biopsy is still the gold-standard method for assessing liver fibrosis. However, it is difficult to perform liver biopsy for all patients who need to be assessed repeatedly due to its invasiveness and prohibitive cost. In addition, biopsy samples are usually

too small to diagnose the disease accurately and diagnostic opinions often differ among pathologists.

Recently, transient elastography (FibroScan®: Echosens, Paris, France) has become available for the assessment of liver fibrosis as a rapid noninvasive method, which can measure liver stiffness from outside of the body (Kawamoto et al, 2006) Briefly, this system is equipped with a probe consisting in an ultrasonic transducer mounted on the axis of a vibrator. A vibration of mild amplitude and low frequency is transmitted from the vibrator to the tissue by the transducer itself. This vibration induces an elastic shear wave that propagates through the tissue. In the meantime, pulse-echo ultrasonic acquisitions are performed to follow the propagation of the shear wave and measure its velocity, which is directly related to the tissue stiffness (or elastic modulus). The harder the tissue, the faster the shear wave propagates (de Ledinghen et al, 2006) The test usually takes less than 15 minutes in total. FibroScan can be used as an initial screening tool to reduce the number of patients requiring liver biopsy and also to measure ongoing response to treatment. In some patients the initial screening results may be sufficiently well-defined to provide a confident assessment of the patient's stage of liver fibrosis.(National Horizon Scanning Centre,2008). Kawamoto et al reported thet the diagnostic accuracy of FibroScan for livers with more than 20% fibrosis area was higher than that for livers with 10% fibrosis area, and optimal cut-off level for FibroScan was 13.6 kilopascal (kPa), which could thus distinguish livers with more than 20% fibrosis area.(Kawamoto et al,2006)

INTRAVASCULAR ULTRASOUND ELASTOGRAPHY

The composition of an atherosclerotic plaque is an important determinant for clinical syndromes. Determinants of ruptured plaques are a large lipid core covered by a thin fibrous cap with a dense infiltration of macrophages. Although some promising invasive and noninvasive techniques are being developed, no technique is currently clinically available to identify these vulnerable plaques. Intravascular ultrasound (IVUS) has proven to be a powerful technique to assess the geometry of the vessel wall and plaque. However, the sensitivity and specificity to detect lipid cores remains low (de Korte, 2002) Intravascular ultrasound elastography is a technique that assesses the local strain in the artery wall and plaque. Although this modality is still in research and needs more investigation, it is very promising to give a helpful information to the clinician and radiologist.

For intravascular purposes, the compression can be obtained from the systemic pressure difference that is already available in intravascular applications. Additionally, well-controlled deformation is possible by using a transducer positioned in a compliant intravascular balloon (Jaros). An ultrasound image of a vessel-phantom with a hard vessel wall and a soft eccentric plaque is acquired at a low pressure . In this case, there is no difference in echogenicity between the vessel wall and the plaque resulting in a homogeneous IVUS echogram. A second acquisition at a higher intraluminal pressure (pressure differential is approximately 5 mmHg) is performed. The elastogram (image of the radial strain) is plotted as a complimentary image to the IVUS echogram. The elastogram reveals the presence of an eccentric region with increased strain values thus identifying the soft eccentric plaque (Jaros).

The elastograms of invitro experiment using specimens taken from excised human femoral arteries showed that the strain in fatty tissue is higher than the strain in fibrous material.(de Korte et al, 2002) A study using Yucatan pig reported that elastography has a high sensitivity to identify fatty material: A maximum sensitivity of 100% with corresponding specificity of 80% was achieved when the threshold was set at a mean strain in the plaque of 0.35% (de Korte et al, 2002)

CLINICAL APPLICATION OF ULTRASOUND ELASTOGRAPHY IN INDONESIA

So far, there is still no report about clinical application of ultrasound elastography in Indonesia. This could be because of not many hospitals has equipped with this new imaging modality, and some types of ultrasound elastography are still investigated so that it has not been use for routine clinical application. Although some kinds of ultrasound elastography have been available in some hospitals, those still need socialization and training, so that radiologist and clinician can be familiar with the equipment.

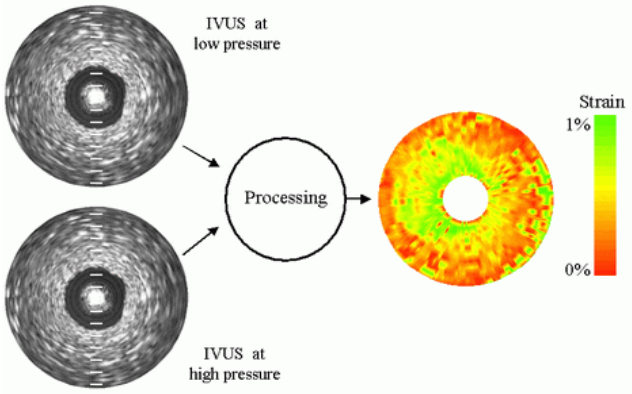

Fig. 10: Echogram (left) and elastogram (right) of a vessel mimicking phantom containing an isoechoic soft lesion between 7 and 11 o'clock. The lesion is invisible in the echogram, while it is clearly depict in the elastogram.

SUMMARY

Ultrasound elastography is very helpful to differentiate cancers from benign lesions especially in the breast, prostate, pancreas and lymph nodes; evaluate fibrosis area in the liver, also assessing strain of arterial wall and arterial plaque. For breast lesion, the sensitivity, specificity, accuracy, and positive predictive value of UE were 89.7%, 95.7%, 93.9%, and 89.7%, respectively. For thyroid lesion, US elastograms may predict malignancy with 96% specificity and 82% sensitivity. Positive predictive value, negative predictive value, and accuracy for elastography of prostatic tumor were 87.8%, 59%, and 76%, respectively. EUS elastography has a high sensitivity, specificity and accuracy (91.7 %, 94.4 % and 92.86 %, respectively) to differentiate between benign and malignant lymph nodes. Positive predictive value, negative predictive value, and accuracy for elastography for pancreatic masses were 87.8%, 59%, and 76%, respectively. From those datas, it seems that ultrasound elastography is a promising technique that might improve the characterization and differentiation between benign and malignant masses based on the tissue elasticity. But its application in local use in Indonesia is still need more training and socialization.

REFERENCES

Anonym. Elastography. Retrieved: January 5, 2009, from http://en.wikipedia.org/wiki/Elastography

de Korte CL, Sierevogel MJ, Mastik F; Strijder C, Schaar JA, Velema E, et al.,2002. Identification of atherosclerotic plaque components with intravascular ultrasound elastography in vivo. Circulation. 105:1627-1630

de Ledinghen V, Douvin C, Kettaneh A, Ziol M, Roulot D, Marcellin P, et al., 2006. Diagnosis of Hepatic Fibrosis and Cirrhosis by FibroScan, Transient Elastography, in HIV/Hepatitis C Virus-Coinfected Patients. JAIDS Journal of Acquired Immune Deficiency Syndromes 41(2):175-179

Emelianov SY, Aglyamov SR, Shah J, Sethuraman S, Scott WG, Schmitt R, et al., 2004, Combined ultrasound, optoacoustic and elasticity imaging. Retrieved: January 8, 2009, from http://www.bme.utexas.edu/research/pil/papers/Emelianov_Photonics West 2004.pdf.

Frey H, 2003. Real time elastography: a new ultrasound procedure for the reconstruction of tissue elasticity. Radiologe 43:850–855.

Giovannini M, 2007. Endoscopic ultrasound (EUS) elastography. Retrieved: January 8, 2009, from http://www.hitachi-medical.co.jp/medix/pdf_sup/sup_09.pdf.

Hiltawsky KM, Kruger M, Starke C, Heuser L, Ermert H, Jensen A, 2001. Freehand ultrasound elastography of breast lesions: clinical results. Ultrasound Med Biol 27: 1461–1469.

Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, 2006. Breast Disease: clinical application of US elastography for diagnosis. Radiology 239:341-350

Jaros J, Ultrasound elastography. Retrieved: January 2, 2009, from (http://physics.uku.fi/opiskelu/kurssit/LUT2/elastography.pdf)

Kallel F, Ophir J, 1998. Limits on the contrast of strain concentrations in elastography. Ultrasound Med Biol 24:1215–1219.

Kawamoto M, Mizuguchi T, Katsuramaki T, Nagayama N, Oshima H, Kawasaki H, et al. 2006. Assessment of liver fibrosis by a noninvasive method of transient

elastography and biochemical markers. World J Gastroenterol July 21; 12(27): 4325-4330.

Konofagou EE, et al, 2003. Elastography: From theory to clinical applications. Summer Bioengineering Conference, June 25-29, Florida, 2003.

Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Mai JJ et al, 2005. Thyroid gland tumor diagnosis at US elastography. Radiology 237:202-211

Miyanaga N, Akaza H, Yamakawa M, Oikawa T, Sekido N, Hinotsu S, et al., 2006. Tissue elasticity imaging for diagnosis of prostate cancer: a preliminary report. Int J Urol. Dec;13 (12): 1514-8.

National Horizon Scanning Centre , 2008. Transient elastography (FibroScan) for evaluating liver fibrosis. Retrieved: January 11, 2009, from http://www.pcpoh.bham.ac.uk/publichealth/horizon/outputs/documents/2008/april/Fibroscan.pdf

Ophir J, 1998. New medical imaging technique improves chances of early cancer detection. Retrieved: December 27, 2008, from www.algor.com/news_pub/cust_app/cancer/cancer.asp

Rago T, Santini F, Scutari M, Pinchera A, Vitti P, 2007. Elastography: new developments in ultrasound for predicting malignancy in thyroid nodules. The Journal of Clinical Endocrinology & Metabolism 92(8): 2917-2922.

Ross DS. 2002. Nonpalpable thyroid nodules: managing an epidemic. J Clin Endocrinol Metab 87:1938–1940.

Săftoiu A, Vilmann P, Hassan H, Gorunescu F. Analysis of endoscopic ultrasound elastography used for characterization and differentiation of benign and malignant lymph nodes. Ultraschall Med. 2006 Dec;27(6):535-42.

Săftoiu A, Vilman P, 2006. Endoscopic ultrasound elastography – a new imaging

technique for the visualization of tissue elasticity distribution. J Gastrointestin Liver Dis 15(2): 161-165.

Salomon G, Köllerman J , Thederan I ,Chun F, Budäus L, Schlomm T, et al., 2008. Evaluation of prostate cancer detection with ultrasound real-time elastography: a comparison with step section pathological analysis after radical prostatectomy. European Urology 54(Issue 6):1354 - 1362.

Stavros AT, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA, 1995. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. Radiology 196:123–134.

Thomas A, Fischer T, Frey H, R. Ohlinger R , Grunwald S, Blohmer J.-U et al., 2006. Real-time elastography—an advanced method of ultrasound: first results in 108 patients with breast lesions. Ultrasound Obstet Gynecol; 28:335–340.

Uomo G, 2008. Ultrasound Elastography: A possible improvement of the paraphernalia of pancreatic imaging. JOP. J Pancreas (Online) 9(5):666-667.

Zhi H, Ou B, Luo B, Feng X, Wen Y, Yang H, 2007. Comparison of ultrasound elastography, mammography, and sonography in the diagnosis of solid breast lesions. J Ultrasound Med 26:807-815.