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● *Original Contribution*

IN VIVO RESPONSE TO COMPRESSION OF 35 BREAST LESIONS OBSERVED WITH A TWO-DIMENSIONAL LOCALLY REGULARIZED STRAIN ESTIMATION METHOD

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Abstract—The objective of this study was to assess the *in vivo* performance of our 2-D locally regularized strain estimation method with 35 breast lesions, mainly cysts, fibroadenomas and carcinomas. The specific 2-D deformation model used, as well as the method's adaptability, led to an algorithm that is able to track tissue motion from radiofrequency ultrasound images acquired in clinical conditions. Particular attention was paid to strain estimation reliability, implying analysis of the mean normalized correlation coefficient maps. For all lesions examined, the results indicated that strain image interpretation, as well as its comparison with B-mode data, should take into account the information provided by the mean normalized correlation coefficient map. Different trends were observed in the tissue response to compression. In particular, carcinomas appeared larger in strain images than in B-mode images, resulting in a mean strain/B-mode lesion area ratio of 2.59 ± 1.36. In comparison, the same ratio was assessed as 1.04 ± 0.26 for fibroadenomas. These results are in agreement with those of previous studies, and confirm the interest of a more thorough consideration of size difference as one parameter discriminating between malignant and benign lesions. (E-mail: elisabeth.brusseau@creatis.insa-lyon.fr) © 2014 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Breast cancer, Correlation coefficient, Strain estimation, Ultrasound elastography.**

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer in women and the leading cause of female cancer deaths worldwide (Jemal et al. 2011). To better describe the burden of this disease, the following estimates reported in the literature can be provided. Throughout the world, breast cancer accounted for 23% (1.38 million) of the total new cancer cases in women and 14% (458,400) of the total female deaths from cancer in 2008 (Jemal et al. 2011). In the United States, an estimated 230,480 cases of invasive breast cancer, along with 57,650 carcinomas in situ, were expected to be newly diagnosed in females in 2011. In addition, 39,520 women were expected to die of their disease the same year (Siegel et al. 2011). Finally, in Europe, 421,000 new cases of breast cancer were estimated to have occurred, and 129,000 women to have died of this disease in 2008 (Ferlay et al. 2010).

Early diagnosis and treatment advances are essential to decrease breast cancer-related mortality (U.S. Preventive Services Task Force [USPSTF] 2009). X-ray mammography is the primary imaging modality for breast cancer screening. To provide an indication of its widespread use, about 36 million screening examinations were conducted in the United States in 2006 (Spelic et al. 2007). This technique, however, also has well-recognized limitations; most particularly, some cancers are missed. Mammography sensitivity is indeed known to be significantly reduced when screening women with dense

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breasts. In addition, this technique has a low positive predictive value, meaning that many mammographic findings referred for biopsy are benign (Rosselli Del Turco et al. 2007; Poplack et al. 2005).

To improve screening and diagnosis, other imaging modalities are used as an adjunct to mammography (Houssami et al. 2009; Lee et al. 2010; Smith and Andreopoulou 2004), among which ultrasound is the most widely employed. This technique is indeed used to further evaluate abnormal findings identified in mammograms (Taylor et al. 2002; Yang and Dempsey 2007). Ultrasound is very valuable in differentiating cysts from solid masses and can also provide additional useful information for tissue lesions. Moreover, several studies on the supplemental utilization of ultrasound to examine women with dense breasts found that this modality is able to detect some cancers not seen with mammography. In these studies, ultrasound-detected cancers presented themselves mainly as small, node-negative invasive carcinomas. Unfortunately, a substantial increase of the number of false positives associated with the utilization of supplemental ultrasound was also reported (Berg et al. 2008; Crystal et al. 2003; Nothacker et al. 2009).

Whether with sonography or mammography, lesion interpretation is based on the observation of specific features in the images. With ultrasound data, these features are, for instance, the lesion's shape, margin, orientation and vascularity. Fibroadenomas, for example, tend to be oval-shaped lesions with their long axis parallel to the skin. Final impressions are summarized by classifying the examined lesion in one of the Breast Imaging Reporting and Data System (BI-RADS) assessment categories, each of these categories being associated with a specific management recommendation (D'Orsi et al. 2003).

Part of current research is aimed at extracting new information from images to improve diagnosis. In this context, ultrasound elastography, which provides information on local tissue elasticity, appears to be a valuable tool, given that breast cancer is characterized by changes in the tissue's mechanical properties (Krouskop et al. 1998; Samani et al. 2007).

In ultrasound elastography, different approaches exist that vary with the mechanical stimulus used, the tissue elasticity-related parameter provided and the estimation method employed (Bercoff et al. 2004; Hoyt et al. 2007; Nightingale et al. 2003; Ophir et al. 1991; Sandrin et al. 2003; Xu et al. 2010). In this article, quasi-static techniques (Varghese et al. 2009), which reveal tissue elasticity by imaging its deformation under compression, are considered.

Since the first studies focusing mainly on the development of signal and image processing methods to locally estimate tissue strain, ultrasound elastography has evolved toward a technique that is now the subject of many clinical studies. The fact that modules dedicated to deformation imaging are now included in some ultrasound scanners used in clinical departments contributes largely to the evaluation of the diagnostic value of elastography. As has been done with the BI-RADS classification, different elastography-specific criteria have been introduced to differentiate between malignant and benign breast lesions. A grading scale or elasticity score, based on the strain pattern in the lesion and the surrounding tissues, can be used. A strain index, a ratio evaluated between the suspicious region and a reference area, can also be assessed (Gong et al. 2011; Itoh et al. 2006; Schaefer et al. 2011; Yerli et al. 2011).

Nevertheless, assessing the real impact of elastography remains a difficult task because of the variability of the results reported in terms of sensitivity and specificity. In a recently published meta-analysis, Gong et al. (2011) underlined the heterogeneity between reported studies and the important part played by study design. Moreover, results are shown to be operator and observer dependent (Burnside et al. 2007; Regner et al. 2006; Yoon et al. 2011). On the other hand, the evaluation of elastography performance compared with, as well as its contribution when combined with, B-mode ultrasound has also been investigated (Cho et al. 2008; Sadigh et al. 2012; Zhi et al. 2007). Further evaluation requires additional studies with larger numbers of patients, with the histologic analysis remaining the reference standard (Kumm and Szabunio 2010; Wojcinski et al. 2010).

Strain estimation methods directly contribute to elastography performance. Different 2-D approaches designed to estimate tissue deformation have been reported. Most of them partition the image into small regions of interest (ROIs), or measurement windows, and assume a 2-D translation motion of these regions with tissue compression (Chen et al. 2009; Doyley et al. 2001; Zhu and Hall 2002). In these methods, any small ROI is therefore supposed to be subjected to a rigid motion. From this motion model, improved techniques have been proposed involving the use of multi-level or multi-scale schemes and/or regularization to produce continuous displacement fields (McCormick et al. 2011; Pellot-Barakat et al. 2004; Shi and Varghese 2007). Strains are then deduced from the gradient of the estimated displacements.

Other methods consider more complex displacements within ROIs and locally use an affine motion model to depict the effect of medium deformation. In addition to a translation, terms describing axial, lateral and shear strains of these regions can thus be directly estimated, unlike the above-mentioned techniques (Liu et al. 2009, Maurice et al. 2004).

We have developed a 2-D locally regularized strain estimation method that in addition to a 2-D translation