Characterization of Invasive Breast Cancer using Quantitative DCE-MRI at 3.0T

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Target Audience: Clinicians and scientists with an interest in quantitative DCE-MRI techniques in breast cancer.

Purpose: Breast cancer is the second most prevalent disease and the leading cause of deaths of women worldwide. Gd-DPTA- based dynamic contrast enhanced MRI (DCE-MRI) has proven a promising non-invasive modality for characterizing the pathophysiological microenvironment of tumors. Pharmacokinetic (PK) modelling can yield results of tumour-vessel permeability, perfusion and extracellular-extravascular volume fraction[1]. A recent study has reported a correlation between the PK parameters and prognostic factors in breast cancer[2]. In this work we exploit the improved spatiotemporal resolution achievable at 3.0T to investigate the relationship between the modelled vascular parameters and their histopathological profile within a cohort of breast cancer patients.

Methods: Data acquisition: In this prospective study, 57 female patients with locally advanced breast cancer underwent DCE-MRI examination prior to surgery. 60 malignant lesions were identified. Imaging was performed on a 3.0T system (MR750, GE Healthcare, Waukesha, WI) using an 8-channel breast coil. T_{10} maps were acquired using a variable flip angle 3D SPGR sequence (TE/TR/α=2.1/5.3ms/2°,3°,5°,10°,15°). Transmit B_1 mapping was performed using a 2D Bloch-Siegert shift method. The dynamic acquisition employed a 3D segmented *k*-space sequence with parallel imaging (acceleration factor ×2), spectral-spatial water excitation, an interpolated voxel size of 0.6x0.6x1.4mm and a 9s temporal resolution. Other parameters included TE/TR/α=3.8/7.1ms/12°, FOV=350mm with an acquisition matrix of 350×350, 112×2.8mm slices, receiver bandwidth = ±125kHz and NEX=0.5. The slice orientation and locations matched the T_{10} and B_1 mapping. A bolus of 0.1mmol/kg Gd-DPTA (Magnevist, BayerSchering, Berlin, Germany) was delivered at 3ms/s followed by a 20 ml saline flush. In total, 43 phases of post contrast-enhanced images were acquired following 5 baseline phases and a total acquisition time of 8 minutes.

Data analysis: Quantitative analysis was performed in OsiriX using the DCETool[4]. ROIs were manually drawn on all consecutive enhancing sections of the tumor. Tissue concentration-time course data was analysed using the two-compartment Tofts model[1] with the modified Fritz-Hansen arterial input function[4], yielding K^{trans} and v_e. Using in-house analysis code developed in MATLAB (v8.0, The MathWorks, Inc., Natick, MA), a 3x3x3 pixel region representing the maximally enhancing 'hot spot' was identified from the functional maps together with whole tumor mean values. Information regarding histological subtype and grade was obtained from the histopathological reports. Distributions of the PK metrics are presented. The non-parametric Kruksal Wallis and Mann-Whitney-U-tests were used to investigate the relationship between the vascular parameters and grade.

Results: All patients (range 28-62, mean age=52 years) were surgically managed within 10 days of the MR examination (range 3-14 days). None of the patients had received any treatment prior to the MRI examination. We examined 34 invasive ductal, 17 lobular, 4 mucinous, 2 papillary and 3 tubular carcinomas, of which 8 were grade 1, 38 were grade 2 and 14 grade 3. Figure 1 shows the (a) post contrast T1W image (b) parametric maps of K^{trans} and (c) v_e of a known cancer. Figure 2 shows the distributions of K^{trans} and v_e for each respective histological subtype and grade. Hotspot K^{trans} and v_e were found to be higher for ductal, lobular and mucinous types. Significance was found between hotspot K^{trans} and v_e in grades 1 and 3 tumours (p=0.050, p=0.047) respectively. However, differences were not significant between grades 1 and 2 (p= 0.128, p=0.06), and grades 2 and 3 tumours (p=0.330, p=0.23) respectively. Also when assessed with regards to the mean values of K^{trans} and v_e, differences between grades were not significant (p=0.42, p=0.30).

Discussion: Both lesion morphology and kinetic pattern are considered for giving a final diagnostic impression. PK analysis will yield K^{trans} and v_e values in line with the histological grade of the tumour. When assessed over the region with highest signal intensity, our results demonstrate an increased vascular permeability associated with fast-growing tumors together with an increase in the interstitial space. This can be explained by the higher rate of cellular proliferation exhibited by the high-grade lesions whereas the low-grade lesions show little proliferation.

Conclusion: Tracer kinetic parameters K^{trans}, v_e obtained at 3.0T can be used for the non-invasive differentiation of the grades of breast cancer. This study indicates that K^{trans} and v_e provide important and independent information concerning tumor biology and microvascular structure that supports the use of these more complex analysis protocols.

References: [1]Tofts *et al*. JMRI 1999;10:223-232. [2]Koo *et al.* JMRI. 2012;36:145-51. [3]Sung *et al.* RSNA 11;2011; 38:454-459 [4]Fritz-Hansen *et al*. MRM 1996;36:225.

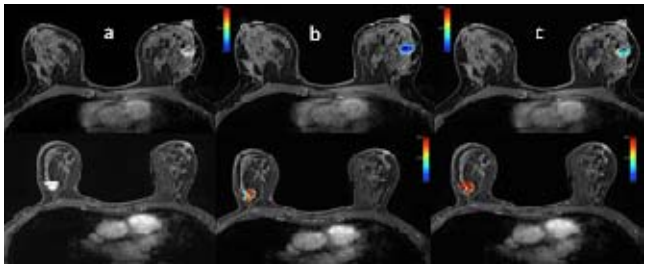

Figure 1 shows the a) T1W image, b) K^{trans} map, and c) v_e map for a grade 1 invasive ductal carcinoma in the lateral aspect of the left breast (top row) and similarly for a grade 3 invasive ductal carcinoma (bottom row)

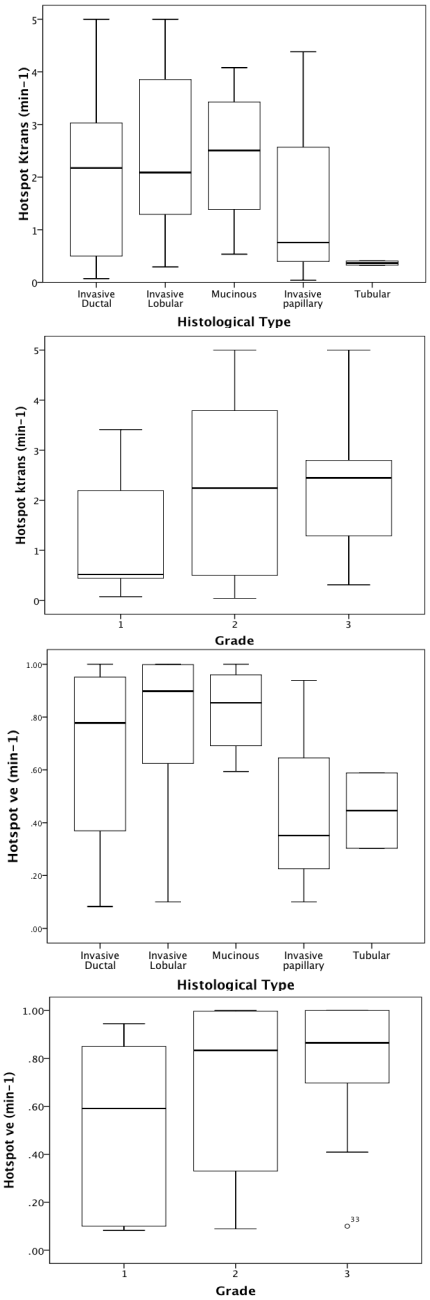

Figure 2 shows the distribution of the hotspot K^{trans} according to histological type (top), grade (middle), and hotspot v_e according to histological type (middle) and grade (bottom). Hotspot K^{trans} and v_e is higher in the more common ductal and lobular types. Hotspot K^{trans} and v_e are higher in the grade 3 tumours.