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Quantification of Breast Stiffness Using Magnetic Resonance Elastography at 3T with a Soft Sternal Driver: A Reproducibility Study

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Abstract

Purpose—Previous studies of breast MR elastography (MRE) evaluated the technique at magnetic field strengths of 1.5T with breast in contact with the driver. The aim of this study is to evaluate breast stiffness measurements and their reproducibility using a soft sternal driver at 3T and compare the results to qualitative measures of breast density.

Materials and Methods—Twenty-two healthy volunteers each underwent two separate breast MRE scans in a 3T MRI. MRE vibrations were introduced into the breasts at 60Hz using a soft sternal driver and axial slices were collected using a gradient echo MRE sequence. Mean stiffness measurements were calculated for each volunteer as well as a measure of reproducibility using concordance correlation between scans. Mean stiffness values for each volunteer were assessed and related to amounts of fibroglandular tissue (i.e. breast lobules, ducts and fibrous connective tissue).

Results—The stiffness values were reproducible with a significant p-value<0.0001 between two scans with concordance correlation of 0.87 and 0.91 for center slice and grouping all slices, respectively. Volunteers with dense breasts (i.e. higher grades of fibroglandular tissue) had mean stiffness values of 0.96 kPa (center slice) and 0.92 kPa (all slices) while those without dense breasts had mean stiffness values of 0.85 kPa (center slice) and 0.83 kPa (all slices) ($p = 0.05$).

Conclusion—Breast MRE is a reproducible technique at 3T using a soft sternal driver. Dense breasts had significantly higher stiffness measurements compared to non-dense breasts.

Keywords

MR elastography; Breast disease; Breast stiffness; Elastography

INTRODUCTION

Breast cancer is the most common form of cancer among women in the United States and the second leading cause of cancer death (1). Mammography and ultrasound are most commonly used for the detection and characterization of breast masses, however, both modalities have limitations. The sensitivity of mammography decreases with increasing breast density while the specificity of ultrasound is limited in its characterization of breast lesions (2,3). Contrast enhanced breast magnetic resonance imaging (MRI) is the most sensitive imaging modality for breast cancer detection and is indicated for screening women at high risk for breast cancer, evaluating extent of disease in patients with a known breast carcinoma and monitoring therapy, and in the additional evaluation of clinical or imaging findings (ACR Practice Parameter for the Performance of Contrast-Enhanced Magnetic Resonance Imaging (MRI) of the Breast Res. 12 – 2013, Amended 2014 (Res. 39)). While breast MRI is highly sensitive for cancer detection it has been historically limited in its use due to a lower specificity because of an overlap in appearances between benign and malignant lesions(4).

It is known that breast cancers are often stiffer than benign lesions and normal surrounding tissues. Breast cancer often shows a desmoplastic stromal reaction with a reactive proliferation of connective tissue and fibroblasts around malignant epithelial cells (5). This tissue reaction forms a basis upon which breast lesions may be detected through palpation. However, clinical breast examination (i.e. palpation) is subjective. The use of elastography in breast ultrasound has been shown to improve exam specificity and is of potential use in reducing unnecessary biopsies of masses with low suspicion of malignancy and assessing histopathologic severity of breast lesions (6–11). Additionally, ultrasound elastography has some limitations such as user dependent, limited spatial resolution, and lack of standardized scoring of tissue stiffness (12).

Magnetic resonance elastography (MRE) is a novel non-invasive technique to measure the spatial stiffness of soft tissues (13–26). MRE images are generated through a three-step process. First, noninvasive vibrations are applied to tissues by a driver that transmits waves. Second, a phase-contrast MRI sequence synchronized to the applied vibrations measure wave displacement. Lastly, the measured wave displacements are mathematically converted to spatial stiffness maps. Previous studies of MRE have shown the potential in improving the diagnosis of breast lesions. Earlier work showed a good distinction between benign and malignant lesion stiffness and that utilizing MRE along with contrast enhanced MRI improved diagnostic accuracy (25–27). MRE may provide important additional information noninvasively which could be used to improve the specificity of contrast enhanced breast MRI and reduce the amount of false positive biopsies performed. However, these studies used a MRE driver, which is in contact with the breast causing bulk motion rather than shear motion, discomfort and compressing the breast.

The aim of this study is to assess the reproducibility of breast MRE in a 3T MRI system using a soft sternal driver, which obviates the need for contact with the breast during the examination and compare subject stiffness measurements against a BI-RADS measure of fibroglandular tissue (FGT).

MATERIALS AND METHODS

The study protocol was approved by the institutional review board and written informed consent was obtained from each study participant. A total of 22 healthy female volunteers (age range 24–64 years) were included in the study.

Experimental Setup

All imaging was performed using a 3T MRI scanner (Skyra, Siemens Healthcare). Each patient laid face down with her non-compressed breasts positioned in the breast coil (Sentinelle 16 channel coil, Siemens Healthcare). The soft sternal driver was attached to the breast coil and connected by pneumatic tubing to the active driver as displayed in Figure 1. 60 Hz vibrations were introduced into the breasts through the soft sternal driver.

Image Acquisition Parameters

A series of axial images were obtained using a gradient echo (GRE) MRE sequence (13). Imaging parameters included: TE=19.94 ms, TR=25 ms, Field of view=320×320 mm², matrix size 256×128, slice thickness=5mm, number of slices=5, MRE phase offsets=4. After the initial scan, to measure reproducibility, each volunteer was asked to step out of the scanner and repositioned in the breast coil within five minutes. The same imaging parameters were utilized for a subsequent scan.

Image Analysis

MRE images were masked to obtain the breast and a curl processing (28) was performed to remove the longitudinal component of wave motion. Additionally, a bandpass directional filter was applied in eight directions with cutoff values of 4–40 waves/FOV to remove the reflect waves (29). 3-D local frequency estimation (30) was performed to obtain a weighted stiffness map using MRE-lab (Mayo Clinic, Rochester MN). The mean stiffness was calculated using a custom made software in Matlab (Mathworks, MA) to report the mean stiffness value encompassing the entire breasts. The high resolution T1 and T2 weighted images were reviewed by three dedicated breast imaging radiologists and the amount of FGT was subjectively scored according to BI-RADS criteria (31). Breasts were classified as being almost entirely fatty (A), having scattered FGT (B), having heterogeneous FGT (C), or extreme FGT (D). The BI-RADS amounts were chosen based on the most frequent scores among the three raters. Subjects were grouped as A/B or C/D based on their scores with the C/D group chosen to represent patients with dense breast tissues.

Statistical Analysis

The reproducibility of MRE-derived stiffness measurements was tested by the concordance correlation method (32) and using Bland-Altman plots (33). To determine association between BI-RADS scores and MRE-derived stiffness measurements, BI-RADS scores were chosen based on the most frequent scores among the three raters and grouped as A/B and C/D. The difference in stiffness between the two groups was compared by using two-sample t-test. A p-value of 0.05 was considered significant.

RESULTS

Good discernible waves were observed using soft padded sternal driver without the need for contacting the breasts. Figure 2 displays the short-axis magnitude image in one of the volunteers as well as a snapshot of one time point of wave propagation in the three spatial directions (X, Y, and Z) as well as the corresponding 3D weighted stiffness map for scan 1 and scan 2.

MRE-derived stiffness measurements of the breast were found to be reproducible. Figure 3 shows the concordance plot of stiffness values for center slice between two repeated measurements, demonstrating a significant correlation coefficient of $r_c = 0.87$ (95% Confidence interval: 0.76–0.98; $p < 0.0001$). Similarly, Figure 4 shows the concordance plot of stiffness values for all slices between two repeated measurements, demonstrating a significant good correlation coefficient of $r_c = 0.91$ (95% Confidence interval: 0.84–0.98; $p < 0.0001$). Additionally, Figure 5 shows the Bland-Altman plot for center slice with a very small mean bias of 0.009 kPa and 95% limits of agreement of –0.11 to 0.12 kPa. Similarly, Figure 6 shows the Bland-Altman plot for all slices with a very small mean bias of 0.01 kPa and 95% limits of agreement of –0.07 to 0.09 kPa.

Higher stiffness measurements were found for subjects with greater amounts of FGT. Thirteen of the volunteers were classified as having either A or B amounts of FGT and nine volunteers as having either C or D amounts of FGT. Volunteers classified as having dense breasts tended towards greater breast stiffness measurements. For the A/B group, the mean stiffness by pooling all subjects for center slice was 0.85 ± 0.11 kPa while for the C/D group it was 0.96 ± 0.13 kPa with a significant p-value ($p = 0.03$), as shown in Figure 7. Similarly, for the A/B group, the mean stiffness by pooling all subjects for all slices was 0.83 ± 0.11 kPa while for the C/D group it was 0.92 ± 0.13 kPa with a significant p-value ($p = 0.05$), as shown Figure 8.

DISCUSSION

This study had demonstrated that MRE-derived breast stiffness measurements were reproducible with a significant correlation between repeat measurements in a 3T system using a soft sternal driver. Additionally, volunteers with dense breasts had significantly higher stiffness measurements compared to less or non-dense breasts.

This study evaluated the use of breast MRE at field strength of 3T. The increased use of higher field MRI scanners allows for greater signal-to-noise and improved spatial resolution though this may affect the generation of MRE images. It was previously reported that the use of MRE for the liver at 1.5T resulted in image degradation when the same scanning parameters were utilized in a 3T system (34). Our study demonstrates that breast MRE is feasible and reproducible at 3T at a frequency of 60 Hz. The frequency of 60 Hz was lower than previously reported breast MRE investigations (65–300 Hz) which may require less power for penetration and improve patient comfort during the examination (25–27,35). However, lower frequencies have longer wavelengths, where spatial resolution might be

compromised while detecting small tumors. Additionally, this study was able to differentiate dense breasts using MRE-derived stiffness measurements at 60Hz.

Previous studies evaluating the use of breast MRE have utilized drivers requiring contact with and compression of the subject's breast (25–27,35). Previous studies also required the use of multiple drivers, one contacting the lateral aspect of each subject's breasts, as opposed to the single driver used in this experimental setup. The use of a sternal driver without requiring contact with or compression of a subject's breast provided several advantages over previous experimental setups. First, the vibrations are introduced into the breast without displacing them, as there is no contact with the breast. Second, contact with a subject's breasts may induce image artifacts during a diagnostic examination secondary to compromised positioning. Skin folds or breast deformation in positioning may cause areas of signal inhomogeneity, anatomical distortions, and poor image quality making image interpretation difficult, which can be avoided (36). Finally, compression of the breast may affect contrast enhancement characteristics of breast tissues and lesions during diagnostic examinations. Previous investigations have shown that breast compression during MRI evaluation may affect breast lesion detection, evaluation of lesion size, as well as imaging interpretation (37). Compression may decrease blood flow and the inflow of contrast material, potentially causing delayed or non-enhancement of malignant lesions.

The differentiation of benign and malignant breast pathology in breast imaging examinations is important for maintaining high sensitivity for cancer detection while avoiding unnecessary biopsies. Given that the specificity of contrast enhanced breast MRI is a factor sometimes cited as limiting its use, endeavors which may decrease false positive results should be investigated. Previous investigations of elastography use in breast ultrasound have shown improvements in specificity without loss of sensitivity (7–10). A previous study combining breast MRE and contrast enhanced MRI demonstrated a 20% increase in specificity while maintaining 100% sensitivity (35). Further investigations utilizing this technology are warranted to assess its value in improving lesion characterization on breast MRI, particularly in lesions with lower likelihoods of malignancy such as areas of non-mass enhancement with relatively benign distributions or circumscribed masses. Additional investigations of MRE may also focus on areas where ultrasound elastography has proven useful in breast imaging. Elasticity imaging has shown useful in predicting the histopathologic severity of breast malignancies as well as monitoring treatment effects in patients undergoing neoadjuvant chemotherapy (11,38,39).

There are some limitations in our study. First, the sample size is small with only 22 volunteers included in the study. Second, the study did not directly evaluate the use of MRE with any specific breast pathology but rather only normal volunteers. While volunteers classified as having dense breasts tended to have greater mean stiffness values the significance of this finding is unclear. Finally, only short-term reproducibility (i.e. on same day) was performed as we were testing the reproducibility of the technique. Despite these limitations good reproducibility of stiffness measurements was observed with significantly higher stiffness for dense breasts.

MRE of the breast is a valid and reproducible technique at 3T with the use of a soft sternal driver. Dense breasts characterized qualitatively by BI-RADS amount of FGT had higher stiffness measurements. Additional studies with larger patient cohorts and a variety of breast lesions are warranted to further define the utility of this technique in differentiating benign and malignant breast pathology.

Acknowledgments

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Figure 1. Experimental set-up. A soft sternal driver is placed on the breast coil in the expected location of the sternum. Vibrations are non-invasively transmitted from the passive driver and into the subject's breasts without contacting the breast.

Figure 2. MRE data in the same volunteer: An example showing the magnitude image, wave images in the X, Y, and Z directions and the corresponding stiffness map for scan 1 and scan 2.

Figure 3. Concordance plot of stiffness values (kPa) for the center slice between the two repeated scans for the 22 volunteers. $r_c=0.87$ (95% CI: 0.76–0.98; $p<0.0001$).

Figure 4.

Concordance plot of stiffness values (kPa) for all slices between the two repeated scans for the 22 volunteers. $r_c=0.91$ (95% CI: 0.84–0.98; $p<0.0001$).

Figure 5. Bland-Altman plot between scan 1 and scan 2 for the center slice with red lines showing 95% limits of agreement (-0.11 kPa to 0.12 kPa) and purple line showing the mean bias (0.009 kPa).

Figure 6. Bland-Altman plot between scan 1 and scan 2 for all slices with red lines showing 95% limits of agreement (-0.07kPa to 0.09kPa) and purple line showing the mean bias (0.01kPa).

Figure 7.

Box plot of stiffness values for the center slice for the 22 volunteers as function of BI-RADS amount of breast FGT with mean stiffness of 0.85 ± 0.11 kPa for A/B group and 0.96 ± 0.13 kPa for C/D group with a significant difference ($p=0.03$) between two groups.

Figure 8.

Box plot of stiffness values for all slices for the 22 volunteers as function of BI-RADS amount of breast FGT with mean stiffness of 0.83 ± 0.11 kPa for A/B group and 0.92 ± 0.13 kPa for C/D group with a significant difference ($p=0.05$) between two groups.