

Appendix E1

Materials and Methods

In Vivo Studies

Between March 2016 and April 2018, 14 female participants with biopsy proven invasive ductal carcinoma (IDC) were recruited for this study. All participants were recruited during their scheduled clinical MRI examination at our institution and the characteristics of the 14 participants are presented in Table 1. Lesion size was measured on postcontrast images and the average size was 3.2 ± 1.0 cm (range, 1.7 ~ 4.5 cm). Based on measurements from the images, different tissue density patterns were observed, including extremely dense tissue ($n = 2$), heterogeneous tissue ($n = 3$), scattered tissue ($n = 4$), and fatty tissue ($n = 5$).

After the MRI scans, region-of-interest (ROI) analysis was performed by one radiologist (A.P.) with 8 years of experience in breast imaging. For healthy study participants, ROIs were directly placed on the proton density maps to assess both T_1 and T_2 relaxation times for fibroglandular tissues. For participants with IDC, lesions were first identified on clinical dynamic contrast enhanced MRI examination. Based on this information, ROIs were drawn on T_2 maps corresponding to solid enhancing component of the lesion, and propagated to the T_1 maps. Note that in MRF, the T_1 maps are intrinsically registered to the T_2 maps, as the two are acquired simultaneously. For participants with more than one lesion, a single representative lesion based on the size of lesions was selected. All the T_1 and T_2 values obtained from breast tumors for the 14 participants with IDC are presented in Table 1. T_1 and T_2 relaxation times in normal tissues were also measured from nine participants with IDC and ROIs were drawn from contralateral nondiseased breast by covering whole breast tissue at one section where the breast tissue covered a large area. No values were obtained from the other five participants with IDC who had almost entirely fatty breast tissue composition.

Volumetric B_1 Mapping with the Bloch-Siegert Method

For volumetric measurement at 3T, substantial B_1 field inhomogeneities are expected for breast imaging (16). To evaluate the influence of this inhomogeneity on the accuracy of T_1 and T_2 quantification using MRF, a volumetric B_1 map was acquired in a separate scan using the Bloch-Siegert method (15). The Bloch-Siegert B_1 measurement was performed on six participants out of the total of 15 healthy participants and it was prescribed to have the same spatial coverage as the MRF scan. A gradient-echo sequence was implemented with a 3D stacks-of-spirals acquisition and the total acquisition time with a matrix size of $128 \times 128 \times 48$ was ~ 52 sec (15). The volumetric B_1 map ($128 \times 128 \times 48$) was first calculated and resized to the same matrix size as the MRF measurement ($256 \times 256 \times 48$). A similar approach to incorporate B_1 information into the matching algorithm was adopted from a previous implementation for abdominal MRF (15). To retrieve tissue properties in considering B_1 variation, a special MRF dictionary that includes an additional dimension of B_1 (50% ~ 150% with a step size of 5%) was generated, as previously introduced in the literature (17). Signal evolution from each voxel were then matched to those entries with the same B_1 value as measured to extract T_1 , T_2 and proton density (M_0). As

a comparison, the standard processing method without using the acquired B_1 information (assuming a uniform B_1 map of 100%) was also performed.

Results and Discussion

The effect of B_1 field inhomogeneity on the accuracy of quantitative measurement using MRF was evaluated on six healthy participants. With the proposed MRF method, quantitative measurement obtained without B_1 correction (T_1 , 1131 ± 109 ms; T_2 , 45 ± 8 ms) provides similar results as compared with those obtained in consideration of B_1 variation (T_1 , 1129 ± 111 ms; T_2 , 45 ± 8 ms). No difference in either T_1 ($P = .09$) or T_2 ($P = .99$) was observed after applying B_1 correction.

Transmit (B_1^+) field inhomogeneity is a well-known problem for quantitative breast imaging, especially with high-field-strength 3T scanners. Compared with our previous study for abdominal MRF (15), our current study used more inversion pulses with various inversion times, which resulted in a higher sensitivity to T_1 , but the range of flip angles was reduced from $[0^\circ 54^\circ]$ to $[5^\circ 12^\circ]$. This low flip angle pattern significantly reduces the sensitivity of the proposed technique to the B_1 field inhomogeneity. In addition, an MLEV-based T_2 -preparation module was also used to minimize the adverse effects of inhomogeneous B_1 field.