Learning objectives

Tissue strain techniques represent an Imaging approach aiming to depict - besides anatomical details - mechanical properties of tissues.

A lot of interest is arising and many methods have been used to try to investigate elastic modulus and to create stress-strain maps. Understanding the different categories they are divided and how they work is an useful tool to help finding new applications.

Background

For centuries clinicians used palpation to evaluate organs; now, after exploring almost all different methods of interaction of ultrasound, x-ray and magnetic fields with tissue in order to express anatomical maps, interest is arising in evaluating mechanical properties of tissues, i.e. viscoelastic characteristics (Fig. 1 on page 7). This is the field of the so-called tissue strain Imaging techniques, while the term "sonoelastography" is usually used to describe the techniques using steady state excitation methods (see below).

Generally speaking they work in a similar way: information is obtained through the application of a force inducing a modification to a tissue which is closely related to its elasticity. The way information concerning elasticity are expressed is different; it can be either a color or a gray-scale map or it can be a number (Fig. 2 on page 8).

A first classification can be made considering the Imaging technique used to measure tissue displacements: most methods are ultrasound-based techniques but magnetic resonance can be used as well.

A) US-BASED METHODS

Two main techniques belong to this group: quasi-static and dynamic methods. In the former methods the distribution of the elastic modulus of the target tissue is inferred through the observation of stress and strain, in the latter through the velocity of the shear waves generated in the tissue.

1 - **Quasi-static methods** share a similar way of working and a similar way of analyzing data. Accurate and precise estimation of the local displacements of tissue with high spatial resolution and high signal-to-noise ratio is required.
To deduce elasticity from stress and strain, in these methods a known stimulus is applied to the target, radio-frequency data are collected and compared to pre-stimulation data (Fig. 3 on page 9) using different algorithms - the simplest being the classical time-delay technique then evolved to more complicated cross-correlation algorithm.

The cross-correlation algorithm between post and pre-compression A-lines is used to obtain an estimation of the local strain (Fig. 4 on page 9). The stress is evaluated considering the applied stress vs. the theoretical stress distribution, in order to obtain an estimation of the local axial stress. Stress/strain gives the local Young's modulus, which can be expressed as elastogram (Fig. 5 on page 10).

One of the problems when dealing with quasi-static methods is that the target tissue must be locally homogeneous because boundaries can have marked effects on the distribution of applied stresses and this can make it problematic to quantitatively image them, giving rise to inaccurate results.

Quasi-static methods can be divided in three categories considering the stimulus which can be applied to the tissue.

a) **Low-frequency excitation**: in this category are found those methods utilizing low-frequency deformation (on the order of 1-10 Hz) to perturb tissue. Since the frequencies are low they do not generate shear waves and can be considered quasi-static in nature.

b) **Steady state excitation**: techniques using a steady state excitation using the ultrasound transducer represent some of the most commonly utilized approaches to elastographic imaging. Steady-state quasi-static deformations have been applied using either under stepper motor control (with the transducer held in a fixture) or freehand compression using the transducer. This is the most-frequently use method of tissue excitation and is usually referred as "sonoelastography".

c) **Steady state physiological excitation**: physiological stimuli due to respiratory, cardiac muscle deformations and cardiovascular sources have been used for elastographic imaging. Physiological deformation sources, however, introduce challenges due to non-uniform deformations caused and need for gating of the data to obtain reproducible results.

2- **Dynamic methods** are based on the detection and tracking of shear waves resulting from mechanical vibration of the tissue (Fig. 6 on page 11). The algorithm used is the time to peak algorithm.

The main problem consisting with dynamic methods is that the shear waves undergo rapid attenuation.
Two main categories can be identified, on the basis of the applied stimulus:

a) **External methods (i.e.: Transient Elastography):** a mechanical push from a piston is used to launch a compression wave into the tissue. The transient distortion of the tissue generates a shear wave that travels laterally away from the line of the compression push in a three-dimensional pattern and the movements of the tissue are visualized by an interrogating ultrasound beam. This produces a line on the monitoring screen whose slope indicates the speed of movement of the shear wave which is related to the Young's modulus.

b) **Internal methods (i.e.: Acoustic Radiation Force Imaging Technique; Supersonic Shear Wave Elastography):** after selecting a range of interest on a gray-scale map an acoustic push pulse is focused directly to it, inducing the generation of the shear waves. The shear waves travel perpendicular to the ultrasonic beam and undergo a rapid attenuation. But before it happens tracking beams are sent to the tissue, parallel to the main axis, continuously until the passing shear wavefront is detected. Different algorithms are used to calculate the shear wave velocity (SWV) and thus the elastic modulus.

**B) MAGNETIC RESONANCE-BASED METHODS**

The principle of MR elastography is very similar to that of sonoelastography. High-frequency vibrations are applied externally to the tissue to induce the generation of shear waves. Tissue displacements are then correlated with the phase shift of the magnetic resonance signals and data are then processed to relate these displacements to mechanical properties.

Several factors can affect the results obtained using MR-based elastography, including the frequency of tissue excitation, tissue temperature and the direction of wave propagation and polarization.

**C) CLINICAL APPLICATIONS**

Since disease is often related to increased tissue stiffness without specific changes in ultrasound b-mode features, many attempts have been made in order to obtain additional information using tissue-strain techniques.

1) **Static techniques**
Among the quasi-static techniques the most used is the steady-state quasi-static excitation, obtained using the transducer to perturb the tissue.

The first and main application to date are in the field of breast and musculoskeletal imaging but interesting results have also been obtained in the evaluation of lymph nodes and - with endocavitary approach - of prostate as well. Results obtained from applications on thyroid nodules are less fair.

a) The normal sonoelastographic pattern of tendons (especially Achilles tendon) has been accurately evaluated in their whole extension and is now well known. It is characterized by a hard homogeneous or relatively homogeneous pattern (Fig. 7 on page 12) whereas the ruptured tendons are characterized by a less-hard, highly heterogeneous structure (Fig. 8 on page 13).

b) Normal fibroglandular breast tissue is markedly stiffer than the normal fatty breast tissue which makes it appear harder on elastographic scans; findings can vary considering the phase of menstrual cycle (Fig. 9 on page 14) and the intake of oral contraceptives. Non considering the cysts - whose b-mode features are typical - sonoelastography may help in the characterization of focal breast masses, included non-palpable lesions. Generally speaking the malignant breast lesions (Fig. 10 on page 14) are stiffer than the benign lesions, like fibroadenomas; invasive ductal carcinomas are much stiffer than any other breast tissue.

c) The results in the evaluation of thyroid nodules are quite contradictory. Malignant nodules are harder than benign nodules (Fig. 11 on page 15, Fig. 12 on page 15) but - according to a recent review - the sensitivity, specificity and positive predictive values are still too low to consider it as an alternative to fine needle aspiration cytology, although sonoelastography can be considered a useful tool.

d) The evaluation of cervical lymph nodes metastases (Fig. 13 on page 16) has been related to interesting results. Metastatic lymph nodes are characterized by a harder pattern and the intra-observer correlation is good.

e) Since its higher cell density than normal tissue, prostate cancer is well-suited to sonoelastographic evaluation. This technique not only allows better depiction and characterization of prostatic nodules but it is proven that real-time elastography-targeted biopsy allows cancer detection in men with PSA values between 1.25 and 4 ng/ml.

2) Dynamic techniques
Methods based on the tracking of however generated shear waves are the subject of rising interest, especially due to their capability of quantifying tissue stiffness.

**a) Transient elastography** is used to evaluate liver stiffness, which is related to fibrosis stage, and according to two recent meta-analyses - has shown high accuracy in the diagnosis of liver cirrhosis. It has several limitations due to patients' overweight and narrow intercostals spaces. Additional problems are its low accuracy in diagnosing significant fibrosis and poor reproducibility for both low and high stiffness values. Unlike the other dynamic techniques transient elastography does not give an anatomical overview to the liver (Fig. 14 on page 17).

**b) ARFI** is a new promising technique which is under investigation in many fields.

- As concerning with the **liver** it is showing results very similar to what has been found for transient elastography. SWV values show a significant positive correlation with the severity of fibrosis, also when dealing with children. Multiple measurements must be taken and mean SWV must be evaluated (Fig. 15 on page 18).

**Spleen:** Spleen stiffness has been investigated as a complementary tool in the assessment of chronic liver disease. As expected as a consequence of portal stasis and hypertension, obtained values are higher as parenchymal hepatic disease worsens and portal hypertension grows (Fig. 16 on page 19).

Some authors attempted to establish a cut-off value of splenic stiffness able to predict the risk of variceal bleeding.

**Pancreas:** Few reports have been published concerning normal and pathological ARFI findings. In normal controls results are slightly different when considering head, body and tail (Fig. 17 on page 19).

Chronic pancreatitis is characterized by higher SWV (Fig. 18 on page 19).

**Prostate:** Preliminary data have been published concerning the possibility of discriminate prostate cancer from benign prostate hyperplasia, which show promising results.

SWV are significantly higher in prostate cancer and benign prostatic hyperplasia than in normal prostate (2.37+/-0.94; 1.98+/-0.82 vs.1.34+/-0.47).

**Thyroid:** mean values obtained from healthy controls are 1.70+/-0.39 for the right lobe and 1.63+/-0.35 for the left lobe. Goiter and thyroiditis are associated with higher values.
(2.03+/−0.48 and 2.29+/−0.78 respectively). Thyroid malignancies are related to a twofold increase of the values of the SWV (Fig. 19 on page 20 a-c).

- **Breast**: ARFI has proven useful in many reports in the evaluation of solid breast masses: malignant lesions are characterized by a SWV significantly greater than the SWV found in benign masses (5.96+/−2.96 vs.2.25 +/−0.59).

  **c) Supersonic shear wave** is only at the beginning, although experimental bases and preliminary results are promising.

- According to preliminary results supersonic shear wave imaging can measure the stiffness of breast tissue, providing highly reproducible qualitative and quantitative data. In detail adding the supersonic shear wave elastographic features to BI-RADS feature analysis improves specificity of breast US mass assessment without loss of sensitivity (Fig. 20 on page 20).

- Supersonic shear wave is a promising tool to evaluate histological deterioration in renal transplants. The level of cortical stiffness is correlated with the global degree of tissue lesions although it is not closely related with the level of interstitial fibrosis (Fig. 22 on page 22).

- Data about diagnostic performances of supersonic shear wave elastography in assessing liver fibrosis are controversial. According to some studies it is more accurate than transient elastography in assessing significant liver fibrosis (> F2), other researchers concluded that data are not yet sufficient to consider it as an alternative to transient elastography. It gives the advantage of providing an imaging evaluation of the parenchyma. Evaluated liver stiffness increases in parallel with the degree of fibrosis.

- Evaluation of cervical lymph nodes has showed that malignant nodes are significantly stiffer than benign nodes, although more studies are needed to confirm these results (Fig. 23 on page 23).

**Images for this section:**
• Young’s Modulus: is the constant of proportionality between stress and strain. Units are the same as stress (i.e. force per unit area) and the most commonly used are are psi, Pa (Pascal), kPa and MPa

• Stress: is defined as force per unit area

• Strain: is the change in length per unit length. Computed as \((L_f - L_0)/L_0\) where \(L_f\) is the final length and \(L_0\) is the initial length

Fig. 1
Fig. 2: Tissue strain techniques share the same way of working: a force (manual or external compression, ultrasound beam) induces a modification to a tissue which is closely related to its elasticity. This gives us certain information which can be expressed either as a color/gray scale map or as a number.

Fig. 3: In quasi static methods a known stimulus is applied to the target and radio-frequency data are collected and compared to pre-stimolation data.
**Fig. 4:** Pre and post compression signals are compared. The early windowed blue segment shows no compression (=no delay) while the later orange segment exhibit distorted RF signal with short delay which is the basis for computing the stress.
**Fig. 5:** Stress/strain gives the local Young’s modulus, which can be expressed as elastogram. Harder tissues are expressed as blue ones, softer tissues as red ones and intermediate areas are expressed in green.
**Fig. 6:** Dynamic methods (ARFI, Supersonic Shear Wave Elastography) work in a similar way (i.e. tracking the shear waves generated by acoustic push pulses). The shear waves travel perpendicular to the exploring ultrasound beam. Their speed depend on the elastic properties of the area, and they undergo rapid attenuation. Before it happens tracking beams are sent parallel to the ultrasonic beam in order to detect the passing shear wavefront. The time between the generation of the shear wave and the detection of the peak is used to calculate velocity.
Fig. 7: Healthy tendons are characterized by a hard (blue) homogeneous or relatively homogeneous (blue-green) pattern
Fig. 8: The ruptured tendons are characterized by a less-hard, highly heterogeneous structure, with elastograms ranging from blue (hard) to red (soft).

Fig. 9: a, b: Breast stiffness vary depending on the different phases of the menstrual cycle. During the menstrual phase the color is green; during the luteal phase the color is mainly blue due to the higher stiffness of the parenchyma.
**Fig. 10:** a-c: malignant breast lesions (c) are stiffer than the benign lesions, like fibroadenomas (b); simple cysts exhibit a homogeneous soft pattern (a)(courtesy of Dr S.Vasori).

**Fig. 11:** Malignant nodules are harder than benign nodules, as it happens in this goiter where the elastogram gives low-stiffness values.
Fig. 12: Since cancer is expected to be harder than benign nodules scars can give hard-tissue misunderstanding signal as it happens in thyroiditis.
**Fig. 13:** Metastatic lymph nodes are characterized by a pattern of the "hard" type.
**Fig. 14:** Transient elastography does not give imaging data but it expresses information giving an elastographic curve whose stepness is directly related to liver stiffness and expressed in kPa.
Fig. 15: ARFI is an interesting non invasive tool in the evaluation of chronic liver disease. SWV values show a significant positive correlation with the severity of fibrosis (a: normal liver, b: liver fibrosis).

Fig. 16: Spleen stiffness can be used in the global assessment of portal hypertension. As expected as hypertension grows (b) SWV grows too.

Fig. 17: a-c: Results obtained from pancreatic gland are slightly different if measured from the head (a), the body (b) and the tail (c).
Fig. 18: SWV measured in chronic pancreatitis are higher than in normal pancreas.

Fig. 19: a-c: When compared with benign nodules (a) thyroid malignancies are characterized by higher values (b: follicular cancer; c: papillary cancer).
**Fig. 20:** According to preliminary results shear wave elastography is highly reproducible and malignant lesions are characterized by harder tissue.
Fig. 21: Shear wave elastogram of a renal transplant. The regions of interest are positioned in the cortex (opencircle) and the medulla (dashed circle) using the B-mode image. The level of cortical stiffness is correlated with the global degree of tissue lesions although it is not closely related with the level of interstitial fibrosis.
**Fig. 22:** Shear wave elastogram of a reactive lymph node: it shows homogeneous blue colour elasticity signal. When considering quantitative information the Q-box has QboxMean 15.8 kPa and QboxMax 22.9 kPa.
Fig. 23: Shear wave elastogram of a metastatic lymph node showing heterogeneous-high signal areas. When considering quantitative information the mean (QboxMean) and maximum (QboxMax) value of the Q-box was 187.6 kPa and 239.5 kPa, respectively.
Imaging findings OR Procedure details

Tissue strain Imaging can be divided in two categories: quasi static and dynamic methods

1) **Quasi static methods** use a known applied stimulus (usually manual compression but it can be also external vibration) to induce a perturbation of the tissue. Images acquired before and after compression are compared using different algorithms (cross-correlation algorithms) to calculate stress/strain maps.

2) **Dynamic methods** can use external vibration (transient elastography, MR elastography) or internal excitation (ARFI, Supersonic Shear Wave Elastography) in order to generate shear waves which travel across the tissue and whose speed depend on the elastic properties of the area. Tracking beams are used to calculate this speed which allows calculation of tissue stiffness.

Conclusion

Tissue strain imaging is a rapidly-expanding field which shows interesting results. Besides the most known and utilized quasi-static US-excitation, showing the best results especially in the evaluation of tendons, dynamic techniques are gaining interest, thanks to their ability to depict different tissue density also as numbers, as it happens for ARFI Imaging and the new-arrived Supersonic Shear Wave Imaging.

When everything will be understood about their way of interacting with in-vivo tissues, many obstacles will be overcome in order to understand what lies behind the traditional gray-scale Imaging.

References


**Personal Information**

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