Ultrasound Diagnosis of Breast Cancer

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Ultrasound is a popular imaging modality for its safety and low cost. Its role in the diagnosis of breast cancer is discussed, and its performance is then compared those of mammography (gold standard) and MRI. Besides conventional B-mode and color or power Doppler ultrasound images, latest development of acoustic radiation force impulse (ARFI) and supersonic shear imaging and their application in breast diagnosis are introduced.

Keywords: Breast Cancer, Sonography, Magnetic Resonance Imaging, Doppler Ultrasound, Acoustic Radiation Force Impulse Imaging, Supersonic Shear Imaging.

1. SONOGRAPHY IN BREAST CANCER DIAGNOSIS

Ultrasound (US) is becoming a popular clinical diagnosis modality in the past decades with the major advances in transducer, electrical circuit, digital signal processing, and system control, and has already been applied to large varieties of diseases because of its uniqueness of low cost, flexibility, non-invasion, and non-ionization. US has the ability to image and evaluate patient’s internal anatomy structure and physiology in real-time with astounding clarity. Therefore, it makes significant contributions to healthcare.

The breast examination by US started from 1951 with an optimistic opinion that US would replace mammography eventually in detecting breast cancer. However, with more comprehensive studies, it illustrates that US is only valid for the discrimination between cysts and solid masses. The performance of US depends on the size, number, location, and properties of the lesions, the operation skills, and the system specifications (i.e., resolution and frequency).

The diagnosis of cysts is clinically and socially important for remarkable reduction on the number of breast biopsies and early therapy, particularly for those non-palpable ones. Aspiration or biopsy is not required to simple cysts, which reduces the healthcare cost, anxiety and discomfort of patients during with surgery. However, for palpable masses, aspiration is advocated due to its less expense, availability at many centers, and often accompanies with therapy, but not much desirable for many women due to its discomfort. US is the appropriate method of lesion diagnosis with accuracy of 96–100% if it is not palpable and applicable for aspiration. A simple cyst usually has smooth walls, sharp anterior and posterior borders, no internal echoes, and posterior enhancement (Fig. 1). Using a gel or fluid offset and aligning the target to the focal region with better resolution could define the anterior wall, especially for superficial lesions. In comparison, posterior enhancement is mostly inconsistent.

Occasionally, diffuse mastitis does not have an appropriate response to antibiotics, which suggests abscess formation. Therefore, mammography may not be appropriate for pain and edema of the breast and will not display a discrete abscess cavity with inflammation-induced higher density. US is an alternative approach for diagnosing and guidance of surgical drainage of abscesses, which have various sonographic characteristics, such as irregular hypoechoic or anechoic cavities, occasional fluid-fluid or fluid-debris levels, posterior enhancement, distortion on surrounding, and overlying skin thickening (Fig. 4).
Fig. 1. A palpable lesion in the left upper inner quadrant of breast shown in (a) oblique and (b) craniocaudal mammograms (arrows), and (c) a simple cyst in the transverse sonogram (arrows) with smooth borders, no internal echoes, posterior enhancement, and lateral shadows from the smoothly curved walls.

US seems a more sensitive imaging modality for positive axillary lymph nodes in the breast cancer that is commonly involved but rarely evaluated than physical examination and axillary mammography with compression. The capability of metastatic nodes by US and physical examination are 72.7% and 45.4%, respectively, with equal specificities of these two techniques (97.3%) in a study of 60 patients. Furthermore, US has success in the guidance of fine-needle aspiration of cyst, biopsy of solid masses, preoperative needle, and wire localization.

Fibroadenomas are smoothly round, oval, or lobulated lesions with homogeneous internal echoes and posterior enhancement while carcinomas are irregular solid masses with internal echoes and attenuated brightness. Therefore, their US images have certain overlaps, and accurate determination is possible with

Fig. 2. A 3-cm palpable fibroadenoma found by biopsy is shown in (a) oblique mammogram (arrows) and (b) the longitudinal sonogram as a well-outlined, slightly lobulated, and homogeneous solid mass (arrows).
conventional sonography.\textsuperscript{16–19} Ratios of the length to the antero-posterior diameter of the cancer and fibroadenomas are significantly different, and the oblong configuration in fibroadenomas is more apparent in superficial position.\textsuperscript{20}

US has been implemented in screening breast cancer, particularly those with dense tissue, in Japan, Europe, and Australia. However, its inability of detecting all types of breast cancers and a substantial number of non-palpable cancers who are visible and invisible at mammography, respectively, prevents US being a valuable screening modality because of its unacceptably high false-negative rate, (0.3–47\% with mean of 20.7\%), which may be even higher for small and clinically occult cancers.\textsuperscript{21} Most importantly, US detection of a significant number of non-palpable carcinomas with good-quality negative mammograms is not always satisfactory. In addition, US has a remarkable false-positive rate in asymptomatic patients because of the shadowing produced by many normal structures\textsuperscript{22} and similar sonographic features between fat lobules and solid tumors.\textsuperscript{23} US diagnosis is unable to exclude malignancy and identify an underlying reason for the asymmetric fibroglandular tissue, but mammography and physical examination.\textsuperscript{8}

In summary, sonography at high quality and high frequency used in a judicious manner is a valuable tool in the clinics. Sonography is applied to the evaluation of circumscribed lesions found in the mammography, palpable masses invisible in the mammography, and a cyst is in the differential diagnosis. The need for biopsy on a simple cyst could be eliminated after the US diagnosis. Otherwise, a biopsy or mammographic follow-up is required no matter of the sonography results, in which US provides not much clinically useful information and, subsequently, is not suggested.\textsuperscript{4}

![Fig. 3. False-negative (a) oblique and (b) craniocaudal mammograms with moderate density but no discrete mass and (c) the longitudinal sonogram of a 4-cm palpable mass in the lower inner quadrant of the right breast, which was revealed as ductal carcinoma in biopsy.](image)

![Fig. 4. Longitudinal sonogram of (a) a mastitis and large area of induration that has an irregular abscess cavity with echoes and posterior enhancement, and (b) a severe mastitis with multiple small (3-9 mm) scattered abscesses (solid arrows), thick skin (open arrows), high echogenicity, structure distortion, and a sharp interface between normal and abnormal tissue (curved arrow).](image)
2. COMPARISON OF MAMMOGRAPHY, SONOGRAPHY AND MRI

The diagnostic sonography in the breast has been investigated for at least 30 years.1 Sonography did not detect any proven cancers that were missed by mammography. Mammography was found superior in detecting 97% of the 64 pathologically confirmed cancers, while sonography can only seek 58% of them. Mammography detected more than 90% in all cancer categories, including those amenable to cure, but the value for sonography is only 48% (40% of the non-palpable malignancies and 8% of the cancers smaller than 1 cm that did not yet spread to axillary lymph nodes). Tumor size and axillary lymph node status are the most important prognostic indicators for breast cancer, and the mammography done far outperformed sonography in detecting the smallest cancers and those that did not yet spread to axillary nodes. A major factor limiting the ability of sonography for non-palpable breast cancers seems to be its inability to image the micro-calcifications (individual particles 0.2–0.5 mm). Mammography-positive sonography-negative cancers usually are small, non-palpable, and have not yet spread to axillary lymph nodes, whereas very rare sonography-positive mammography-negative cancers are always detectable by physical examination and more likely to have metastasized. Therefore, upgrading to state-of-the-art mammography is preferred to improving the cancer detection ability rather than purchasing an US system.24

The role of sonography in breast diagnosis is an ongoing investigation.25 US is a widely accepted method for discriminating cysts from solid masses and guiding interventional procedures. Sensitivities and accuracy of the US in the discrimination between benign and malignant breast nodules are not high enough to reply on, and its value in comparison or addition to mammography is still in debate.26 Thus, US is not recommended as a screening tool due to the failure in establishing its efficacy.27

US was performed to detect (1) circumscribed lesions (possible cysts), (2) palpable lesions visible in mammography, (3) palpable lesions not visible in mammography, and (4) non-palpable lesions visible in mammography in a 2-year prospective study of 4,811 cases. As a result, 1,103 cases (23%) were reclassified their suspicion levels of malignancy.25

US can achieve a certain improvement in breast cancer diagnosis as an adjunct to mammography. Although it not very dramatic for the total cohort of patients, such an improvement was considerable for the subgroup of patients, especially among the young patients with low sensitivity of mammography. Mammographic classification based on a relatively high threshold for biopsy provides US opportunity of increasing sensitivity. If further advances are achieved in US diagnosis, especially for diffusely growing cancers, a further acceptance of US in the breast cancer diagnosis is expected.25

Young breasts, despite low occurrence, are more sensitive to radiation so that the limited exposure is desired. US imaging is usually performed in the initial study. No further evaluation is necessary for a cyst. If the mass is solid or invisible in sonography, at least one mammogram will be obtained to seek micro-calcifications. Although mammography allows detection of almost all palpable masses, adequate positioning may not be possible for very deep lesions adjacent to the chest wall or in a slim woman with a mass at the extreme periphery of the breast. Altogether, US is not a substitute for mammography, nor does a negative sonogram rule out carcinoma.4

3. DIAGNOSIS OF MICROCALCIFICATION

The identification of micro-calcification (i.e., smaller than 0.5 mm) on mammography has been widely studied and is indispensable in the early detection of breast cancer.23 35–45% of discovery of non-palpable breast cancers depends on the presence of clusters of micro-calcification on mammography.2 Micro-calcifications are brighter reflectors than the surrounding breast parenchyma without an acoustic shadow in sonography.9 In a study of 89 tumors found in 84 patients, micro-calcifications were visible in 44 breast cancers using high resolution ultrasound (HRUS, 49%), 40 cancers using X-ray mammography (XRM) (45%) and 46 breast cancers on histology (53%).28 HRUS has the sensitivity of 95%, specificity of 87.8%, and accuracy of 91% in the detection of micro-calcification. The corresponding values for histology are 80%, 71.4% and 75.3%, respectively. Therefore, US is a sensitive and reliable diagnosis modality for micro-calcification in breast cancer presented within a mass lesion.28 HRUS detected micro-calcification in 6 cancers that were negative on XRM, among them 4 were positive on histology. These false positives may be due to the requirement of sufficient deposition of calcium phosphate for the identification of micro-calcifications for XRM but not necessary for US. In addition, XRM is a survey of the entire breast, whilst US is tomographic and its multi-section analysis may increase detection accuracy.28

Calcifications that occur within masses are more visible on US, which is partially because most malignant solid nodules provide a great echogenicity. In contrast, sonography for benign calcifications with many hyperechoic and heterogeneous fibers are less reliable. Hence, malignant are more visible in the sonography than benign calcifications. Although the sensitivity of sonography for calcifications is lower than that of mammography, sonographically visible calcifications within a solid mass have high possibility of malignant.29

The different types of ductal carcinoma in situ (both comedo and non-comedo) correlate with mammographic patterns of micro-calcifications and the latter inconsistent foci of micro-calcifications. Malignant micro-calcifications within ductal carcinoma in situ and microscopically invasive ductal carcinoma, which do not have associated sonographically demonstrable masses, are difficult to identify on US.28

4. DIAGNOSIS OF LYMPH NODE METASTASES

The presence of axillary lymph node metastases in breast cancer is an important symptom in assessing prognosis and determining the treatment plan. Axillary staging is conventionally performed by axillary lymph node dissection. The use of sonography in detecting metastases is feasible and would reduce the number of false-negatives at sentinel node biopsy.30

In the studies including palpable and non-palpable nodes, if the size (>5 mm) or node visibility in sonography was used as the criterion for positivity, sensitivity varying between 66.1% (95% confidence interval: 52.6–77.9%) and 72.7% (49.8–89.3%), with no heterogeneity between them, including both
gold standard of axillary lymph node dissection and sentinel node biopsy. However, the variation of specificity is from 44.1% (34.3–54.3%) to 97.9% (88.7–99.9%), and heterogeneity is found between the results. If the lymph node morphology was used for positivity, variations of sensitivity and specificity are from between 54.7% (41.7–67.2%) and 80.4% (73.9–86.2%) to 92.3% (74.9–99.1%) and 97.1% (90–99.6%), respectively. Whist in the studies, including only non-palpable nodes, if the node size in sonography (>5 mm) or its visibility was used as a criterion for positivity, sensitivity varies from 48.8% (39.6–58%) to 87.1% (76.1–94.3%) and specificity from 55.6% (44.7–66.3%) to 97.3% (86.1–99.9%). If the node morphology was used as the criterion for positivity, variations of sensitivity and specificity were from 26.4% (15.3–40.3%) and 88.4% (82.1–93.1%) to 75.9% (56.4–89.7%) and 98.1% (90.1–99.9%), respectively. In the US guided biopsy, the sensitivity varies between 43.5% (33–54.7%) and 94.9% (88.5–98.3%) and specificity between 96.9% (91.3–99.4%) and 100% (96.2–100%), although sensitivity is reduced because it is necessary to visualize the node or to fulfill the sonographic criteria for malignancy.

Therefore, sonography is moderately sensitive and specific in the diagnosis of axillary metastases in breast cancer. However, it cannot be used as a sole method for decision, whether to perform axillary lymph node dissection. When suspicious metastatic axillary nodes are found, a US guided biopsy can be performed, which increases the specificity (100% vs. 96.5% use of sonography alone) at the cost of certain aggression and extra resources. Subsequently, about half of the axillae with metastases would be detected with a high specificity (96.5%) and a good sensitivity (48.4%), and then those positive patients would undergo axillary lymph node dissection. The remaining negative would be candidates for sentinel node biopsy, which improves the negative predictive value of the sentinel node biopsy because of the lower prevalence of metastases and thereby increases the certainty of sonography-based diagnosis.

5. SURVEILLANCE OF WOMEN AT HIGH FAMILIAL RISK FOR BREAST CANCER

Breast cancer susceptibility gene (BRCA) mutation carriers, who exhibit adverse histopathologic features of biologic aggressiveness, has a lifetime risk for up to 65–80% to develop breast cancers rather than sporadic ones. A comparative cohort study was carried out to investigate the effectiveness of mammography, US, and MRI in 529 women with increased familial risk. Annual conventional mammography was performed with at least two views (medio-lateral oblique and cranio-caudals) per breast, and additional or spot compression views where appropriate. Diagnoses were coded according to the Breast Imaging Reporting and Data system (BI-RADS) diagnostic categories. Breast ultrasound was performed with 7.5- to 13-MHz probes. Standard contrast-enhanced MRI of both entire breasts was performed on a 1.5 T system after injection of 0.1 mmol/kg gadopentetate dimeglumine.

43 breast cancers were identified in the total cohort (34 invasive, 9 ductal carcinoma in situ). Overall sensitivity of diagnostic imaging was 93% (40 of 43); overall node-positive rate was 16%, and one interval cancer occurred (1 of 43, or 2%). In the analysis by modality, sensitivity was low for mammography (33%) and US (40%) or the combination of both (49%). MRI offered
Fig. 6. (A) Mammogram and (B) sonogram of suggestive of cancer (arrowhead) on a 53-year-old patient with a family history of breast cancer and personal history of benign breast biopsy on the left breast revealed no clinical findings. (C) MRI showed only scar tissue on the left (arrowhead), but revealed a suspicious lesion in the right breast (long arrow), which was an invasive ductal cancer, pT1b, G3, N0, M0 by biopsy. Absence of cancer in the left breast was confirmed by 4-year follow-up.

a much higher sensitivity (91%). The sensitivity of mammography in the higher-risk groups was 25%, compared to 100% for MRI. Specificity of MRI (97.2%) was equivalent to that of mammography (96.8%).33 Mammography, either alone or combined with sonography, seems insufficient for diagnosis of early breast cancer in patients who are at increased familial risk with or without BRCA mutation. If MRI is used for surveillance, a significantly higher sensitivity, specificity, and positive predictive value (PPV) could be achieved for diagnosis of intraductal and invasive familial or hereditary cancer at a more favorable stage.33 Indeed, not even half of all cancers were prospectively diagnosed with a combination of mammography and sonography, whereas breast MRI alone diagnosed 91% (39 of 43). However, MRI is still an investigational technique for surveillance and screening of asymptomatic women with normal conventional diagnosis. Apart from cost, the most important reason of breast MRI is low PPV, low specificity, and allegedly low sensitivity for ductal carcinoma in situ (DCIS). However, MRI has the highest sensitivity for invasive as well as intraductal cancers, which was not achieved at the expense of similar specificity as that of mammography.33 Combined with mammography, sonography can compensate some but not all the shortcomings of mammography with a substantial number of false-positive diagnoses. In comparison to surveillance by MRI, mammography was of limited and US of no additional value. US screening may, however, be useful in the long interval between the annual surveillances.33

Altogether, surveillance with MRI allows an earlier diagnosis of familial breast cancer and has better performance than mammography or the combination of mammography with high-frequency sonography.

6. DOPPLER ULTRASOUND

The well-known phenomenon of tumor angiogenesis is associated with an increase in malignancy.34,35 These abnormalities included tumor stains, irregular large caliber vessels, and either prolonged or rapid emptying of vessels presumably due to blood pooling, leaky vessels, and/or arterio-venous shunts. Among the established breast diagnosing techniques, mammography and sonography have undisputed contributions. However, no adequate information on the growth pattern and the prognosis of breast humps are available. Doppler US has been investigated to differentiate benign lesion from malignant solid breast masses from their different Doppler characteristics, (i.e., symmetric signals in normal tissue, no signals in cysts, and higher maximum systolic and end-diastolic pressures in malignant tumors)36–38 with high sensitivity and specificity despite considerable overlap in the benign and malignant types.39,40 Highly sensitive color Doppler on even minute tumor vessels could map the tumor blood flow both quantitatively and qualitatively.

Color Doppler in 2 of 39 malignant breast disease patients with the tumor size of 0.6–8.0 cm (median 2.0 cm) did not show any vascularity. In comparison, no blood vessels were
found in 10 of 73 benign masses (0.3–4.7 cm with the median of 1.4 cm). In patients with puerperal mastitis, abscess, phylloides tumor, and haemangioma, vascularization was extremely high. Benign and malignant breast lesions have significantly different Doppler US features. There is a remarkable overlap of carcinoma and benign tumor in peak flow velocity. The discrepancies between reported studies may be related to the US system and the scanning techniques. The accuracy for smaller blood vessels, especially for poorly vascularized masses, could be improved using a high-frequency and high-resolution system. Furthermore, color Doppler may also be able to reduce the number of biopsy and histological evaluations for patients with suspicious mammograms.

In another prospective study, the color Doppler flow images of 55 proven breast cancers were performed, and 82% of them were classified on a three-level scale of vascularity (minimal: 14%, moderate: 29%, marked: 53%), suggesting its clinical potential use. 4% of the flow images had no detectable flow. 69% of the normal breasts had moderate or marked vascularity (minimal: 28%, moderate: 41%, marked: 28%), and 3% were avascular. Because of poor distinction between normal tissues and cancer, more sensitive Doppler methods are required for the low vessel flow that is rather specific for malignancy.

Power Doppler sonography has advantages over color Doppler type with high sensitivity in the detection of vascular flow. Power Doppler findings were considered positive when at least one vessel was associated with the solid breast mass (Fig. 7). In one study comprising 176 breast cancers in 176 patients (27–91 years, mean ± std: 56 ± 15 years), 65% and 10% of the cases were invasive ductal carcinoma and invasive lobular carcinoma, respectively. Among them, 73% showed vascularity and 27% showed no vascularity on power Doppler sonography. The sizes of the lesions in which power Doppler sonography revealed vessels and no vessels were 7–80 (21 ± 15) mm and 3–55 (14 ± 14) mm, respectively (p < 0.01); however, these two categories overlapped. Tumor vascularity revealed by power Doppler sonography correlated strongly with detection of lymph node involvement and lymphatic vascular invasion with sensitivities of 93% and 90%, but low specificities of 32% and 35%, respectively. More importantly, patients with breast cancer in whom vessels were not revealed by power Doppler sonography were also unlikely to have lymph node involvement and lymphatic vascular invasion with negative predictive values of 90% and 87%, respectively.

In conclusion, Doppler US could detect moderately small vessels around and within tumors, even if they were too small to be displayed on conventional B-mode images. Although only cancer patients were involved, the presence of similar vessels in the normal breast indicates Doppler imaging as a technique with a presumably higher specificity but much lower sensitivity.

7. ACOUSTIC RADIATION FORCE IMPULSE IMAGING

The limitations of palpation and biopsy as well as CT, MRI, and US imaging require a noninvasive, cost-effective, safe, and accurate modality for detecting changes in tissue pathology. Several groups have developed elasticity-based imaging modality in order to exploit the relationship between pathology and tissue’s mechanical properties.
Acoustic radiation force is due to the momentum transfer from the propagation of acoustic waves to the dissipative medium.\textsuperscript{44} The absorption is in the direction of wave propagation, whereas the reflection depends on the angular scattering properties of the target.\textsuperscript{45} Under plane-wave assumptions, the generated radiation force in the tissue is:\textsuperscript{44, 46}

\[ F = \frac{2\alpha I}{c} \quad (1) \]

where \( F \) is a force per unit volume, \( \alpha \) is tissue attenuation, \( I \) is the acoustic intensity, and \( c \) is the sound speed of tissue.

Acoustic radiation force impulse (ARFI) imaging, a novel transient elastography method, generates radiation force inside the tissue, detects the consequent localized displacements by correlating the ultrasonic echoes, and then estimate the mechanical properties of target.\textsuperscript{47} All tissues are inherently viscoelastic and response differently to mechanical excitation, on the order of ten micrometers, which can be monitored both spatially and temporally and is inversely proportional to local tissue stiffness. The tissue volume exposed to radiation force is determined by the focal characteristics of the transmitting transducer, and the temporal profile of the force is dependent on transmitted pulse shape, usually with the duration less than 1 ms. In this method, a single diagnostic transducer is used both to apply localized radiation forces inside the tissue and to track the resulting tissue displacements, which guarantees good alignment and ease of real-time implementation. ARFI imaging has many potential advantages, such as identifying and characterizing a wide variety of soft tissue lesions, atherosclerosis, plaque, and thrombosis in clinics.

There is good correlation between the ARFI image and the matched B-mode image in the breast at the depth of 5–25 mm (Fig. 8(a)). In the ARFI image, the boundary of an infected lymph node as a palpable lesion appears stiffer than its interior and the tissue above it (i.e., smaller displacements). The oval structure in the B-mode image immediately above and to the left of the lesion (upper arrow) is outlined as a softer region of tissue than its surroundings in the ARFI image. The transient response to ARFI excitation depends on tissue structure and mechanical properties. In Figure 8(b) the region of tissue spanning 13–18 mm moves further, and exhibits a later peak displacement than the others, which is slightly darker in the matched B-mode image.

Peak displacements of ARFI images range from 5 to 13 \( \mu \text{m} \) \textit{in vivo}, and the lesion in the B-mode image exhibits a stiff outer boundary and a softer interior in the matched ARFI image (Fig. 9). Core biopsy of this lesion demonstrated an infected lymph node with a more liquid abscessed component. While these findings are circumstantial, they do suggest potential correlation between the clinical pathology and the ARFI image. The discrepancy of the brightness in the B-mode image and detected stiffness indicates no direct relationship between them as expected.

There is no speckle in the ARFI images. Thus, the traditionally defined speckle SNR of a conventional US imaging system is in general lower than that of the ARFI imaging system. Comparison of the contrast of the ARFI and B-mode images yields variable results. The applied radiation force and resulting tissue displacements are predominantly in the direction of wave propagation. With the current imaging geometry, only these axial displacements are tracked, and the anticipated error is ±0.14 \( \mu \text{m} \).\textsuperscript{44} While useful information might be derived from the lateral displacement, tracking of such small lateral displacements (\(<1 \mu \text{m}\)) is extremely challenging. The increase in displacement estimation error with depth rather than the decreased SNR does not degrade image quality.\textsuperscript{49} The resolution of an ARFI imaging system depends on transducer specifications and configuration, the number and location of pushing beam, spatial relationship of pushing locations and tracking beams, and the pulse length and kernel size in the tracking algorithm as well as the tissue property itself, and is at least comparable to that in the conventional B-mode imaging.

The acoustic energy required to generate detectable displacements \textit{in vivo} is large (\(<1,000 \text{ W/cm}^2 \) \textit{in situ}), but its duration is short (0.7 ms in each pushing location). So the radiation force-induced displacement in soft tissue is detectable while maintaining a temperature increase below 1 °C.\textsuperscript{50, 51} Altogether, the operating parameters of ARFI imaging are safe, and will not result in an increased risk to the patient.

In summary, ARFI imaging is feasible \textit{in vivo} for the diagnosis of breast. Differences in displacement maps are correlated with tissue structure as observed in the matched B-mode images.

The transient response of tissue varied with tissue type and its

![Fig. 8.](image-url)
visco-elastic behavior. Although these findings are preliminary, they present several opportunities for ARFI imaging with a considerable clinical promise.

8. SUPERSONIC SHEAR IMAGING

Supersonic shear imaging (SSI) is another transient elastography approach and combines the remote palpation of the ARFI technique and the ultrafast echographic imaging approach, which provides a quantitative elasticity map with less dependence on operator in comparison to static elastography.52, 53 The initial clinical investigation illustrates its potential as an adjunct for sonography.

SSI generates a remote radiation force by focused ultrasonic beams as ARFI. Consequently, a transient shear wave will be formed by the remote tissue vibration. Several pushing beams at increasing depths are transmitted to generate a quasi-plane shear wave front that propagates throughout the region-of-interest (Fig. 10). After that, successive raw radiofrequency (RF) data is acquired at an ultrafast frame rate (2,000 frames/s). Contrary to conventional sonography formed using line-by-line scanning, ultrafast echoic images are achieved by transmitting a single quasi-plane ultrasonic wave which has slight diffraction along the transducer elevation direction and then performing the imaging process (i.e., beam forming, array signal processing) only in the receiving mode. Because of the memory limit, only 128 successive ultrafast echoic images can be stored at a total duration of 30 ms.54, 55

3 successive SSI sequences were performed to locate the lesion (Fig. 11). The first SSI sequence was performed using pushing
Fig. 12. Comparison between the B-mode ultrasound and the elasticity image obtained in the SSI with colorbar presenting the shear wave speed (0–9 m/s, $E = 0$–240 kPa) with the delineation between soft fatty tissues (∼7 kPa) and breast parenchyma (∼30 kPa) in normal breast tissue.

beams centered along the central line, which allowed elasticity imaging on both left and right parts. Then, the second and third SSI sequences were performed with a left and a right pushing line, respectively, and allow elasticity imaging in the middle of the imaging plane.

In the initial clinical trial, a total of 15 lesions were assessed quantitatively for its elasticity at an image window of 38 × 44 mm². The elasticity map displays the local shear wave speed $c_s$ on a color scale ranging from 0–9 m/s with the corresponding Young’s Modulus, $E = 3pc_s^2$, ranging from 0–240 kPa. Elasticity maps exhibit good concord with the spatial heterogeneities and structures in normal breast tissue and provide quantitative highlighting for benign and malignant lesions. In general, benign solid and malignant lesions in that study had a mean Young’s modulus of 45–80 kPa and 100 kPa (in some cases >180 kPa), respectively. It is known, however, that some cancers such as the mucinous subtype can be rather soft, and some mature fibroadenomas can be extremely stiff.

8.1. Normal Breast Tissue

The quantitative elasticity in normal breast tissue clearly delineated the different structures of breast. Young’s modulus ranged between 3 kPa for fatty tissues to 45 kPa in the parenchyma. Figure 12 compares the US gray scale and Young’s modulus image, which presents a fibrous mass (benign lesion corresponding to a fibrocystic disease). The Young’s modulus is easily recovered in the normal breast tissue areas. There is nice delineation between fatty tissue (∼7 kPa) and breast parenchyma (∼40–50 kPa) on both the US grayscale and elasticity images. These characteristic values were found in all healthy patients.55

Fig. 13. Comparison between B-mode ultrasound and quantitative elasticity map in the SSI mode for infiltrating ductal carcinoma grade III. Hypoechoic lesion with indistinct margins, slightly posterior shadowing classified as BI-RADS category 5.
8.2. Malignant Lesions

A typical example of a BI-RADS category 5 lesion and its corresponding elasticity map is shown in Figure 13. The B-mode US depicted a 10-mm hypoechoic mass with indistinct margins and posterior shadowing, which strongly indicates a high suspicion of malignancy and is confirmed in the pathologic diagnosis as an infiltrating ductal adenocarcinoma (grade III with a high mitotic activity). SSI clearly exhibits higher stiffness of the lesion with mean elasticity value of 150–175 kPa and better delineation of the lesion margins than B-mode US images. The lesion size measured on the elasticity map was confirmed by the pathologic analysis (8 × 10 mm). In addition, the Young’s modulus in the SSI enables a satisfactory discrimination between fatty tissues (∼5 kPa), breast parenchyma (∼40 kPa), and lesion location (∼170 kPa) in the resolution of roughly 1.5 mm.

The potential ability of the SSI for the guided percutaneous procedures (core biopsies or fine needle aspirations) with clinically satisfactory location precision was illustrated in Figure 14 for a small, slightly hypoechoic nodular lesion with indistinct contours measuring 5 mm, which was classified as BI-RADS category 4. This lesion is rather difficult to discriminate on B-mode US because of its low echogenicity contrast in comparison to the normal parenchyma after local anesthesia, thus necessitating multiple sampling. In comparison, the elasticity map clearly delineates a small and stiff region (∼165 kPa) and properly depicted margins with an average 5 mm diameter. This lesion size was confirmed after biopsy by the pathologist.

8.3. Benign Solid Lesions

SSI was also able to detect benign solid lesions such as fibroadenomas or fibrocystic disease changes. In all cases, these lesions were detected on the elasticity mapping as rather soft structures with mean Young’s modulus ∼80 kPa for, whereas malignant lesions exhibited mean elasticity >100 kPa. A hypoechoic,
Fig. 16. Comparison between B-mode image and quantitative elasticity map in the SSI of (a) hypoechoic lesions with lobulated margins, discretely reinforcing ultrasound beam, classified as BI-RADS category 4, which was diagnosed as a cyst containing inflammatory cells and debris in fine-needle aspiration, and (b) another patient with a benign cyst nodule.

homogenous, lobular-shaped lesion classified as BI-RADS category 4 can be observed in Figure 15. SSI describes structures with different elasticity in good concord with the structures depicted in the B-mode image, but comparable elasticity with the surrounding healthy tissues ($E$:8–15 kPa). Biopsy was performed under US guidance and led to a histologic diagnosis in favor of fibrocystic disease.

8.4. Benign Cysts

SSI was also useful in the diagnosis of cystic lesions. Figure 16(a) corresponds to hypoechoic lesions with lobulated margins and a discreetly reinforced US beam, which was classified as BI-RADS category 4. Fine-needle aspiration was performed under US guidance, and a yellow-colored liquid was evacuated, which led to a histologic examination as a cyst containing inflammatory cells and debris. The SSI elasticity map provided local Young's modulus in healthy surrounding tissues except in the lesion, which is consistent with the fact that shear waves do not propagate in liquids. All data corresponding to non-propagating shear waves are intrinsically filtered by the imaging post processing algorithm. Two reasons for this filtering can be evoked. First, the strong acoustic streaming induced in the liquid can lead to a de-correlation of the successive US data. Second, the strong modification of the shear displacement versus the propagation direction yields to a de-correlation of shear displacement time profiles at neighboring locations, resulting in a false time-of-flight estimation. This de-correlation can be in both cases filtered, leading to an absence of Young’s modulus estimation in the liquid. Figure 16(b) corresponds to another more clearly hypo-echoic cystic lesion which is identified as a liquid area surrounded by soft tissues in the SSI.

In summary, quantitative mapping of breast tissue elasticity is feasible in vivo using the SSI approach. Discrimination between breast fat and parenchyma and identification of malignant lesion, benign solid lesion, cystic lesions are feasible, reliable, and clearly visible. This novel imaging modality is significantly less operator dependent than static elastography as the mechanical excitation that interrogates breast tissues is induced by the system itself. It could have a potential in clinics for breast lesion diagnosis.

9. CONCLUSION

High-frequency high-quality sonography system has significant technical improvements with high resolution, great contrast, large
dynamic range, less speckle noise, high frame rate, and multiple ultrasound imaging modality (i.e., color Doppler and real-time three-dimensional scanning) in the past decades. Although digital signal/image processing techniques aided the automated tumor/cancer detection and enhanced the outcome, the superiority of state-of-the-art mammography over sonography has been shown in a variety of clinical studies. However, in the detection and diagnosis of benign lesions, for example, a distinction between cystic and solid masses, mammography is not necessarily the preeminent examination, and sonography is the useful procedure of choice. Meanwhile, development of novel ultrasound-based elastography, especially the transient type that generates remote pushing force to the target, enables the detection of the mechanical properties of tissue, which has higher sensitivity, specificity, and contrast than the conventional B-mode ultrasound images. Although the preliminary results are very promising, its role in breast cancer diagnosis will be carried out in multiple and randomized clinic centers and then be compared with mammography for performance evaluation.

References and Notes

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