Can Diffusion Weighted Imaging/Apparent Diffusion Coefficient Mapping and Dynamic Contrast Magnetic Resonance Imaging provide Histological Phenotyping of Breast cancer in Basal and Luminal subtypes?

M. A. Jacobs[1], R. H. El Khouli[2], K. J. Macura[1], S. Mezban[1], I. Kamel[1], and D. A. Bluemke[2]
[1]The Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, Baltimore, Maryland, United States,
[2]Department of Radiology and Imaging Sciences, National Institutes of Health, Bethesda, Maryland, United States

Purpose: To prospectively investigate the feasibility of using Diffusion Weighted Imaging (DWI) with Apparent Diffusion Coefficient (ADC) mapping and Dynamic Contrast Enhancement (DCE) magnetic resonance imaging (MRI) for histological phenotyping of breast cancer lesions into basal(ER-/PR-/HER2-Nu-;Triple Negative (TN)), basal-like(only HER2-Nu+), and luminal-type (luminal A-ER+/PR+/ HER2-Nu-; luminal B- ER+/PR+/HER2-Nu+) subtypes.

Methods: Eighty-four patients with suspicious mammographic and ultrasound findings were prospectively studied underwent MR imaging at 3T. MR sequences were axial Fat Suppressed (FS) T_2 spin echo (SE), T_1 fast spoiled gradient echo (FSPGR). Fat-suppressed 3D T1-FSPGR pre- and 10 post-contrast images (16sec temporal resolution) were obtained after injection of GdDTPA contrast agent (0.1mmol/kg) for kinetic modeling. DWI was acquired using SE-EPI(TR/TE=5000/90ms,128x128,b=0,600s/mm^2,NEX=1). Total data acquisition time was about 45 min. Trace ADC maps were constructed and ADC values (mean±SD) and ratios of glandular and lesion tissue were obtained. DCE-MR was classified by morphology and temporal time curves[1]. Breast lesions were categorized by histological phenotyping based upon hormonal markers, HER2-Nu by FISH, and Ki-67 proliferation index (%). The types of lesions were basal(ER-/PR-/HER2-Nu-;Triple Negative (TN)), basal-like(only HER2-Nu+), and luminal-type (luminal A=ER+/PR+/ HER2-Nu-; luminal B=ER+/PR+/HER2-Nu+). The different ADC map and DCE values between lesion types were evaluated using an unpaired 2-sided t-test. Statistical significance was set a $p<0.05$.

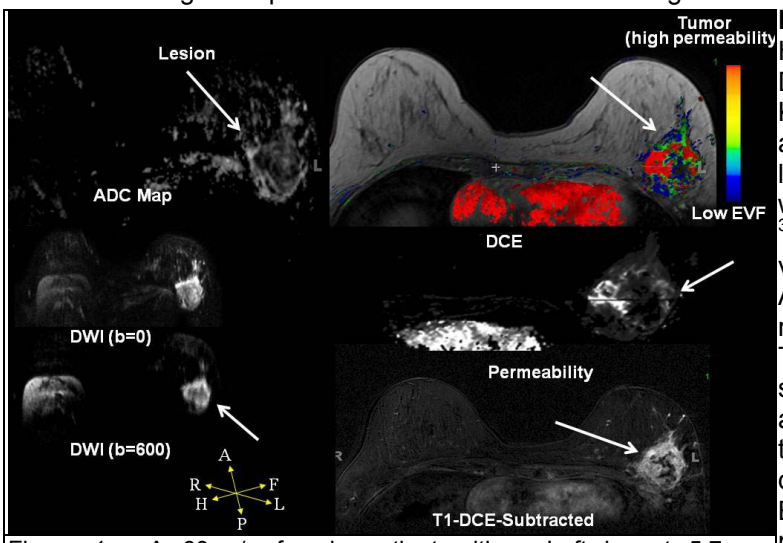

Figure 1. A 68 y/o female patient with a Left breast 5.7 cm heterogeneously enhancing mass underwent multiparametric MR imaging. The lesion characterization demonstrated high permeability with low ADC maps values. The final histological characterization was a triple negative lesion (basal).

Results: There were 18 basal type lesions (TN=13; HER2-nu+=5), 35 luminal type(Type A=28; Type B=7), 7 DCIS, and 22 benign lesions. The mean ADC value and Ki-67 for basal lesions were $0.98\pm0.39\times10^{-3}$mm^2/s; 62% and for basal-like $0.84\pm0.15\times10^{-3}$mm^2/s; 45%. For both luminal A and B lesions, the ADC map value and Ki-67 was $1.1\pm0.21\times10^{-3}$mm^2/s; 37% and $1.1\pm0.42\times10^{-3}$mm^2/s; 15%, respectively. For DCIS, the ADC map value was $1.4\pm0.45\times10^{-3}$mm^2/s. For benign lesions, the ADC map value was $2.1\pm0.26\times10^{-3}$mm^2/s. Similar results were noted for the L/GT ratios. Interesting, for TN and HER2-Nu+, DCE-MR morphology and time series analysis had no benign findings, only intermediate and malignant scoring(type 2/3). However, the luminal types, DCIS, and benign lesions all presented with different "grades" of morphology and uptake curves. Benign lesions, generally, had benign features, such as persistent enhancement and smooth features.

Discussion: This study revealed that DWI/ADC mapping coupled with DCE-MR has the potential to characterize the different phenotypes of breast lesions. Indeed, Basal (TN) and Basal-like lesions had decreased ADC values and only highly suspicious DCE-MR findings. Whereas, luminal A and B had higher ADC values than basal lesions and lower Ki-67. Both DCIS and benign lesions had significantly higher ADC values. ADC mapping is a measure of the movement of water [2-6], whereas, DCE-MR adds a measure of the vascular characteristics of tumor environment within breast tissue [1,7]. Thus, combined DWI/ADC mapping, and DCE-MR provides radiological biomarkers of molecular environment and could provide targets for image-guided biopsy of highly aggressive tumor regions.

References: :[1].El Khouli RH, *Semin Roentgenol* 2008;43:265-281. [2] Moseley ME, *AJN.* 1990;11:423-429. 3]. Guo Y, et. al, JRMI. 2002, 15(6): 693-704 [4] [Woodhams R et. al, *Magn. Reson. Med. Sci.* 2005; **4**: 35-42 [5] Chenevert TL. *JNCI* ;2029-2036. 2000. [6] Padhani AR *Neoplasia* 2009;11:102-125 [7] Tofts PS, *JM RI* 1997;7(1):91-101,

Acknowledgement: NIH grants: 1R01CA100184; P50 CA103175; and 5P30CA006973(IRAT)