● *Original Contribution*

IMPLEMENTATION OF ELASTOGRAPHY SCORE AND STRAIN RATIO IN COMBINATION WITH B-MODE ULTRASOUND AVOIDS UNNECESSARY BIOPSIES OF BREAST LESIONS

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Abstract—The aim of this study was to evaluate whether the combination of B-mode ultrasound, elastography score (ES) and strain ratio (SR) improves diagnostic performance with respect to breast lesions. One hundred thirty lesions were prospectively evaluated by B-mode ultrasound and strain elastography, followed by fine-needle aspiration cytology/biopsy in 117 woman who were scheduled for regular breast BUS. The median ES (4.5 vs. 2.9, $p < 0.001$) and SR (4.9 vs. 2.3, $p < 0.001$) were significantly higher for malignant than for benign lesions. A sensitivity of 90.5% and specificity of 93.2% for the ES (cutoff point = 3.8) and a sensitivity of 87.5% and specificity of 87.6% for the SR (cutoff point = 3.5) were obtained. Elastography combined with B-mode ultrasound improved the specificity, accuracy and positive predictive value. Receiver operating characteristic curves yielded a higher value for the combined technique for diagnosis of breast lesions. Routine use of such a diagnostic algorithm could reduce the number of unnecessary biopsies. (E-mail: Bojanic.kristina@gmail.com)   © 2016 World Federation for Ultrasound in Medicine & Biology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Key Words: Breast lesions, Ultrasonography, Strain elastography, Elastography score, Strain ratio, Diagnostic accuracy, Breast Imaging Reporting and Data System.

INTRODUCTION

Breast cancer is the most common cancer among women worldwide, with nearly 1.7 million cases diagnosed in 2012 (International Agency for Research on Cancer 2012). Breast cancer is also the most common cancer in women in Croatia, where it accounts for 26% of all cancer sites in females (Šamija and Strnad 2015).

Early detection of malignant lesions is critical for the successful management of breast cancer. Today, conventional B-mode ultrasound (BUS) plays a decisive role in the diagnostic pathways using the standardized Breast Imaging Reporting and Data System (BI-RADS) lexicon developed by the American College of Radiology (ACR) (Mendelson et al. 2013). The distinct BI-RADS assessment category also implies which further clinical action should be taken.

Lesions graded as BI-RADS 3 are probably benign, and short-term follow-up is recommended. Nevertheless, malignancy is eventually diagnosed in about 3% of these lesions, resulting in a delayed diagnosis of cancer in a considerable number of patients (Sadigh et al. 2012a). On the other hand, a recent prospective study evaluating screening ultrasonography reported a BI-RADS 3 category in about 20% of patients, and 16.6% were ultimately sampled for biopsy with a low malignancy rate of 0.8% (Barr et al. 2013). BI-RADS 4 lesions have a

low to moderate probability of cancer (3%–94%) and biopsy/fine-needle aspiration cytology (FNAC) should be considered. However, with BI-RADS category 4, approximately 15% of findings are histologically malignant, and a much larger proportion of patients undergo invasive diagnostic procedures that might not be necessary if better imaging methods were available for accurate diagnosis confirmation (Liu et al. 2014). Presently, biopsy is used as a supplement for other diagnostic methods in the evaluation of breast lesions, but the rate of cancer detection in biopsies ranges from only 10% to 30% (Chiou et al. 2006; Duncan et al. 2000).

Fine-needle aspiration cytology is still widely practiced in the assessment of breast masses in both palpable and non-palpable lesions because it provides a rapid, accurate and cost-effective diagnosis in many countries, including Croatia (Radhakrishna et al. 2013). UK guidelines state a complete sensitivity >80%, positive predictive value of malignancy >95%, false-negative rate <5%, false-positive rate <1%, inadequacy rate of 3 <25% and suspicious rate <20%, confirming that FNAC as a very good and effective diagnostic modality (Wells et al. 1994).

According to Medina-Franco et al. (2005) and Abdullateef (2014), FNAC in the hands of an experienced examiner achieves very high sensitivity and specificity and low false-positive and false-negative rates and is associated with no significant complications. They concluded that the diagnostic accuracy of FNAC for breast lesions is very high with minimal complications. A positive predictive value of 100% allows establishment of a therapy based on its results. Furthermore, the Croatian health care system is financially limited, and FNAC is the method of choice for diagnosis of invasive breast lesions. Therefore, a suitable predictor of malignancy in BI-RADS 3 and 4 lesions would be beneficial and of great clinical relevance. To improve diagnostic accuracy, strain elastography (SE) was introduced (Ophir et al. 1991). It is a non-invasive technique in which stiffness or strain images are used to detect or classify anatomic areas with different elasticity patterns. This technique, based on tissue stiffness/elasticity, helps in the differential diagnosis of benign and malignant breast lesions (Moon et al. 2011) that conventional ultrasound methods cannot detect, thus improving the accuracy of diagnosis of breast cancer (Pons et al. 2015) and reducing the number of unnecessary biopsies of BI-RADS 3 and 4 lesions.

According to the European Federation for Ultrasound in Medicine and Biology (EFSUMB) guidelines and recommendations on the clinical use of ultrasound elastography from 2013, elastography was initially recommended to increase diagnostic confidence in determination of benign or malignant lesions, as well as to re-grade benign-appearing stiff lesions and consider them for biopsy, but not to downgrade a lesion that would

be sent for biopsy on the basis of ultrasound descriptors alone (BI-RADS 4A or higher) (Cosgrove et al. 2013).

Recent studies and a meta-analysis (Sadigh et al. 2012a, 2012b, 2013) indicated that ultrasound elastography provides higher image quality compared with BUS or mammography during breast cancer diagnosis, which can increase specificity and reduce false-positive results, making it useful for avoiding breast biopsy (Barr 2014; Faruk et al. 2015; Sadigh et al. 2012a). Strain elastography allows evaluation of the elastography score (ES) as a qualitative parameter of relative stiffness of the lesion (Barr 2012) and the strain ratio (SR, fat/lesion ratio [FLR]) as a semiquantitative ratio of the stiffness of the lesion to that of fat (Barr 2012; Yoon et al. 2014). According to the World Federation for Ultrasound in Medicine and Biology (WFUMB) guidelines and recommendations for clinical use of ultrasound elastography, SR is a semiquantitative method for numerically evaluating how many times stiffer a target mass is compared with subcutaneous fat (Barr et al. 2015). Although some studies have reported that the SR is a highly valuable and more objective parameter for differentiating malignant and benign breast lesions (Shyam et al. 2012; Thomas et al. 2010; Yoon et al. 2014), others have confirmed that the SR has poor reliability and does not improve elastographic accuracy (Kumm and Szabunio 2010; Yerli et al. 2011). Additionally, only a few studies have investigated the usefulness and accuracy of SE with different-sized breast lesions (Giuseppetti et al. 2005; Itoh et al. 2006; Liu et al. 2014).

Therefore, a prospective study was designed to evaluate whether the combination of conventional B-mode ultrasound, ES and RS improves diagnostic performance and increases confidence during examination of women with breast lesions in everyday clinical practice. We also wanted to examine the influence of lesion size on the degree of elasticity. Additionally, we aimed to determine whether ES and SR, as strong predictors of malignant and benign changes, could downgrade BI-RADS 3 and 4 lesions and reduce the rate of unnecessary invasive diagnostic procedures.

METHODS

Patients

The study was reviewed and approved by the Health Center Osijek Review Board (Approval No. 03-382/14). All participants signed an informed consent form before being included in the study. One hundred seventeen women scheduled for regular breast ultrasound examination from January 2014 to May 2015 at the Department of Ultrasound Diagnostics at the Health Center Osijek were included in the study. To be included the women had to