Intravoxel incoherent motion MRI may reveal microvascular variation of fibroglandular tissues in breast cancer

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Purpose: Angiogenesis plays a crucial role in tumor growth. Global and local blood vessel analysis based on DCE-MRI has revealed the increased vascularity of the ipsilateral tumor-bearing breast [1,2]. However, due to the limited spatial resolution of breast DCE-MRI, microvascularity of breast cannot be well characterized. Intravoxel incoherent motion (IVIM) offers a new means to study the tissue microvascularity by analyzing the pseudo-diffusion effect generated by the microscopic blood flow in a randomly oriented capillary network [3]. Previous IVIM studies all focused on the differences between normal tissues and benign/malignant breast tumors for the purpose of tumor detection and characterization [4,5]. We hypothesize that microvascular variation in fibroglandular tissues (FGTs) may be associated with ipsilateral breast cancer prior to the increased macroscopic hypervascularity as revealed by DCE-MRI, and this microvascularity effect can be investigated through IVIM-MRI.

Methods: IVIM-MRI was conducted (prior to contrast injection) in addition to the clinical breast-MRI protocol (T1w, T2w, DCE-MRI) on 21 histology-confirmed female breast cancer patients on a 3T clinical scanner (Tim Trio, Siemens Healthcare, Erlangen, Germany) using a fat-suppressed single-shot EPI sequence with research ethics approval and received consent forms. IVIM Imaging parameters were: axial view, voxel size=1.82x1.82mm^2, slice thickness=3mm, TE/TR= 102/5800ms, NEX=4, SENSE=2, eight b-factors=0, 50, 100, 150, 200, 400, 600, 1000s/mm^2. ROIs were carefully drawn on left and right breast FGTs and avoided lesion and major blood vessels by referring to DCE-MRI images and MIP vascularity map. True diffusion D, pseudo-diffusion D* and pseudo-diffusion fraction f in each ROI were calculated pixel-wisely using a customized MATLAB program (MathWorks, Natick, MA, USA) based on segmented non-negative least-square bi-exponential curve fitting. ADCs were also calculated using 3 b-factors (0, 400, 1000s/mm^2) by mono-exponential non-negative least-square fitting. For both IVIM parameter and ADC fitting, voxels with the goodness-of-fit R^2<0.98 were excluded for analysis. Ipsilateral D, D* f and ADC mean values of FGT in tumor-bearing breast were compared to contralateral breast values using Wilcoxon signed rank test with a significance level of 0.05.

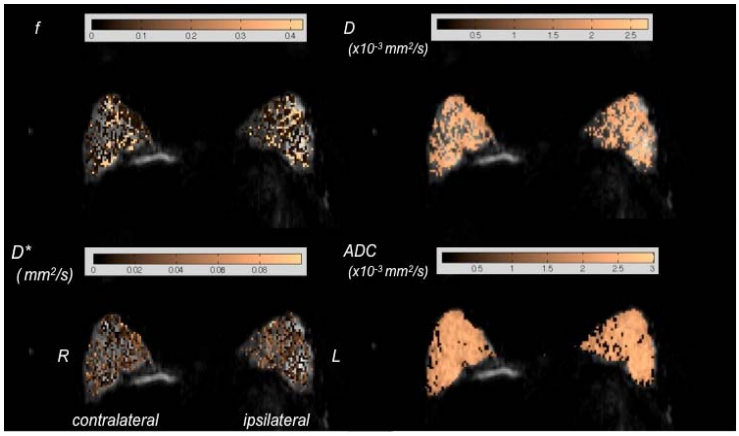

Fig.1. IVIM parameter and ADC maps of an IDC breast cancer patient. Note that the tumor is not depicted in this slice.

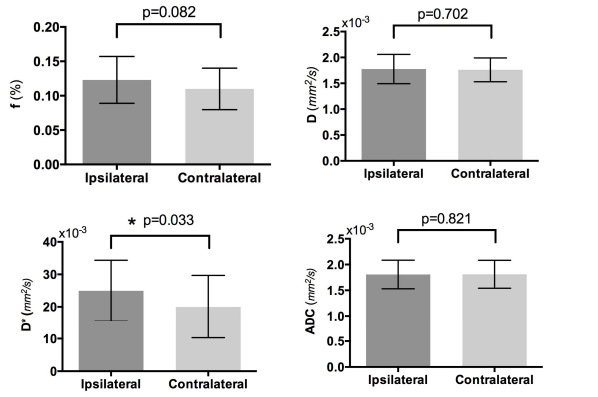

Fig. 2. Bar plots of mean IVIM parameter and ADC of ipsilateral and contralateral breast FGTs in all 21 patients

Results: Figure 1 shows the IVIM parameter and ADC maps of an IDC breast cancer patient. The ipsilateral (left) and contralateral (right) breast FGT's f, D*, D and ADC were 0.098±0.063 vs. 0.082±0.055, 30.80±30.62 vs. 25.60±23.52 ×10^{-3}mm^2/s, 2.16±0.25 vs. 2.15±0.23 ×10^{-3}mm^2/s and 2.25±0.28 vs. 2.20±0.26 ×10^{-3}mm^2/s, respectively. Figure 2 illustrates the bar plots of mean IVIM parameter and ADC of ipsilateral and contralateral breast FGTs in all patients. D and ADC values were very close in both breast FGTs without apparent differences (both p>0.70). In contrast, ipsilateral f (0.123±0.034) was slightly higher than contralateral f (0.109±0.030) while this difference was not yet statistically significant (p=0.079). Furthermore, ipsilateral D* (24.96±9.37×10^{-3}mm^2/s) was significantly higher than contralateral D* (19.98±9.69×10^{-3}mm^2/s) with a p=0.033.

Discussion: To the best of our knowledge, this is the first study to investigate the microscopic vascular variation of breast FGT associated with breast cancer. The increase of f and D* in ipsilateral breast FGTs may indicate the increased capillary density and the faster blood flow within the capillary networks associated with the tumor growth, yet it is still unknown whether these increases occur prior to the tumor formation or they are the consequence of tumor growth. We postulate that the microvascularity information revealed by IVIM-MRI may potentially serve as a sensitive imaging biomarker for breast cancer risk assessment, characterization and/or prognosis. This study is majorly limited by the marginal statistical power due to the small sample size, so a rigorous clinical assessment based on larger patient cohorts is warranted. The microvascular variation in FGTs may also be correlated to macrovascularity change, cancer sub-types and background parenchymal enhancement (BPE). These should be further investigated in future studies.

References: [1] Sardanelli F et al, Radiology 2005;235:791-797; [2] Han M, et al. AJR 2012;199:921-928; [3] Le Bihan D, et al. Radiology 1988;168:497-505; [4] Sigmund EE et al, MRM 2011;65:1437-1447; [5] Bokacheva L, et al. JMRI 2014;40:813-823.