ELASTOGRAPHY, PROGRESSION FACTOR IN LIVER ULTRASOUND

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ELASTOGRAPHY, PROGRESSION FACTOR IN LIVER ULTRASOUND (ABSTRACT): Elastography is a method which, using ultrasound, obtains images and measurements of tissue elasticity when applying a force on it. As an imaging method it was developed to quantify objectively the pathological changes related to the presence of an abnormal tissue, compared to the surrounding tissues, giving information about the elasticity/stiffness of the examined tissue, the degree of fibrosis, the degree of stiffness compared to tumor free tissue. The tissue analysis can be done through a compression technology "eSie touch elasticity imaging" (with applications for the surface elastography) or ARFI technology – “acoustic radiation force imaging” (the diffusion impulse of the acustic force). The ARFI method allows valid, accurate and flexible evaluation of liver stiffness and it is correlates with the fibrosis stage. The liver elastosonography, through new technologies available, has reached the level of the fibroelastocaster and magnetic resonance imaging. The ultrasound elastography application quickly advances, starting with the researches in this field. At present, it has analysed the most various fields of application, from the breast, prostate, thyroid, pancreas imaging to the study of abdominal lymphnodes and peripheral vessels, gastrointestinal stromal tumors, primary and secondary liver tumors, the evaluation of uterine cervix, from cardiology to gastroenterology and urology, both in adults and in pediatrics. Key words: ELASTOGRAPHY, ULTRASOUND EVALUATION, IMAGING METHOD.  

The ultrasound evaluation is a non invasive, unpainful, repetitive investigation method which allows to have a good exploration of the tissues and organs, especially in children, where the patient’s compliance is different from the adult’s, often much lower.

Beside the simultaneous multichannel processing of information, the panoramic and harmonic ultrasound, the elastography is a new way of representing the ultrasound information, a noninvasive evaluation concept of tissues nature (1,2). The method consists of applying a longitudinal pressure on a tissue and displacement measuring reflectance of the tissue nuclei. The representation of these displacements through colors, allows an information extract, which, in the end, facilitates the differentiation with high probability of benign from malignant tissue (2).

The method initially started and deve-
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veloped as applications on breast, but now it has applications in liver, prostate, thyroid, abdominal lymphnodes, peripheral vessels, myocardial and other directions of clinical application (3).

The ultrasound elastography refers to ultrasound methods which can produce images or measurements of tissue elasticity - the ability to resist deformation, deformations of tissues to the application on its strengths. The force applied to the tissue can be of several types (4):

- the force applied by the ecografist’s hand;
- the force applied by an external mechanical device;
- the force given by the physiological movements of the human body - breath, the cardiac activity, pulsed movements of large arteries;
- the force applied by a certain ultrasound issued by the ultrasound probe which makes the exploration itself.

The response to the application of this force will vary according to the tissue elasticity.

The elastography as an imaging method was developed in order to objectively quantify the pathological changes related to the presence of an abnormal tissue, compared to the surrounding tissues (5). This new method of diagnosis gives informations related to the elasticity/stiffness of the examined tissue, degree of tissue fibrosis (eg. pre-stage liver cirrhosis), respectively the degree of stiffness of a tumor tissue compared to the free one, with promising results to differentiate between benign and malignant lesions or in assessing the tissue changes over time (4).

The manual palpation or the subjective “palpation” through ultrasounds was used for many years in order to give a qualitative assessment of the tissue stiffness, but the need to obtain a direct image led to the development of elastography (4).

The mechanical properties of the soft tissues which depend on their content, include elastic modulus (Young’s modulus), Poisson’s report and the shear properties of the tissue. These properties totally differ from the elastic modulus which governs the propagation of the ultrasounds. For example, the normal breast tissue is stiffer than the one made of fibroadenoma, and the breast cancers have shown how to shear up to seven times higher than in the normal tissue. The imaging potential resulted from this high contrast led to the development of some ultrasound investigation methods (4).

For these different approaches there have been developed:
1. The application of low frequency vibration energy and concomitant Doppler detection of the wave disturbance;
2. Image of local response to a load applied to estimate the parameters by direct comparison between pre and post data compression;
3. The calculation of these parameters.

This new ultrasonographic diagnosis method is not available using the conventional sonographic image and it represents the most important development in the ultrasound technique since the appearance of the Doppler images. The information related to the tissue stiffness is complementary and independent of the information related to the acoustic impedance provided by the B-mode image (grayscale) and the one related to the vascular flow provided by the Doppler in age. Technically described since the last decade, the method was introduced just at the beginning of 2008, as an application of the latest ultrasound devices which include a wide range of analytical applications related to tissue strain or request and which allow visual qualitative and quantitative measurements of the tissue stiffness/elasticity (6).

The extent of the tissue analysis can be done by two different technologies:
- Compression elastography “eSie touch elasticity imaging” (with applications
for the surface elastography – Real time exploration especially the breast. The acquisition of radiofrequency (RF) signals during compression or because movements of inspiration/expiration, allows obtaining images generated by the tissue tension, which is proportional with its stiffness (4);

• An other example is ARFI – “acoustic radiation force imaging” (the diffusion impulse of the acoustic force) in which an acoustic impulse is triggered in the tissue in order to assess/interrogate the mechanical properties of the tissue stiffness/elasticity. The waves propagate like waves sideways when throwing a stone in the water. It has 2 possibilities of evaluation:
  - Virtual touch tissue imaging – a method through which a diagram of the tissue stiffness is obtained, with a gray scale (reverse as the classical examination 2D);
  - Virtual touch tissue quantification - through which it is appreciated the speed of the transverse propagation of the waves triggered, allowing the quantification of the tissue elasticity.

The ARFI method does not impose a certain degree of compression on the tissue, done by the examiner and which can vary (by hand fatigue), but it takes over the patient’s respiratory movements, which means rhythmic and constant movements.

By means of the elastography using compression it can assess just the superficial tissues, while with the ARFI method the tissue elasticity can be assessed starting with a depth of 1.5 cm up to 8 cm.

Unlike the conventional sonography B-mode which gives us anatomical details based on differences in the acoustic impedance, the Virtual Touch image describes properties referring to the tissue stiffness. In this respect, the Virtual Touch image is closer to a tissue evaluation through a physical palpation than through the conventional ultrasound evaluation.

There are three steps in the process of Virtual touch acquisition:
• First an ultrasound image B-mode is obtained;
• Then in a very short time (approximatively 100 microseconds) a push impulse is given;
• The issued impulse produces a displacement force, depending on the tissue’s properties where it moves (so, in a soft tissue the waves move quickly, but in a stiff tissue it moves less or not at all). After the pushing pulse stops, the tissue relaxes and returns to its original shape. The captured ultrasound waves at a time are compared with the reference image, thus calculating the tissue displacements resulted from the pushing force (6).

VIRTUAL TOUCH TISSUE IMAGING (VIRTUAL TOUCH)

An image of the Virtual Touch soft-ware is actually a qualitative gray-scale map of the relative tissue stiffness (elastograma) for a user defined ROI (the region of interest). This information is calculated by examining the relative displacement of the tissue elements due to an acoustic pulse push. Thus, on elastograma the shining regions correspond to the tissue which is more elastic (less stiff) and the dark regions correspond to the stiff tissue.

If an image of the Virtual Touch soft-ware and a conventional image in B-mode are displayed together, the apparent limits of the tissue can differ, because the production of images is done through different mechanisms (6).

THE ADVANTAGES OF THE VIRTUAL TOUCH SOFT

The elastography methods previously available needed manual compression of the tissue or were based on the physiological needs of the body (cardiac activity, respiratory movements, and so on). These approaches
could limit the depth of the image location and easing the artifacts.

The application of the Virtual Touch soft allows an image by the independent combination of the multiple axial lines, obtained from the information of the tissue dislocation, starting with the left axial line within ROI, the tissue being described through a conventional ultrasound signal. Then, a push impulse is applied along this line, the captured conventional radiation being applied along the same line in order to obtain the signal of the dislocated tissue. Thus we can calculate the differences in tissue position every point along the axial line, between relaxation and compression (6).

The calculated differences are related to the maximum tested at a spatial location of tissue due to the tissues elastic properties in that area. The more elastic a tissue is, the bigger its dislocation is. The process above is repeated for each axial line within ROI as it is with a conventional B-mode scanning. Finally, all the calculated dislocations all over ROI are transformed in elastograma, describing the relatively tissue stiffness.

Generally, the stiffer the tissue is, the bigger the wave velocity is as it passes through this region. Overall, the measured speed of the wave is an intrinsic tissue property, which can be reproduced. The cut waves are generated and pass the tissue perpendicular, as some small waves resulted by throwing a pebble in a pond. In contrast with the classical ultrasound waves axially oriented, the cut waves do not interact directly with the convertor. Besides this, unlike the conventional ultrasound waves, the cut waves are attenuated approximately 10,000 times faster and thus needing a higher measurement sensitivity. Still, as the wave which is cut in front passes through the tissue, the generated dislocations are detectable, using ultrasound captive waves. Observing the front wave in more locations, and correlating these measurements with the past tense, the speed of the cut wave can be quantified (6).

**VIRTUAL TOUCH TISSUE QUANTIFICATION**

The ARFI technology can be used to measure a numerical value of the wave speed, by implementing the Virtual Touch tissue quantification.

For the Virtual Touch tissue quantification, first, it is identified an anatomical area using a ROI situated on a conventional image obtained through ultrasounds. An impulse of acoustic pushing is applied laterally, inducing a wave-cut which goes through ROI. The captured radiation, sensitive to more than 1/100 sound wave length, is applied adjacent to the push impulse. These radiations are continuously transmitted until the wave cut front is detected. The time between the cut-wave generation and the peak detection is used to calculate the speed of the cut wave. Multiple measurements are done for a given spatial location, for the reported value to ensure the quality measurement (6).

The tissue image and the Virtual Touch quantification is the first and the only implementation of the acoustic radiation image generated by the pulse force, which can be used with the conventional ultrasound in researches about the density and elasticity of the liver tissue. By this way, the previous elastography evaluations which were difficult and with variable results, become correct and practical (6).

It is important the fact that the technique of the Virtual Touch programme brings new information about the tissue, which can be used for diagnosis and in the therapeutic clinical applications.

**CLINICAL APPLICATIONS OF THE ELASTOGRAPHY**

The researches related to the ultrasound elastography quickly advances and the techniques utility too. At present, it is analysed in the most various fields, from cardiology
to urology and gastroenterology, in adults and children too. Elastography begins trial in clinical practice and as a tool for cancer diagnosis (7).

Elastography was used in different studies to obtain images in vivo of the prostate and in the breast imaging, to view the elasticity of different tissues and to determine different degrees of stiffness, being able to distinguish the malignant tumor tissue from the benign tumor tissue. The researchers managed to classify correctly the lesion of the prostate using this technique (8,9).

The usefulness of this technique has been interested also in the exploration of malignant tumors of the cervix and thyroid (10,11,12,13,14,15).

Elastography may be used in transvaginal ultrasound assessment of the female pelvis (16). There are only a few reports in the literature on the in-vivo use of real-time transvaginal elastosonography in the field of gynecology, being a promising tool that can provide detailed mapping and characterization of uterine fibroids, that could improve the gynecological ultrasound evaluation of size, volume and delineation of uterine fibroids before surgery or embolization (16,17).

The combination of elastography with highly sensitive conventional B-mode sonography has the potential to further improve the diagnosis of metastatic enlarged cervical lymphnodes (18).

Thyroid elastography is useful to make a correct differential diagnosis between malignant and benign thyroid nodules (10,11,12,13,14,15).

This method of ultrasound exploration is used in the evaluation of superficial lymphnodes stiffness, too (10,11,12,13,14,15).

USING ELASTOGRAPHY IN HEPATOLOGY

Elastography of the liver through new technologies available, has become comparable to fibroelastoscanner (for assessing liver fibrosis) and to the nuclear magnetic resonance.

Normal liver tissue is soft and flexible. With inflammation, however, many of the cells die and are replaced by collagenous fibrils and the tissue gets stiffer. The process is often slow-extending over decades in many cases. Precise, noninvasive measurement of liver stiffness, a simple application of elastography, promises to be a safe, inexpensive method to monitor the progress of liver patients (19).

Real-time elastography is a noninvasive method based on use of ultrasound promising in preoperative assessment of liver fibrosis in chronic hepatitis, in nonalcoholic fatty liver disease (NAFLD) and in cirrhosis (20,21).

Elastography imaging of the small liver nodules in cirrhosis might be used as a non-invasive tool for accurate diagnosis, as well as selection of patients for curative therapy, but not for screening. Its utility in patients with non-vascularised nodules, can help to eliminate the false negative diagnosis of contrast enhanced imaging of the liver and to improve their outcome. Real-time elastography is a promising sonography-based noninvasive method for the preoperative assessment of liver fibrosis both in liver diseases with considered fibrosis and in cirrhosis, having a highly sensitivity and specificity. It is considered fibrosis if the media of 3-5 successively determinations in the same area is over 2 (21,22).

Real-time elastography is a promising method for the non-invasive diagnosis of early hepatocarcinoma. Blue color at elastography and hypervascular aspects are independent predictors of hepatocarcinoma (22,23).

THE ARFI ELASTOGRAPHY METHOD IN HEPATOLOGY

The new ultrasonographic method of ARFI
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elastography allows valid, accurate and flexible evaluation of liver stiffness. Elastography of the left liver lobe is also possible which may be especially helpful in obese patients (24).

ARFI allows SWV quantification (SWV-shear wave velocity), in strong correlation with the fibrosis stage. Steatosis does not influence SWV (24,25). The maximal performance of the method consists of the prediction in severe fibrosis and cirrhosis. The diagnostic accuracy is strongly comparable to transient elastography only for the prediction of severe fibrosis and cirrhosis, whereas for earlier stages, TE performs better (25).

Both ARFI and TE have excellent predictive values in the presence of the cirrhosis, even if the liver elasticity determined by TE better correlates with the histological fibrosis in patients with chronic liver disease HCV and HBV (with hepatitis C, respectively B), compared to the values obtained through ARFI (26).

ARFI elastography has very good accuracy for the assessment of liver fibrosis and is superior to other noninvasive methods (APRI Index, FibroMax) for staging liver fibrosis (27).

Images obtained with ARFI elastography provided additional qualitative information regarding the stiffness and tumor margin of liver tumors. By measuring shear wave velocity, the quantification of stiffness was made possible and showed the potential to differentiate malignant hepatic tumors from hepatic hemangiomas (28).

CONCLUSION

Using conventional real-time ultrasound equipment with modified software (for example virtual touch tissue imaging, virtual touch tissue quantification și eSie touch elasticity imaging), elastography has been reported to be useful for differentiation and characterization of various malignant tumors, such as breast, prostate, thyroid, pancreas, lymphnodes, gastrointestinal stromal tumors, primary and secondary liver tumors, the evaluation of uterine cervix (23).

REFERENCES

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