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● *Original Contribution*

QUANTITATIVE ASSESSMENT OF BREAST LESION VISCOELASTICITY: INITIAL CLINICAL RESULTS USING SUPERSONIC SHEAR IMAGING

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Abtract—This paper presents an initial clinical evaluation of *in vivo* elastography for breast lesion imaging using the concept of supersonic shear imaging. This technique is based on the combination of a radiation force induced in tissue by an ultrasonic beam and an ultrafast imaging sequence capable of catching in real time the propagation of the resulting shear waves. The local shear wave velocity is recovered using a time-offlight technique and enables the 2-D mapping of shear elasticity. This imaging modality is implemented on a conventional linear probe driven by a dedicated ultrafast echographic device. Consequently, it can be performed during a standard echographic examination. The clinical investigation was performed on 15 patients, which corresponded to 15 lesions (4 cases BI-RADS 3, 7 cases BI-RADS 4 and 4 cases BI-RADS 5). The ability of the supersonic shear imaging technique to provide a quantitative and local estimation of the shear modulus of abnormalities with a millimetric resolution is illustrated on several malignant (invasive ductal and lobular carcinoma) and benign cases (fibrocystic changes and viscous cysts). In the investigated cases, malignant lesions were found to be significantly different from benign solid lesions with respect to their elasticity values. Cystic lesions have shown no shear wave propagate at all in the lesion (because shear waves do not propage in liquid). These preliminary clinical results directly demonstrate the clinical feasibility of this new elastography technique in providing quantitative assessment of relative stiffness of breast tissues. This technique of evaluating tissue elasticity gives valuable information that is complementary to the B-mode morphologic information. More extensive studies are necessary to validate the assumption that this new mode potentially helps the physician in both false-positive and false-negative rejection. (E-mail: Mickael.tanter@espci.fr) © 2008 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Elastography, Ultrasound, Breast, Cancer, Acoustic radiation force, Shear wave imaging.**

INTRODUCTION

Today, breast cancer remains a major public health problem. It has the highest morbidity incidence for women, with an estimated 1 million new cases per year and 478,000 deaths per year worldwide. X-Ray mammography, which is the "gold standard" examination for breast cancer screening, relies on a sensitivity that is appropriate for fatty breasts but less accurate in dense breasts. Dense breast have a high proportion of glandular tissue that is difficult to discern on mammography. The specificity of mammography remains moderate, leading to many false positives and useless interventions for lesions proven *a posteriori* to be benign by histology (Kolb 2002; Sardanelli 2004).

Other imaging techniques such as ultrasound (US) and magnetic resonance imaging (MRI) also possess limits. Ultrasound is strongly operator dependent. Dynamic MRI with the injection of contrast agents has a high sensitivity for breast cancer detection (>90%) but suffers from a mediocre specificity, typically 50–80% according to the type of cancer (Kuhl 2007). Consequently, although it is strongly subjective, the act of manual palpation remains today a major procedure for the clinical examination and is included in the workflow of breast screening. In Greek ancient ages, physicians practiced palpation of body parts to determine tissue

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stiffness. They knew that a hard deformed mass within an organ was often related to the presence of an abnormal lesion. Today, palpation is not only useful for screening and diagnosis but also during interventions to effectively guide the surgeon toward the pathologic area. It is well known that breast cancer lesions tend to feel harder during palpation than benign breast masses. However, this difference is subjective and is often difficult to assess. Therefore, it can be suggested that a quantitative imaging of local hardness heterogeneities may provide a more accurate discrimination of cancers from benign masses. Nevertheless, it must be kept in mind that some fibroadenomas can be very stiff and some cancers (necrotic or mucinous subtype) can be quite soft (Samani 2007).

In the last 15 years, various techniques based on the use of ultrasound (Ophir 1991; Parker 1992; Skovoroda 1995; Levinson 1995; Fatemi 1998; Nightingale 2001; Bercoff 2003) or MRI (Muthupillari 1995; Chenevert 1998; Kruse 2000; Sinkus 2000, 2005a, 2005b; Plewes 2000) have been developed by various research teams to quantitatively measure the local mechanical response of tissues under external stress. All proposed approaches are based on the same three-phase methodology: (i) organs are mechanically stressed by either external or internal forces, (ii) tissue movement induced by these forces is measured with ultrasound or MRI and (iii) elastic properties of tissue are estimated quantitatively or qualitatively from the measured displacements of tissue.

A pioneer in this field, static elastography (Ophir 1991,1996, 2000; Konofagou 2002) is an ultrasound-based method enabling the acquisition of relative stiffness of images in soft tissues. Elastograms are created by comparing the ultrasound radiofrequency signal obtained before and after a slight compression of the tissue. The results of the comparison are displayed as an image where hard areas appear dark and soft areas appear bright. The breast is the application of choice for this technique, because it is readily accessible to compression with an US transducer.

Static elastography, like all imaging modalities, has certain limitations. The main pitfall of this modality is that it does not provide a quantitative assessment of the local stiffness, but instead displays a map of the local tissues strain, the so-called "elastogram." Even for a simple one-dimensional model, the underlying link between local strain ε and stiffness E is strongly dependent on the local stress σ *via* the well known relation $E = \sigma/\varepsilon$. Therefore, the stiffness map will be comparable to the elastogram only in the case of a homogeneous stress field in the whole region-of-interest. In general practice, the operator induces light pressure at the surface of the breast with the transducer, and the elastogram is generated. The operator's compression pressure strongly influences both the elasticity image and the resulting elasticity score. Despite these technical limitations, this technique seems promising and could lead to a specificity improvement of ultrasound imaging for breast cancer diagnosis (Garra 1998; Hyltawsky 2001; Frey 2003; Hall 2003; Barr 2006). However, when elasticity results are used for diagnosis, images obtained with the application of strong pressure may lead to a misdiagnosis (Itoh 2006). Images with minimal perturbation of strain relationships can be obtained by lightly pressing the probe to the breast. In addition, this technique requires practice to be able to exert light pressure on the same cross-sectional surface of the breast and therefore cannot be considered as an operator-independent technique. Magnetic resonance (MR) elastography (Muthupillari 1995; Kruse 2000; Sinkus 2005a, 2005b) overcomes most of the limitations of static elastography while providing a 3-D quantitative mapping of several elastic properties of breast tissues, such as shear modulus, shear viscosity and anisotropy. Contrary to static elastography, MR elastography is based on the use of shear waves induced in tissues by external surface vibrators working at low frequency (~50 Hz). However, because of the acquisition time (~10 to 15 min) MR elastography is limited to static organs and also precludes a freehand applicability.

Several years ago, transient elastography (Catheline 1999; Sandrin 1999, 2002a, 2002b; Gennisson 2002; Tanter 2002; Bercoff 2003) was proposed to merge the advantages of MRI and static elastography into an echographic system, to provide both a quantitative assessment of elasticity and reduced operator dependence compared with static elastography along with the real-time aspect and freehand capabilities of ultrasound compared with MRI. This technique is based on the use of an ultrafast ultrasound acquisition imaging system (5000 frames/s), which enables the real-time visualization of transient shear waves propagating in the human body. Promising results were obtained *in vivo* in the context of breast cancer detection (Bercoff 2003). However, the clinical applicability of this method was limited because it used large and bulky external vibrators.

To overcome this limitation, the ultrafast echographic imaging approach was coupled with the remote generation of a supersonic shear wave in tissues using a modified sequence of ultrasonic beams transmitted by the echographic probe (Bercoff 2002, 2004a, 2004b). This transient elastography approach, called supersonic shear imaging (SSI), provides a way to apply both the mechanical vibration and the ultrafast imaging of the resulting shear wave propagation by using a conventional ultrasonic probe.

The concept of remote palpation induced by the radiation force of an ultrasonic focused beam is not new and was introduced in the medical imaging community