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Ultrasound elastography and contrast-enhanced ultrasound in infants, children and adolescents

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ABSTRACT

Objective: To describe prerequisites, use, and safety of ultrasound elastography and contrast-enhanced ultrasound in infants, children, and adolescents.
Method: This review deals with two latest developments in ultrasonography in children. The principle of strain elastography, transient elastography, and acoustic radiation force imaging is discussed, including limitations, and advantages of the different techniques in diagnosing focal and diffuse organ disease. The intravesical (contrast-enhanced voiding ultrasonography) and intravascular use of contrast-media to outline blood, and urinary flow is described, with special emphasis on indications, off-label use, and diagnostic gain. Examples of indications for performing the advanced ultrasound techniques are presented.
Summary and conclusion: Latest developments in ultrasound machine engineering, and the availability of contrast-media that interact with ultrasound waves allow for assessment of tissue stiffness/elasticity properties, blood, and urinary flow. Thereby ultrasound is capable not only to depict morphology, but gives the additional information on organ, and focal lesion perfusion, and urinary flow dynamics. The information gap to other cross-sectional techniques such as magnetic resonance imaging, that make potential harmful sedation, and anaesthesia in the youngest children necessary, thereby gets closer.

1. Elastography in children

Palpation is well known technique in medicine; one of its tasks is to determine whether a mass is hard or soft in comparison to the neighbourhood. But it is a subjective method and there are difficulties with deep lesions. Elastography is an ultrasound (US) technique that provides a noninvasive and pain-less assessment of tissue stiffness; it can be performed in a real-time US examination. This modality has the ability to assess subtle changes across the entire organ but also focal lesions. Diseases which involve fatty or collagenous deposits increase or decrease tissue elasticity [1]. Numerous studies have used different elastography techniques to measure the stiffness in adults. These studies were predominantly performed in the liver to evaluate hepatic fibrosis and cirrhosis which are known to significantly reduce the elasticity of the liver. Other organs have also been evaluated including the thyroid, prostate, breast, pancreas, kidneys including transplanted kidneys, and lymph nodes. Little is known up to now about the usefulness of elastography in children.

The term “elastography” describes metrics used to measure mechanical properties of biological tissues, and their pictorial representation. The stiffness of a lesion or a material will be measured by stretching the material with a defined force. A graph of the change in length divided by the original length (strain) is then plotted against the force per unit area (stress) [2]. The ratio of stress/strain is called the Young’s modulus [3] (Table 1).

The majority of currently available methods are based on an external force [4]. In strain elastography the subject is stressed by a force generated by an external mechanical impulse or endogenous stress like physiological motion (cardiovascular movement pulsation, breathing). A semiquantitative index of stiffness (strain ratio) may be estimated by comparing the strain within the lesion (region of interest – ROI) to the strain of an adjacent reference region [5,6]. The reduction in stress with increasing depth is a limitation of strain elastography, which means that lesions in a depth of more than about 5 cm are not compressed sufficiently to be visualized on the strain image [2]. Transient elastography (TE) is a method developed only for liver diagnosis. Without B-mode control a low-frequent vibration push (50–500 Hz) will be transmitted over an intercostal space by a piston which is mounted with a single-

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Table 1
Young's modulus for organic and non-organic material.

Material	Young's modulus
Diamond	1220 GPa
Wood (oak)	11 GPa
Cortical bone	10 kPa
Healthy soft tissue	0.5–70 kPa
Liver	0.4–6 kPa

element US transducer (FibroScan®, Echosens, Paris, France). TE is limited in patients with adipositas or in patients with a very narrow intercostal space or with ascites. In acoustic radiation force imaging (ARFI) a high mechanical index pulse produces itself displacement of particles up to 20 μm across the direction of travel. The resulting shear waves travel much more slowly than US waves (1–10 m/s) [7,8]. Measuring shear wave velocity (SWV) must be cautiously performed because it is sensitive to mechanical and functional parameters such as external pressure, vascularization, vascular pressure, and anisotropy [9,10]. Schenk et al. could show that there is no direct correlation between real-time elastography and transient elastography [11]. So, it cannot be recommended to transfer results between different elastography techniques; cut-off values are system-specific and cannot readily be compared across different machines [12].

An overview of all the available techniques is given in Fig. 1.

2. Potential indications for elastography in children

Focal lesions

Based on the known of high stiffness in malignancies this technique can be used in focal lesions to differentiate between healthy tissue and a malignant lesion. Most often the free-hand technique with linear transducers will be used for compression elastography. An important feature is that malignant lesions may appear larger on the elasticity map than on the fundamental B-mode image [13]. In the evaluation of focal testicular lesions tissue elastography allows detailed evaluation of the cellular texture [14,15]. For example, in seminoma, a hard lesion can be clearly visualized by strain elastography; also in embryonal cell carcinoma (blue in colour scale) whereas segmental testicular infarction, inflammation, and hematoma are "soft" (red/green on colour scale). In abscesses a heterogeneous pattern can be found. There were also studies for evaluation of the efficacy of sonoelastography in differentiating benign and malignant focal thyroid, parotid and other salivary gland lesions in children and adults [16,17]. The data are very variable regarding sensitivity and specificity in differentiating malignant from benign lesions, ranging from 73% to 98% and 71% to 100%, respectively [18–20]. Shear wave elastography is also used for the evaluation of cervical lymph nodes. Malignant nodes were stiffer (median 25 kPa; range 6.9–278.9 kPa) than benign nodes (median 21.4 kPa; range 8.9–30.2 kPa); but there was a large overlap [21]. And potentially elastography could be helpful to differentiate between acute inflammation with a decrease in bowel wall stiffness and chronic, fibrotic alterations of the thickened bowel wall which should be associated with increased stiffness [22,23].

Fig. 2 shows focal thyroid inflammation in strain imaging, Fig. 3 shows shear-wave elastography of the liver.

Diffuse tissue changes

The assessment of diffuse liver disease is important for prognosis and therapeutic management, especially in patients suffering from chronic diseases which may alter the liver architecture. Cystic fibrosis or α-1-antitrypsin or metabolic disease deficit are typical paediatric examples. Liver biopsy is up to now the "gold-standard" for fibrosis assessment and classification. Transient elastography (TE) using the Fibroscan is presently the best-studied technique for liver elastography using an impulse which is emitted directly through the skin in an intercostal approach in the midclavicular line of the transducer. For children a probe with a smaller diameter (S-probe) can be used. There are reference values for TE in children for different age groups (0–4 years 4.4 kPa, 6–11 years 4.73 kPa, 12–18 years 5.1 kPa) [24]. Numerous studies could demonstrate a good correlation between TE and histological degree of fibrosis [25–29]. For the ARFI approach, the examiner has to choose a ROI in the right lobe of the liver with an intercostal or subcostal access. A real-time B-scan is used for placement of the ROI to avoid disturbing structures like large intrahepatic vessels or the liver capsule. Evaluation is obtained with free breathing or apnea depending on whether

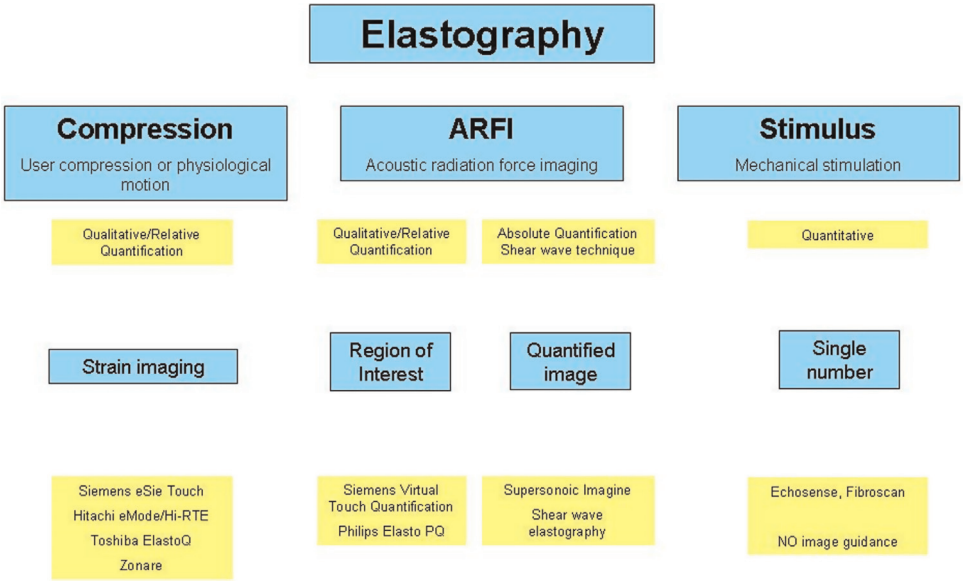

Fig. 1. Ultrasound elastography methods.