Published in final edited form as:

Acad Radiol. 2012 May ; 19(5): 526–534. doi:10.1016/j.acra.2011.11.003.

High-Resolution Diffusion-Weighted Magnetic Resonance Imaging in Patients with Locally Advanced Breast Cancer

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Introduction

Diffusion-weighted magnetic resonance imaging (DW-MRI) provides a non-invasive, non-contrast, three-dimensional method to measure the random motion of water molecules, quantified as the apparent diffusion coefficient (ADC), in vivo. DW-MRI is a promising tool for characterizing micro-structural properties of breast lesions, with applications to both diagnostic and prognostic studies. Decreased ADC has been reported in malignant tumors relative to normal breast tissue [1, 2]. In patients with locally advanced breast cancer, DW-MRI has been shown to have value in predicting response to neoadjuvant chemotherapy [3–7].

Despite this promise, DW-MRI of the breast has yet to be fully integrated into clinical practice. Some prognostic studies have found little value in breast DW-MRI in monitoring treatment response [8–10]. Tumor response to treatment is likely to be heterogeneous and high spatial resolution could improve the ability to capture heterogeneity in diffusivity. High resolution DW-MRI could improve prognostic and diagnostic applications in the breast, but obtaining higher resolution is technically challenging with current commercially available sequences. Most commercially available DW-MRI sequences are echo planar imaging (EPI)-based and spatial resolution is limited by the imaging field-of-view and number of phase and frequency encoding steps that can be acquired before the signal decays. Acquired in-plane resolution in DW-MRI of the breast is generally 2 mm or worse. EPI sequences are also prone to distortion. In breast EPI, distortion and other artifacts are particularly a problem due to changes in magnetic susceptibility at the air-tissue interfaces at the anterior and lateral borders of both breasts, as well as in the adjacent lung.

Imaging with a reduced field-of-view (rFOV) has the potential to provide two significant advantages for breast imaging: 1) improved spatial resolution and 2) reduced distortion. It

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has the potential to reduce distortion by decreasing the required readout duration for imaging and by allowing for air-tissue interfaces to be excluded from the shim volume, reducing susceptibility-induced artifacts. rFOV DWI-MRI has been applied to other anatomic regions such as the spine [11–13] and brainstem [14], but to our knowledge it has not been reported in breast tumors. An alternative approach to reducing distortion is the use of parallel imaging [15, 16]. However, parallel imaging requires estimating the coil sensitivities, a process that may lead to artifacts in the resulting images due to motion (for example, breathing, cardiac motion).

An rFOV DW-MRI sequence with higher in-plane resolution was developed for the spine [17], and was later used for evaluating diffusion outside the central nervous system [18]. This sequence utilizes a 2D echo-planar RF excitation pulse that simultaneously controls the slice and slab thicknesses, where the latter is the reduced-FOV direction during imaging. By reducing the FOV in the phase-encode direction of the EPI readout, we can decrease the number of k-space lines required to achieve a high-resolution image, while significantly reducing off-resonance induced artifacts with the shortened readout. Because only the FOV of interest is excited, there is no need for additional outer volume suppression pulses [13] with potentially high specific absorption rates. Furthermore, this method is compatible with contiguous multi-slice imaging, and hence does not require a slice skip as in [12], which is especially important while imaging small and/or potentially heterogeneous structures such as the tumors in the breast. We aimed to apply this custom-built rFOV DW-MRI sequence to the breast for quantitative DW-MRI of breast tumors.

In this study we investigated the impact of rFOV DWI-MRI on quantified and clinically interpreted DW-MRI data in locally advanced breast tumors, with the goal of improving tumor characterization. Our long-term goal is the ability to better measure tumor response to neoadjuvant chemotherapy and to better predict long-term patient outcomes. In this study, we compared quantitative and qualitative measures of tumor heterogeneity derived from rFOV versus standard FOV DW-MRI acquisitions. We also compared overall image quality. We hypothesized that the increased in-plane resolution in rFOV DW-MRI would improve characterization of tumor heterogeneity while the rFOV would reduce distortion and improve image quality.

Materials and Methods

Patients

The study population consisted of patients with invasive breast cancer enrolled in magnetic resonance imaging (MRI) studies to evaluate response to neoadjuvant chemotherapy. The studies were approved by the Institutional Review Board and compliant with HIPAA. All patients signed informed consent. Only patients with locally-advanced breast cancer scanned with rFOV DW-MRI, standard diffusion, and dynamic contrast-enhanced (DCE) MRI at the same MR exam and prior to surgery were included in the study. Additional inclusion criteria were adequate image quality for quantitative analysis and MR tumor volume $\geq 0.1 \text{ cm}^3$ [19, 20]. Analysis of diffusion in tumors with longest diameter as small as 0.5 cm has previously been reported [21]. Patients were scanned between December 2009 and July 2010. Analysis was retrospective.

Imaging

All scanning was performed on a 1.5 T GE Signa HDx scanner (GE Healthcare, Waukesha, WI) with 40 mT/m maximum gradient strength and 150 mT/m/ms maximum slew rate. An eight-channel bilateral breast radiofrequency coil was used (Sentinelle Medical, Inc,

Toronto, Canada). The diffusion sequences were acquired following contrast-enhanced imaging.

Contrast-enhanced imaging—Bilateral, axial, dynamic-contrast enhanced (DCE) MR images were acquired using a fat-suppressed T1-weighted three-dimensional fast gradient recalled echo (3DFGRE) sequence. Parameters were as follows: TR = 5.9–9.2 ms, TE = 2.6–4.5 ms, flip angle = 10°, FOV = 260–340 mm, acquisition matrix = 512 × 320, 512 × 192, or 384 × 224, slice thickness = 2 mm, number of slices = 92–124, and number of averages = 0.8. Gadopentetate dimeglumine (Magnevist, Schering AG, Berlin, Germany) was administered as a contrast agent at a dose of 0.1 mmol/kg body weight, followed by a saline flush of 10 mL saline. Images were acquired prior to contrast injection and at multiple timepoints post-injection.

Diffusion-weighted imaging—The standard diffusion-weighted imaging sequence used at our institution, a 2D, fat-suppressed, echo planar diffusion-weighted sequence, was acquired bilaterally in the axial orientation. The imaging parameters were: TR/TE = 6000/108.5 ms, FOV = 400 mm × 400 mm, acquisition matrix = 128 × 128, in-plane resolution = 3.125 mm × 3.125 mm, slice thickness = 3 mm, number of slices = 20 (with the exception of 1 patient who had 8 slices), number of excitations = 6, acquisition time = 4.4 min. Diffusion-weighting gradients were applied in 6 non-collinear directions with b = 600. Images were also acquired with b = 0.

A reduced field-of view (rFOV), 2D, fat-suppressed, echo planar diffusion-weighted sequence [17] was acquired unilaterally in the axial and/or sagittal orientation (in the final cohort, only 1 patient was scanned exclusively with sagittal rFOV). In this customized sequence, a 2D spatially selective RF excitation pulse and a 180° refocusing pulse were used to reduce the field-of-view in the phase encode direction while simultaneously suppressing the signal from fat. Parameters were: TR/TE = 4000/64.8 ms, FOV = 140 × 70 mm, acquisition matrix = 128 × 64, in-plane resolution = 1.094 mm × 1.094 mm, slice thickness = 4 mm, number of slices = 8, number of excitations = 16, acquisition time = 4 min. Diffusion-weighting gradients were applied sequentially in 3 orthogonal directions with b = 600. Images were also acquired with b = 0. A 16-slice option was developed for use in patients with large tumors. Parameter changes in the 16-slice option were as follows: TR = 3000, acquisition time = 6.6 min.

Image Processing

ADC maps for standard diffusion were constructed off-line using in-house software. The apparent diffusion coefficient (ADC, or D) for each voxel was calculated under the assumption of monoexponential signal decay of the original signal (S_{b0}) to S_{b600} with application of the diffusion gradients using the relationship in Equation 1 [22]:

$$S_{b600} = S_{b0} e^{-bD} \quad \text{Equation 1}$$

Acquired images for rFOV diffusion were first phase corrected and complex averaged using an automated method, and then ADC maps were constructed automatically at the scanner using the relationship in Equation 1 and previously reported methods [17].

Image Analysis

Quantitative Analysis—Tumor regions-of-interest (ROIs) were manually delineated on a central slice of rFOV images in consultation with a board-certified radiologist specializing in breast imaging. ROIs were placed using in-house software programmed in Interactive

Data Language (Version 7.0, ITT Visual Information Solutions, Boulder, Colorado). Care was taken to capture areas that were hyperintense on DCE-MRI subtraction images (pre-contrast subtracted from post-contrast), and generally hyperintense on DW-MRI and hypointense on ADC. ROIs were drawn to approximate tumor boundaries, so as to capture as much tumor as possible and to avoid inclusion of surrounding tissue. Areas of necrosis or fibrosis, based on lack of enhancement on DCE-MRI data, were excluded. Areas with obvious partial volume averaging of adjacent structures were also excluded by visual assessment. The same ROIs were mapped to the standard diffusion ADC maps. In cases of misregistration between the two acquisitions, ROIs were adjusted so as to cover the tumor. In some cases, differences in slice thickness between the rFOV and standard diffusion led to mapping of the ROI to more than one slice on standard diffusion; in these cases, the slice with the most tumor was selected. In the few cases in which rFOV and standard FOV were acquired in different orientations, the standard FOV images were reformatted and resampled to match the rFOV image series. The standard FOV images were selected for reformatting due to the fact that voxels were approximately isotropic.

For the tumor regions delineated by ROIs on rFOV and standard FOV ADC maps, histograms were constructed for the tumor ADCs, with bins of width $100 \times 10^{-6} \text{mm}^2/\text{s}$ [4], from $0-5000 \times 10^{-6} \text{mm}^2/\text{s}$. Despite the fact that $5000 \times 10^{-6} \text{mm}^2/\text{s}$ is above the diffusivity of free water at body temperature, this value was chosen as the upper limit to allow for exploratory analysis. Since the two sequences differed in resolution and FOV, histogram frequencies were normalized to the total number of tumor voxels [23]. The number of occupied bins (nbins) for tumor ADCs obtained from standard and rFOV diffusion sequences was calculated. The mean, median, minimum and maximum ADC, skew, kurtosis, and 12.5th, 25th, 75th, and 87.5th percentile ADCs were calculated. Measurements of lower (12.5th, 25th) and upper (75th, 87.5th) ADC percentiles may be important due to the fact that viable, invasive cancers have lower ADCs than normal tissue and changes in lower and upper ADC ranges may have potential in predicting treatment response. All histograms were constructed and analyzed in MATLAB (Version R2007a, MathWorks, Natick, Massachusetts).

Qualitative Analysis—Two board-certified radiologists specializing in breast imaging (and who did not take part in the ROI delineation above) qualitatively compared anonymized images from rFOV and standard FOV DW-MRI sequences for each patient. Reviewers were blinded to tumor histology and sequence type. Standard and rFOV images were referred to as sequence 1 and sequence 2. Sequence number was varied from case to case to improve blinding; however, complete blinding to sequence type was not possible due to the visual differences between images. For each patient, reviewers were shown 1 slice from rFOV and standard diffusion, covering the tumor and matched in spatial coordinates between sequence 1 and sequence 2. Reviewers were asked to rate 5 characteristics for each exam. On DW-images ($b=600$), tumor morphologic detail, tumor heterogeneity, lesion conspicuity, and overall image quality were rated; on T2-weighted images ($b=0$), overall image quality was rated. For each characteristic, readers determined if the characteristic appeared better on sequence 1, better on sequence 2, or if it appeared to be similar between the two sequences [24]. Reviewers were given the option of requesting additional slices, dynamic-contrast information, or re-windowing of the images.

Statistics

Tumor ADC means and histogram parameters were compared pair-wise for rFOV and standard FOV acquisitions. The paired Wilcoxon signed rank test was used ($\alpha=.05$). Tumor ADC means were compared between rFOV and standard FOV acquisitions with a Bland-Altman plot [25] and the 95% confidence interval for the agreement between the two

methods was calculated. Differences between the rFOV and standard DW-MRI mean tumor ADC measurements were also assessed in the subgroup of patients scanned after initiation of neoadjuvant chemotherapy using the paired Wilcoxon signed rank test at $\alpha=.05$. Similarly, differences were assessed in patients scanned prior to initiation of chemotherapy. All statistics were performed in MATLAB (Version R2007a, MathWorks, Natick, Massachusetts). Adjustment for multiple comparisons was not made as this analysis was exploratory.

Results

Patient accrual and tumor characteristics

During the study period, 16 patients with breast tumors $>0.1 \text{ cm}^3$ were scanned with rFOV and standard diffusion. Of these patients, 3 did not meet initial inclusion criteria due to image quality problems (in one exam fat suppression failed, one exam had an artifact and one had significant noise at the level of the tumor). Of the remaining 13 patients meeting inclusion criteria, two were excluded from analyses due to small tumor size and difficulty in identifying tumor on a single slice. The remaining 11 patients were included in both quantitative and qualitative analyses. Mean age was 53 (range 37–66).

All 11 patients were diagnosed with invasive breast cancer on pathology from biopsy and in all cases, the disease was considered locally advanced. Patients were scanned for either pre-chemotherapy tumor assessment (N=5) or post-chemotherapy tumor assessment (N=6). Tumor characteristics are described in Table 1. MR tumor longest diameter ranged from 1.3 – 9.3 cm.

Quantitative assessment of tumor ADC distributions

In the 11 patients included in this analysis, the mean tumor ADC calculated from rFOV DW-MRI was $1094.8 \times 10^{-6} \text{ mm}^2/\text{s}$ (SD=120.1) and mean tumor ADC calculated from standard FOV DW-MRI was $1132.8 \times 10^{-6} \text{ mm}^2/\text{s}$ (SD=117.2). Mean tumor ADC was not significantly different between methods ($p=0.58$, Table 2). When the difference between the mean ADCs was plotted against the average of the two methods (Bland-Altman Plot, Figure 1), the limits of agreement were -207.38 to $283.26 \times 10^{-6} \text{ mm}^2/\text{s}$ and more than 95% of the differences in the data were within these limits, suggesting that measurements of mean tumor ADC with the two methods were comparable. In the subgroup of patients scanned prior to initiation of chemotherapy (N=5), the average measurement for mean tumor ADC was 1084.8 (SD=101.9) in rFOV derived data and 1061.9 (SD=101.6) $\times 10^{-6} \text{ mm}^2/\text{s}$ in standard DW-MRI derived data ($p=0.44$). In the subgroup of patients scanned after initiation of chemotherapy (N=6), average measurement of mean tumor ADC was 1103.2 (SD=142.6) $\times 10^{-6} \text{ mm}^2/\text{s}$ in rFOV derived data and 1191.9 (SD=100.0) $\times 10^{-6} \text{ mm}^2/\text{s}$ in standard DW-MRI derived data ($p=0.31$).

In further analysis of the tumor ADC distributions obtained with the two methods (N=11), the 12.5th percentile tumor ADC and minimum tumor ADC were significantly different between rFOV and standard FOV DW-MRI ($p=.042$, $.003$, respectively), with a trend towards a lower 12.5th percentile and minimum ADC in the rFOV acquisition (Table 1). The maximum ADC ($p=.002$), ADC range ($p<.001$), and number of occupied bins ($p<.001$) were also significantly different in the rFOV acquisition relative to the standard FOV. All other variables, including skew and kurtosis, were not significantly different between acquisitions.

Qualitative analysis

Qualitative ratings from both readers showed a preference for rFOV in all five categories; however, Reader 2 showed a stronger preference for rFOV than Reader 1 and rated rFOV as

the preferred series for all cases and all categories. Reader 1 rated tumor heterogeneity as the same on rFOV and standard in 3 cases, lesion conspicuity as the same in 1 of those 3 cases, and preferred lesion conspicuity on standard in 1 and on rFOV in 1 of the 3 cases. Reader 1 concurred with Reader 2 for all other cases and categories.

Case studies

Images are shown for two cases in which readers rated rFOV better than standard FOV DW-MRI in all qualitative areas (Figures 2 and 3). In the first case, despite qualitative improvements with rFOV DW-MRI, tumor ADC histograms (Figure 2) appear similar, although differences in skew and nbins can be measured. In the second case, histograms (Figure 3) appear markedly different, congruent with the qualitative differences identified by the radiologists.

Discussion

The results of this study indicate that rFOV diffusion improves depiction of locally advanced breast tumors as compared to standard FOV diffusion, and that these improvements are reflected in both quantitative and qualitative differences in tumor representation on DW-MRI. Two radiologists specializing in breast MRI independently assigned higher image quality and tumor depiction ratings to rFOV DW-MRI than to standard FOV diffusion. Radiologists saw improvements in clinically significant image quality characteristics, consistent with the fact that rFOV DW-MRI restricted the image FOV, resulting in increased image resolution and simultaneously decreased susceptibility to artifacts.

Our results also showed statistically significant differences between the two sequences in quantitative measurements of the tumor ADC distribution. The fact that the distributions differed in the lower ADC range is consistent with the fact that a higher resolution would yield less partial volume averaging. Decreased partial volume averaging of low-ADC tumor with high-ADC normal tissue would result in lower ADCs in rFOV as compared to standard FOV DW-MRI. Low-ADC regions are assumed to be highly cellular, corresponding to viable tumor, precisely the tumor region that would be of interest in treatment monitoring and diagnostic applications. In clinical studies outside the breast, low-ADC, measured as the minimum ADC, has been found to be informative. In osteosarcoma, minimum ADC differed between patients responding and not responding to chemotherapy, while mean ADC did not [26]. In a DW-MRI study of patients with glioma, minimum ADC was shown to correlate with cellularity [27] and in a study of patients with astrocytoma, pre-treatment minimum tumor ADC was identified as a potential marker of survival [28]. These studies suggest that minimum ADC is valuable in a variety of cancers. While additional study in the breast is needed, improved measurement of minimum tumor ADC with rFOV DW-MRI could be valuable for diagnostic and treatment monitoring applications related to breast cancer.

In this study, the maximum tumor ADC also differed between standard and rFOV DW-MRI. Maximum tumor ADC may be useful in identifying necrotic tumor regions, as such regions would be expected to have decreased cellularity and thus increased ADC. Further study in this area is also warranted.

The fact that the mean ADC did not differ significantly between the two sequences suggests that both sequences were measuring the same bulk tumor, and regardless of resolution, the bulk tumor would be presumed to have the same mean ADC. The statistically non-significant difference in the mean ADCs compares to the results of Zaharchuk, et al, in which a similar mean ADC was found with rFOV and full-FOV DW-MRI in imaging of the spine [29]. Since most treatment monitoring studies track mean tumor ADC, use of rFOV

DW-MRI instead of standard FOV diffusion would not change the results such studies. Furthermore, our qualitative results suggest that such studies might be improved with use of rFOV DW-MRI. In addition to mean ADC, other ADC histogram parameters have been shown to have value in tracking treatment response in the breast [4], as well as outside the breast [30], and in distinguishing different disease subtypes [31].

The promising results of this study are tempered by the small study size. Larger studies are needed to include a broader range of histopathologic subtypes. Most tumors in this study were large due to the focus on locally advanced breast cancer. Following completion of chemotherapy, locally advanced breast tumors may be significantly smaller in size and a higher-resolution sequence could potentially have value in identifying remaining areas of high cellularity; however, the role of rFOV DW-MRI in assessing small residual tumors was not assessed in this small study. In addition, rFOV DW-MRI could have value in imaging smaller invasive or in situ, tumors, but further study is needed to assess the role of rFOV DW-MRI in diagnostic studies and in prognostic studies related to tumor response in smaller tumors.

A source of potential variability in the data results from the fact that the tumor was represented by one only region of interest (ROI) on one slice in the image volume. Single-slice ROI delineation is not uncommon [9, 21]. However, the same volume of tumor imaged with standard diffusion cannot always be imaged with rFOV diffusion because rFOV diffusion is limited to a 140 mm × 70 mm × 32–64 mm acquisition volume. In this study, to reduce discrepancies, ROIs were automatically registered between rFOV and standard DWI series and ROI location and tumor morphology were verified, with adjustments made as needed.

This study was limited in that the parameters for rFOV and standard FOV diffusion were not exactly matched. Due to study and practical constraints, the slice thickness for rFOV diffusion was 4 mm while the slice thickness for standard FOV diffusion was 3 mm. Despite this difference, rFOV voxels were still over 6 times smaller than standard FOV voxels because of the substantially smaller in-plane resolution. In addition, partially due to the longer readout duration, the TE in the standard FOV diffusion sequence was longer than in the rFOV sequence. Despite the difference in TE, theoretical SNR of the standard FOV sequence is still higher than for the rFOV, as the SNR scales linearly with the voxel volume and the square root of the readout time.

Even though image quality with rFOV diffusion was qualitatively better than with standard FOV diffusion, image quality was not consistent within rFOV exams, especially early in the study and three exams suffered from poor quality and needed to be excluded. We have since optimized rFOV DW-MRI to help reduce variable image quality. This sequence utilizes a narrow-bandwidth water-selective excitation, underscoring the importance of accurate identification of the center frequency of water.

Despite the limitations of this study, the quantitative and qualitative results suggest that, compared to standard FOV diffusion, rFOV diffusion is able to better depict the diffusivity of locally advanced breast tumors at a sub-centimeter level. This improvement is important because changes in diffusion are thought to occur before changes in tumor size [3]. Improved identification of treatment-induced diffusivity changes could allow for better assessment of tumor response and better tailoring of therapies to a patient's response. In addition, a higher-resolution sequence could potentially have value in identifying smaller areas of high cellularity, which could represent tumors that may not have otherwise been detected. Prognostic studies evaluating tumor response to treatment may benefit from rFOV diffusion. These benefits must however be substantiated by assessing the ability of rFOV

diffusion measurements to predict clinical outcomes. The rFOV diffusion sequence is associated with potential disadvantages, such as unilateral coverage and additional scanning duration if it is used as an adjunct to standard diffusion. These disadvantages may be outweighed by its potential value, but large, prospective studies comparing the predictive abilities of rFOV diffusion prognostic markers to those of standard FOV diffusion are needed.

Conclusion

In conclusion, the depiction of invasive breast tumors with rFOV DW-MRI is qualitatively and quantitatively different than the depiction with standard FOV DW-MRI. Our results show that image quality and tumor depiction is improved with rFOV diffusion as compared to standard. These findings are consistent with the fact that rFOV diffusion decreases artifacts due to air-tissue interfaces and improves resolution, resulting in decreased partial voluming. This decrease in partial voluming was reflected in statistically significant differences maximum tumor ADC, the number of occupied bins, and importantly, in minimum and 12.5th percentile tumor ADC, measures of the low ADCs expected in most invasive breast cancers to represent viable tumor. High resolution DW-MRI of the breast is promising and further study relating measurements to clinical outcomes is needed.

Acknowledgments

The authors acknowledge funding from R01-CA69587 (NH), R01-CA 116182 (NH) and the California Breast Cancer Research Program Dissertation Award (LS).

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Figure 1.

Bland-Altman plot of mean tumor ADC calculated with rFOV and standard FOV DW-MRI. For each case, the average mean tumor ADC measure ($1/2 * (\text{mean ADC calculated from rFOV} + \text{mean ADC calculated from standard FOV})$) is plotted against the difference between mean tumor ADC measures calculated from rFOV and standard FOV DW-MRI. Differences in measurements of mean ADC ($10^{-6}\text{mm}^2/\text{s}$) are within 1.96 SD (dotted lines) of the mean difference (dashed lines). The 95% confidence interval for the limits of agreement (dotted lines) is -207.38 to $283.26 * 10^{-6}\text{mm}^2/\text{s}$.

Figure 2.

Images and tumor ADC distributions for Case 1. Overall image quality is improved on (a) T2-weighted (T2w, b=0) and (b) diffusion-weighted (DW) images for rFOV DW-MRI compared to standard FOV (d) T2w and (e) DW images. Both radiologists also rated (b) rFOV diffusion as superior to (e) standard in depiction of morphologic detail, tumor heterogeneity, and lesion conspicuity. Despite improvements in tumor depiction, tumor ADC distributions derived from ADC maps for (c) rFOV and (f) standard diffusion, respectively are similar (g, h, respectively).

Figure 3.

Images and tumor ADC distributions for Case 2. Overall image quality is improved on (a) T2-weighted (T2w, b=0) and (b) diffusion-weighted (DW) images for rFOV DW-MRI compared to standard FOV (d) T2w and (e) DW images. Both radiologists also rated (b) rFOV diffusion as superior to (e) standard in depiction of morphologic detail, tumor heterogeneity, and lesion conspicuity. Tumor ADC distributions for rFOV and standard (g, h, respectively) derived from ADC maps (c, f) differ between acquisitions, with an increased number of occupied bins and a decreased minimum ADC in rFOV vs. standard FOV DW-MRI.

Table 1

Characteristics of Tumors in rFOV DW-MRI Study

Characteristic	# Tumors (%)
Histopathological subtype:	
Invasive ductal carcinoma	10 (91%)
Invasive lobular carcinoma	1 (9%)
Tumor Grade:	
Grade 1	0
Grade 2	8 (73%)
Grade 3	3 (27%)
MR Tumor Size:	
MR tumor volume (cm ³)	14.5 (SD = 16) (Range 0.4 – 46.6)
MR longest diameter (cm)	Mean 4.4 (SD = 2.6) (Range 1.3 – 9.3)

Table 2

Comparison of ADC Distribution Parameters between rFOV and Standard FOV DW-MRI Acquisitions

Tumor ADC Variable	Mean, rFOV	SD, rFOV	Mean, standard FOV	SD, standard FOV	Mean % difference* in rFOV relative to standard FOV	p-value
Mean ADC	1094.8	120.1	1132.8	117.2	-2.83	0.577
Skew	0.43	0.51	0.36	0.59	23.68	0.638
Kurtosis	3.52	1.09	3.37	1.35	13.11	0.320
Minimum ADC	231.18	269.0	603.73	306.62	-38.61	0.003
12.5th percentile ADC	749.59	169.1	870.18	192.65	-9.98	0.042
25th percentile ADC	877.50	139.9	962.4	150.52	-7.76	0.083
50th percentile ADC	1071.1	116.7	1102.6	118.29	-2.35	0.638
75th percentile ADC	1288.0	130.1	1295.5	100.92	-0.25	0.765
87.5th percentile ADC	1470.4	148.3	1451.2	93.25	1.65	0.765
Maximum ADC	2149.7	272.6	1780.2	190.83	21.92	0.002
ADC range	1918.5	446.2	1176.5	398.46	78.31	0.001
# Occupied bins	19.73	4.3	11.91	3.78	76.96	0.001

* % difference = (rFOV measurement - standard FOV measurement) / standard FOV measurement * 100 for each exam