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 = 0,30,70,100,200,300,400,500,800 s/mm². 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.

Lesions were first analyzed 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. The two groups, the largest being a slower Dp 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 fp and CE-MRI 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.

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 metastatic, 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/mm², 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 Dp 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 fp 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).

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 monoeponential behavior of weakly perfused normal fibroglandular tissue. The IVIM parameter set provides simultaneous markers of cellularity (D0), vascular blood volume (fp), and blood velocity (Dp). 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 Dp (higher cellularity), higher fp (high blood volume), and lower Dp (slower blood velocity) may provide useful information for grading breast lesions.

References