Statistical Assessment of Diffusion Weighted Signal Decay in Breast Cancer Tumors at 3T: Mono-exponential or Bi-exponential?

Jing Yuan[1], Gladys G. Lo[2], Oi Lei Wong[1], Helen H.L. Chan[2], Abby Y. Ding[1], Ting Ting Wong[3], and Polly S.Y. Cheung[3]

[1]*Medical Physics and Research Department, Hong Kong Sanatorium & Hospital, Happy Valley, Hong Kong, China,* [2]*Department of Diagnostic & Interventional Radiology, Hong Kong Sanatorium & Hospital, Happy Valley, Hong Kong, China,* [3]*Breast Care Center, Hong Kong Sanatorium & Hospital, Happy Valley, Hong Kong, China*

Purpose: Intravoxel incoherent motion (IVIM) MRI [1] has been proposed for breast cancer (BC) diagnosis by investigating microvascularity-induced perfusion (or pseudo-diffusion, D*) and true water diffusion (D) based on a bi-exponential model [2,3]. In contrast to the robustness of ADC calculation based on a mono-exponential model, quantification of IVIM parameters of D* and its fraction f, is difficult, suffering from inherent ill-conditioning of bi-exponential fitting in theory and limited SNR in practice [4]. Simply applying bi-exponential model for least-square fitting of DWI signal usually yields higher goodness-of-fit (GOF) value. However, this only reflects the flexibility of bi-exponential model with more parameters to fit, but does not necessarily mean IVIM-MRI better characterizes DWI signal decay, nor even ensures that bi-exponential decay really exists. In this study, we prompt to statistically assess the DWI signal decay in breast malignant tumors via F-test approach, in order to find the optimal model for better DWI signal characterization in BC.

Methods: DWI was conducted along with a clinical breast-MRI protocol on 39 female BC patients with 30 histology-confirmed (BIRADS6) and 10 high-suspicious (BIRADS5) malignant tumors using a 3T Siemens Trio MRI scanner. DWI imaging parameters were: voxel size =1.82x1.82mm^2, thickness=3mm, TE/TR=102/5800ms, NEX=4, SENSE=2, b=0, 50, 100, 150, 200, 400, 600, 1000s/mm^2. ROIs were carefully drawn on tumors by referring to DCE-MRI. IVIM parameters (segmented bi-exponential fitting), ADC (8 b-factors) and adjusted GOFs (R^2) were calculated both voxel-wisely and on ROI-averaged signal basis. To statistically compare mono- and bi-exponential fitting, F-test was applied with the null hypothesis that the simpler mono-exponential model is correct. F-ratio and the associated p-value were calculated based on residual sum-of-squares, degree of freedom and F-distribution. A significance level of 0.05 was used.

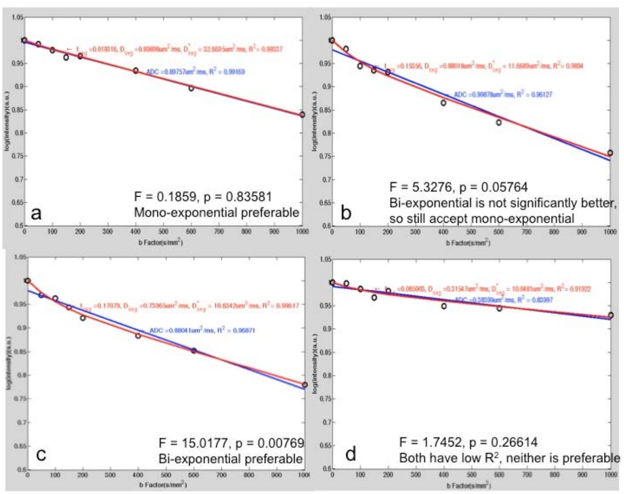

Fig.1. Statistical comparison of mono- and bi-exponential fitting

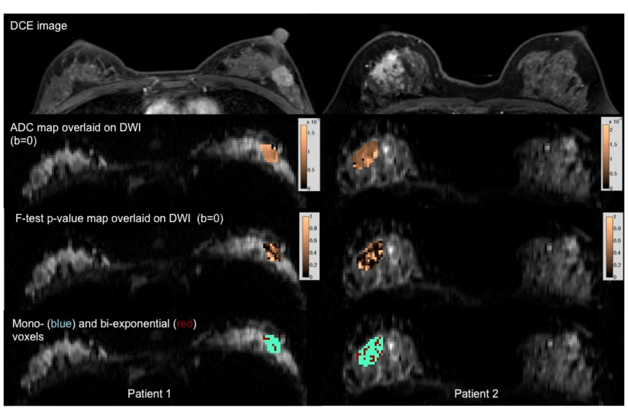

Fig. 2. Voxel-wise fitting in one IDC (left) and one ILC tumor (right)

Results: Regarding ROI-averaged analysis, F-statistics showed that mono-exponential model was preferable only for 14 tumors (Fig.1ab) while bi-exponential model was significantly better in fitting DWI signals of 24 tumors (Fig.1c). 2 other tumors yielded relatively low R^2 for both models so neither one was optimal (Fig.1d). Based on voxel-wise fitting, heterogeneities of F-ratio and p-value were obtained in tumors. Figure 2 illustrated voxel-wise fitting results in one IDC tumor (left) and one ILC tumor (right). In general, fewer voxels were significantly better fitted by bi-exponential model than by mono-exponential models according to p-value maps, regardless of the ROI-averaged signal characteristics. For those voxels better fitted by mono-exponential model, their estimated f and D* were highly heterogeneous, indicating the large uncertainty of quantification by bi-exponential fitting.

Discussion: Accurate and precise estimate of IVIM parameters, especially D* and f, requires very high SNR and many data points, which are usually restricted by the limited clinical scan time. We rigorously compared mono- and bi-exponential fitting of DWI signal in malignant BC tumors via F-test. With clinically achievable SNR, F-statistics indicated that mono-exponential should be sufficiently good for voxel-wise analysis although a few number of voxels were significantly better fitted by bi-exponential model. When bi-exponential voxel-wise fitting was applied, the obtained f and D* should be interpreted carefully as these values could be inaccurate and highly uncertain, depending on SNR, b-factors, fitting algorithm and setting. In contrast to voxel-wise results, ROI-averaged fitting revealed that more tumors were significantly better characterized by bi-exponential decay. This is believed to be attributed to the much higher SNR due to signal averaging, while the underlying tumor heterogeneity was missing. In this sense, IVIM-MRI is clinically useful to characterize BC angiogenesis for diagnosis. This study is majorly limited by the small sample size of BC malignant tumors. DWI signal characterization should be further investigated for different tumor sub-types and grades.

References: [1] Le Bihan D, et al. Radiology 1988;168:497-505; [2] Sigmund EE et al, MRM 2011;65:1437-1447; [3] Bokacheva L, et al. JMRI 2014;40:813-823; [4] Cho JY, et al. MRM, in press.