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● *Technical Note*

SMALL BREAST LESION CLASSIFICATION PERFORMANCE USING THE NORMALIZED AXIAL-SHEAR STRAIN AREA FEATURE

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Abstract—Breast cancers that are found and confirmed because they are causing symptoms tend to be larger and are more likely to have already spread to the lymph nodes and beyond. Thus, early detection and confirmation are of paramount importance. The normalized axial–shear strain area (NASSA) feature from the axial-shear strain elastogram (ASSE) has been shown to be a feature that can identify the boundary-bonding conditions that are indicative of the presence of cancer. Recently, we investigated and reported on the potential of the NASSA feature for breast lesion classification into fibroadenomas and cancers. In this article, we investigate the size distribution of the lesions that were part of the previous study and analyze classification performance specifically on small lesions (<10 mm diameter). A total of 33 biopsy-proven malignant tumors and 30 fibroadenomas were part of the study that involved three observers blinded to the Breast Imaging Reporting and Data System (BIRADS) ultrasound scores. The observers outlined the lesions on the sonograms and the lesion size (maximum circle-equivalent diameter in millimeters) was computed from this outline. The ASSE was automatically segmented and color-overlaid on the sonogram, and the NASSA feature from ASSE was computed semi-automatically. Receiver operating characteristic curves were then generated for the subset of cases involving small lesions. Box plots were produced for the two different lesion size groups, small and large, from a logistic regression classifier that was built previously. The results of our study show that approximately 38% and 22% of the fibroadenomas and cancers, respectively, were small. Furthermore, it was found that the NASSA feature resulted in a perfect classification of the small lesions, both in the training data and in the cross-validation. For lesions <10 mm the difference in fibroadenoma and cancer mean scores was 0.73 ± 0.13 ($p < 0.001$), whereas lesions >10 mm had a difference of 0.52 ± 0.24 ($p < 0.001$). The results also showed that the small lesions actually had better classification than the larger lesions (>10 mm). These results suggest that the ASSE feature can work equally well, even on small lesions, to improve the standard ultrasound BIRADS–based breast lesion classification of fibroadenoma and malignant tumors. (E-mail: Arun.K.Thittai@uth.tmc.edu) © 2013 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Axial-shear strain, Benign, Bonding, Breast cancer, Elastography, Fibroadenoma, Malignant, NASSA, ROC, Small lesion, Sonogram, Ultrasound.**

INTRODUCTION

It is estimated that almost 1.6 million new cases of cancer will be diagnosed in the United States in 2011 (American Cancer Society 2011a). Of the estimated 774,370 cases of cancer diagnosis in women, breast cancers are the most common (30%). Furthermore, the breast is the second leading site (15%) of cancer deaths in the United States (American Cancer Society 2011a). Although the use of screening mammography is widespread, breast cancer continues to develop with palpable masses in a majority of cases (55%–68%; Seltzer 1992; Reeves et al. 1995). A recent report by Mathis et al. (2010) concluded that despite the frequent use of screening mammography, 43% of breast cancers appeared as a palpable mass or an otherwise symptomatic presentation. Breast cancers that are found and confirmed because they are causing symptoms tend to be larger and are more likely to have already spread beyond the breast (American Cancer Society 2011b). Thus, early detection and confirmation are of paramount importance.

Mammography serves as the current standard for breast cancer screening. Although breast ultrasound is not routinely used for screening, it is often used to evaluate breast problems that are found during a screening

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or diagnostic mammogram or on physical examination (American Cancer Society 2012; Stavros et al. 2004). Sonography is considered a helpful addition to mammography when screening women with dense breast tissue, which is difficult to evaluate with a mammogram alone (American Cancer Society 2012). In addition, ultrasound is particularly useful for differentiating between cystic or solid lesions. Ultrasound has become a valuable tool for imaging because it is widely available, noninvasive, and less expensive compared with several other competing imaging modalities. However, there is still an overlap between benign and malignant features on sonograms (Stavros et al. 2004), and biopsy outcomes serve as the gold standard. It is of interest to note that the Breast Imaging Reporting and Data System (BIRADS) features used in conventional sonography (American College of Radiology 2003), unlike those used in palpation, do not relate directly to either (1) the elastic properties of the tumor or (2) the bonding characteristics at the boundary between the tumor and the host tissue (Fry 1954).

Ultrasound elastography was introduced in the early 1990s (Ophir et al. 1991) to provide a way to visualize mechanical properties of the target tissue. The axial-strain elastography (ASE), or elastography, provides information relating to the elastic property of the target tissue (item 1 above). Specifically, contrast between different tissues is produced when tissue regions with different stiffness parameters experience different levels of axial strain than those in surrounding tissues; a stiffer tissue region will generally experience less strain than a softer one (Céspedes et al. 1993; Ophir et al. 1999). Several groups have reported on the usefulness of ASE in the classification of breast tumors as benign or malignant (Burnside et al. 2007; Barr 2012; Garra et al. 1997; Hall et al. 2003; Itoh et al. 2006; Regner et al. 2006; Svensson et al. 2005).

We introduced axial-shear strain elastography to image and exploit the tumor-host tissue boundary bonding characteristics (item 2 above; Thitaikumar et al. 2005, 2007). It is important to note that the contrast mechanism in the axial-shear strain elastogram (ASSE) is due to the shear stress transfer that occurs at boundaries having elastic contrast (Thitaikumar et al. 2007). Thus, the ASSE images fundamentally new information relating to the bonding conditions at that boundary. An important advantage of the ASSE technique is that it is the only technique among all other elasticity imaging techniques discussed in literature (cf. ASE, shear wave elastography, ARFI; Parker et al. 2011) that is able to image this important boundary bonding condition as a separate entity and exploit this information for breast lesion classification into benign versus malignant. The normalized axial–shear strain area (NASSA) feature computed from the ASSE has been shown to be a feature that could identify the boundary bonding conditions that are indicative of the presence of cancer (Thitaikumar et al. 2007, 2008). Recently, we investigated and reported on the potential of the NASSA feature for breast lesion classification into fibroadenomas and cancers (Thittai et al. 2011). However, no analysis on the effect of lesion size on the results was performed or reported. Therefore, the aim of this work was to investigate the size distribution of the lesions that were part of the previous study and to analyze classification performance specifically on small lesions (<10 mm diameter) compared with larger lesions.

It is important to recognize that the potential to metastasize has a high degree of correlation to the tumor size and therefore influences the recurrence rates and ultimately patient survival (Gibbs et al. 2004; Valagussa et al. 1978). The detection and subsequent characterization of small breast lesions is therefore of paramount importance (Gibbs et al. 2004). Studies have shown encouraging survival with lesions <10 mm. For example, Rosen et al. (1993) showed that infiltrating ductal or lobular lesions <10 mm in diameter correlated with a good prognosis and that the relapse-free survival at 20 years was 88%. More recently, Sivaramakrishna and Gordon (1997) extrapolated the log-normal relationship between tumor size and probability of metastasis to include small breast lesions; they showed that tumors detected at 20 mm in diameter had a 25.5% probability of metastasis, whereas tumors detected at 5 mm in diameter had a 1.2% probability of metastasis. Therefore, any additional image, like ASSE, that might aid in detection and noninvasive classification into benign or malignant will have a significant effect on breast lesion management.

MATERIALS AND METHODS

We performed an analysis of the lesion size distribution in the data that were part of previously reported observer study (Thittai et al. 2011). Briefly, the data set consisted of *in vivo* digital radiofrequency data of breast lesions that were originally acquired for evaluating standard axial elastograms. The patient study was compliant with the Health Insurance Portability and Accountability Act and had appropriate institutional review board approval. Informed consent was obtained from all participating patients, who were informed that the radiofrequency data collected would be used at a later time for the creation of elastograms. The elastographic data were acquired using a Philips HDI-1000 US scanner (Philips Healthcare, Andover, MA, USA) with an L4-7 transducer probe operating at a center frequency of 5 MHz. The setup consisted of a precision digital motor system for controlled compressions. The acquisition protocol involved multi-compression with step sizes of 0.25%, up to a maximum total compression of