Vascular and cellular biomarkers from intravoxel incoherent motion (IVIM) MRI in locally advanced breast cancer lesions

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Background

Breast cancer is a complex disease threatening millions worldwide. Grading or diagnosing breast lesions is done histologically, requiring invasive biopsy procedures that suffer from limited sampling. MRI provides a suite of noninvasive assays for quantitative tumor characterization, including diffusion-weighted imaging (DWI). Conventional tumor DWI uses restriction of the apparent diffusion coefficient (ADC) by tumor cellularity as a marker of aggressiveness [1,2]. We hypothesize that highly sampled DWI can also be sensitized to tumor hypervascularity via "pseudodiffusion", a.k.a. intravoxel incoherent motion (IVIM) [3,4]. We present breast cancer lesion IVIM and compare it to perfusion imaging.

Methods

25 patients undergoing bilateral breast examination in a full body Siemens 3 T MRI scanner and 7 element breast coil array were scanned with a diffusion-weighted imaging (DWI) protocol, using a twice-refocused, bipolar gradient single-shot turbo-spin echo (TSE) sequence: TR/TE = 2000 / 103 ms, 108 x 128 matrix, 18 matrix axial slices, 2.7 x 2.7 x 4 mm voxel, single direction diffusion weighting b = 0,30,70,100,150,200,300,400,500,800 s/mm^2. Sagittal T1-weighted 3D VIBE images were collected before and after contrast administration, and at 5 time points during contrast uptake. Axial post-contrast images were collected for comparison with axial DWI. Vascular kinetics were classified from lesion contrast enhancement time course. Other clinical data included pre-MRI fine needle aspiration (FNA) biopsy for initial diagnosis, and post-MRI tissue biopsy for pathological analysis.

DWI data were first analyzed with a monoexponential model to generate ADC maps. Lesions were identified using post-contrast axial T1-weighted image hyperintensity (vascular enhancement), the DWI b=0 image hyperintensity (fluid content), and/or ADC map hypointensity (restricted diffusion) (Figure 1). Regions of interest (ROI) were drawn on DWI maps enclosing the full lesion and amplitudes were collected. ROI data were analyzed with a biexponential model including a vascular compartment with volume fraction f_p and pseudodiffusivity D_p and a tissue compartment with volume fraction (1-f_p) and diffusivity D_t [3].

$$\frac{M}{M_0} = [(1-f_P)\cdot\exp(-b\cdot D_t) + f_P\cdot\exp(-b\cdot D_p)] \qquad (1.1)$$

Each decay curve was analyzed both with a monoexponential model and Eq.(1.1), generating four parameters: ADC, D_t, f_p, D_p. Normal fibroglandular tissue, distinguishable in N=10 patients on DWI, was fit with a monoexponential model to extract ADC. Lesion contrast enhancement curves were sampled from dynamic CE-MRI, and the initial slope was estimated from the difference of the first two points.

Results

25 patient scans showed N = 46 lesions. 16 benign lesions (1 cyst, 4 fibrocystic change, 2 papilloma, 3 fibroadipose tissue, 2 fibroadenoma, 4 other) were not measurable on DWI. DWI was collected from 3 of 4 (3/4) ductal carcinoma in-situ (DCIS), 1 metaplastic, 1 invasive lobular, 1 adenocarcinoma, 2 other cancer, and 11/19 invasive ductal carcinoma (IDC) lesions. Contrast enhancement was available for 15/19 lesions with DWI data. Figure 1 shows an example DCIS breast lesion in this study, including a contrast-enhanced (CE) image, DWI b=0 and b=800 s/mm^2, ADC map, contrast enhancement curve, and DWI signal decay. The lesion DWI decay curve is slower and less monoexponential than the normal fibroglandular tissue, motivating the IVIM model fit (Eq. 1.1). Table 1 shows quantitative results for this study where the most malignant subtype, invasive ductal carcinoma (IDC), is compared to other malignant lesions. Each of the 4 parameters shows nonsignificant but suggestive differences between the two groups, the largest being a slower D_p in IDC. ADC values of normal fibroglandular tissue were found to be significantly different from the lesion group ($p<0.01$). Two MRI vascularity measures (perfusion fraction f_p and CE-MRI initial slope) were correlated (Fig. 2). While the whole group correlation is weak (r=0.4), it is higher within IDC (r=0.97).

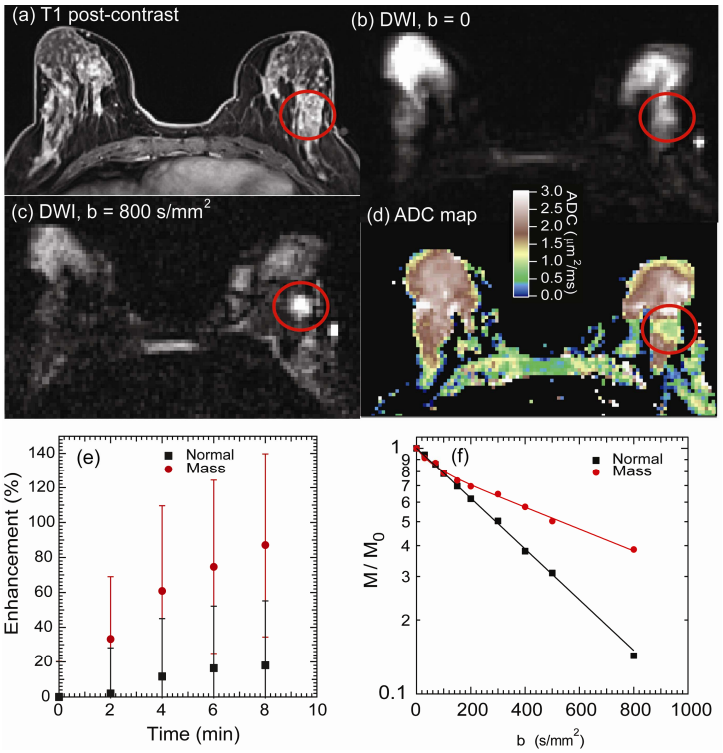

Figure 1: Breast lesion imaging. (a) T1 post-contrast image. (b) DWI unweighted (b=0),(c) DWI b=800 s/mm^2, (d) ADC. (e) Contrast enhancement and (f) DWI decays for mass and fibroglandular tissue.

	Normal FG tissue (n=10)	All lesions (n=19)	IDC (n=11)	Other (n=8)	% diff.	p
ADC (μm^2/ms)	2.50± 0.29	1.43 ± 0.37	1.37 ± 0.31	1.43 ± 0.47	4.5	0.74
D_t (μm^2/ms)	N.A.	1.16 ± 0.35	1.13 ± 0.29	1.21 ± 0.43	6.8	0.66
f_p (%)	N.A.	11.0 ± 4.9	10.9 ± 5.1	11.1 ± 5.1	1.8	0.94
D_p (μm^2/ms)	N.A.	13.4 ± 5.7	12.5 ± 6.9	14.7 ± 3.7	16.2	0.38

Table 1: Breast lesion DWI parameters. % difference and t-test p-value refer to comparison of IDC w/ other malignant lesions.

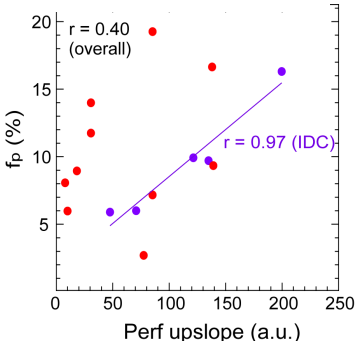

Figure 2: Correlation of f_p with CE-MRI initial slope.

Discussion

Hypervascularity of tumor lesions has been recognized in breast DWI [5-8] but not fully quantified. This preliminary study presents the first quantification in breast lesions revealing distinct vascular and parenchymal compartments, in contrast to the monoexponential behavior of weakly perfused normal fibroglandular tissue. The IVIM parameter set provides simultaneous markers of cellularity (D_t), vascular blood volume (f_p), and blood velocity (D_p). The lesions were clearly differentiated from normal fibroglandular tissue, and some promising trends appear for isolating the most aggressive group (invasive ductal carcinoma) from other malignant lesions. If statistically validated, the trends of lower D_t (higher cellularity), higher f_p (high blood volume), and lower D_p (slower blood velocity) may provide useful information for grading breast lesions.

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