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● *Clinical Note*

ULTRASOUND DETECTION OF MICROCALCIFICATIONS IN SURGICAL BREAST SPECIMENS

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Abstract—The objective was to evaluate a commercial image processing technique (MicroPure, Canon Medical Systems, Tustin, CA, USA) for detection of microcalcifications in breast surgical specimens. Twenty women scheduled for surgical excision of an area with breast calcifications were enrolled, their surgical specimens underwent grayscale ultrasound (US) and MicroPure examination using an Aplio XG scanner (Canon). Four independent and blinded readers analyzed 54 US and 54 MicroPure digital clips to determine the number of calcifications and scored image quality and artifacts on a 10-point scale. All readers saw significantly more microcalcifications with MicroPure than with US, 14.0 ± 12.0 versus 3.0 ± 3.2 ($p < 0.0001$). Three readers preferred MicroPure image quality over that of US ($p < 0.009$) and *vice versa* for one reader ($p = 0.003$). Three readers saw fewer Cooper's ligament artifacts with MicroPure than with US ($p < 0.0001$); one reader saw no significance difference between them ($p = 0.58$). In conclusion MicroPure identified more breast microcalcifications than grayscale US in *ex vivo* surgical breast specimens. (E-mail: flemming.forsberg@jefferson.edu)

Key Words: **Ultrasound, Breast, Microcalcification, Surgical specimen.**

INTRODUCTION

Mammography is an X-ray imaging method that is considered the gold standard for breast cancer screening (Carney et al. 2003; Machado et al. 2012, 2014; Park et al. 2016; Setz-Pels et al. 2011; Tan et al. 2015). Microcalcifications have a recognized association with breast cancer, and they are an important and reliable mammographic feature for the diagnosis of early non-palpable cancer (Bent et al. 2010; Cheung et al. 2002). Patients with suspicious findings on mammography are usually referred for breast biopsy to determine the nature of the lesion as benign or malignant and whether further treatment is needed (Anderson et al. 1997; Bozzini et al. 2008; Bruening et al. 2010; Gufler et al. 2000; Hashimoto et al. 2001; Huang et al. 1999; Mandelson et al. 2000; Moon et al. 2000, 2002; Nagashima et al. 2005; Shin et al. 2010; Soo et al. 2002; Yang et al. 1997). Biopsies can be performed by open surgery (excisional or incisional biopsy) or by minimally invasive core-needle methods that can be guided by stereotactic mammography or by ultrasound (US) (Bruening et al. 2009, 2010).

Ultrasound is considered a reliable modality for differentiation between a cyst and a solid breast lesion, thus obviating unnecessary biopsies. For non-palpable breast masses, sonography alone has a high sensitivity but a low specificity; reported specificities vary from 29% to 46% (Thibault et al. 2000). A US-guided biopsy is commonly used in the case of sonographically visible breast lesions. Thanks to real-time, high-resolution imaging, the biopsy needle can be seen penetrating the target, thus ensuring accurate sampling. With a 7.5 MHz transducer, small masses and areas of parenchymal distortion seen on mammograms can be localized. Rizzatto et al. reported a 40% success rate in localizing masses measuring up to 5 mm using a 7.5 MHz probe (Cheung et al. 2002; Rizzato et al. 1993). In 1992, (Hastrich et al) used a 7.5 MHz probe with axial resolution of 0.4 mm to evaluate isolated microcalcifications in patients; they could identify 45% of these microcalcifications, which ranged from 0.1 to 0.5 mm (Cheung et al. 2002; Hastrich et al. 1992; Teh et al.

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2000). However, identifying isolated microcalcifications within echogenic breast tissue is very difficult.

Microcalcifications appear as bright spots on US, but because the speckle pattern and some tissue structures seen on US look like microcalcifications, traditional US imaging is not considered an accurate method for the clinical evaluation of suspicious microcalcifications. Microcalcifications are more likely to be seen on US when they are located inside solid masses, because the solid masses are usually hypoechoic and therefore can provide a hypoechoic background that improves the visualization of the bright echoes associated with microcalcifications (Gufler et al. 2000; Hendrick 2010; Machado et al. 2012, 2014; Moon et al. 2000, 2002; Nagashima et al. 2005; Park et al. 2010; Soo et al. 2002). The evaluation of isolated microcalcifications within normal breast tissue is considered to be more difficult with US, because of the lack of contrast between normal parenchyma and the microcalcifications (Anderson et al. 1997; Gufler et al. 2000; Hashimoto et al. 2001; Hendrick 2010; Huang et al. 1999; Machado et al. 2012, 2014; Moon et al. 2002; Nagashima et al. 2005; Park et al. 2010; Rickard 1996; Soo et al. 2002, 2003; Yang et al. 1997).

Ultrasound is used to guide percutaneous core biopsies or wire localizations for surgical biopsies of breast masses. For patients, there are many advantages to a US-guided procedure compared with a mammographically guided procedure. In addition to the fact that a US study does not involve radiation (Hendrick 2010), making it a more tolerable choice for pregnant and lactating women, a US-guided procedure permits the patient to stay in a comfortable and more physiologic position without compression of the breast. The real-time aspect of US provides an advantage for the radiologist, who can see the needle progress during the entire procedure, making the procedure safer and quicker. A US-guided approach for the evaluation of microcalcifications would enable more patients to undergo US procedures instead of mammographic procedures.

An innovative imaging technology that improves visualization of microcalcifications on US is MicroPure (Canon Medical Systems, Tustin, CA, USA), which is based on speckle reduction techniques with a constant false alarm rate (CFAR) filter. By combination of spatial and frequency compounding to reduce speckle, images with high-contrast resolution and high tissue uniformity can be created (Machado et al. 2012, 2014; Park et al. 2016; Tan et al. 2015). CFAR is a special interpolation filter that extracts only isolated high-brightness echoes against a heterogeneous background of clutter (Machado et al. 2012, 2014; Park et al. 2016; Tan et al. 2015). Combining the two image processing techniques allows microcalcifications to be separated from artifacts in normal breast tissue. The final MicroPure image presents high-brightness dots (suspected of being microcalcifications) within a dark blue or purple color overlay on the B-mode image. This display mode further improves the ease of detection of the microcalcifications (Machado et al. 2012, 2014; Park et al. 2016; Tan et al. 2015).

Our group performed a pilot study (Machado et al. 2012) on the use of MicroPure for the identification of clusters or isolated microcalcifications in patients with breast microcalcifications seen on mammography. The results of that study were promising, with a statistically significant increase in the mean number of microcalcifications seen on MicroPure images compared with grayscale US, using mammography as the reference standard (on average 1.9 ± 1.7 vs. 0.7 ± 1.1, $p < 0.009$). The purpose of this study was to evaluate the use of MicroPure imaging for the identification of breast microcalcifications in surgical specimens and to compare the results with those of fundamental grayscale US, using X-ray imaging of the specimen as the reference standard.

METHODS

Patients

This study was a prospective, clinical trial conducted from July 2010 to October 2014 and involving 20 adult female patients from the Breast Imaging Center at Thomas Jefferson University Hospital who had breast calcifications identified on a prior mammographic study and who were scheduled to have a surgical excision of the area containing calcifications. The mean age of the patients participating in the study was 57 years (range: 41–79 years), and all provided written informed consent. The study was approved by the university's institutional review board and was compliant with the Health Insurance Portability and Accountability Act.

This study was supported in part by Canon Medical Systems. The sponsor provided the Aplio XG scanner and grant support for this study. The authors of this article had sole control of the data generated by this trial and the information provided for publication.

Data acquisition

After the surgical procedure (performed as part of the patients' standard of care), the surgical specimen was retrieved and scanned with an Aplio XG scanner (Canon Medical Systems) with a 14 MHz broad bandwidth linear array and grayscale US, as well as MicroPure imaging were acquired. No compounding or other image processing techniques were applied. The time gain compensation and 2D gain setting were optimized separately for each imaging technique. Sagittal and transverse still images and digital clips of the surgical excision specimen were obtained with conventional grayscale and MicroPure US imaging by a radiologist with more than 10 years of experience. A total of 22 surgical specimens were scanned because two patients