Effects of Temporal Resolution on Breast Cancer Diagnostic Accuracy by Quantitative Dynamic Contrast-Enhanced MRI

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Introduction High spatial resolution imaging is needed for accurate breast tumor morphology assessment. Clinical dynamic contrast-enhanced (DCE) MRI data are often acquired with high spatial but low temporal resolution because of trade-off between the spatial and temporal resolutions for the conventional gradient echo sequence. As a result, qualitative or semi-quantitative analysis of the DCE-MRI time-course data is often used in clinical contrast kinetics interpretation. However, the results are often dependent on data acquisition details, contrast reagent (CR) dose and/or injection rate, *etc.* These contribute to the limited specificity and study irreproducibility characterizing current clinical breast DCE-MRI protocols (1). Quantitative analysis of DCE-MRI time-course using a pharmacokinetic model to extract pharmacokinetic parameters (*e.g.*, K^{trans} and v_e) is more desirable. These parameters are physiological quantities, in principle independent of the above factors. It has been shown (2,3) that, with relatively high temporal resolution DCE-MRI data, Shutter-Speed Model (SSM, accounting for finite transcytolemmal water exchange kinetics) analysis (4) significantly improves breast cancer diagnostic accuracy compared to Standard Model (SM, assuming effectively infinitely fast exchange kinetics) analysis (5) and the clinical MRI protocol. The SM analysis can also yield CR dose-dependent parameter values (2). Further, the newly discovered DCE-MRI biomarker, ΔK^{trans} [$\equiv K^{trans}$ (SSM) – K^{trans} (SM)], achieves near perfect specificity at 100% sensitivity (2,3). ΔK^{trans} is a measure of K^{trans} underestimation due to the SM's neglect of finite water exchange kinetics (a shutter-speed effect) (2).

Temporal resolutions of 60-120 s are typical for clinical breast DCE-MRI protocols. In this study, by resampling research DCE-MRI time-course data, we sought to evaluate the effects of poorer, clinical temporal resolution on quantitative DCE-MRI breast cancer diagnostic accuracy.

Methods In a recent study (3), 74 patients who had 77 suspicious breast lesions (3 patients presented 2 lesions each) underwent IRB-approved research DCE-MRI examinations prior to their clinically scheduled biopsies. These lesions were deemed suspicious based on the previous clinical breast MRI exams that included tumor morphology assessment and qualitative evaluation of contrast kinetics. The research DCE-MRI acquisitions were conducted at 1.5T using a 3D SPGR gradient echo sequence to acquire 14-20 serial sagittal image volume sets continually, spatially covering the whole breast with the suspicious lesion(s) to be biopsied. Depending on the breast size, the inter-sampling interval (temporal resolution) ranged from 13 to 44 s. At the start of the second volume set acquisition, Gd CR was delivered intravenously [0.1 mmol/kg at 2 mL/s]. ROIs circumscribing the enhanced lesion and within an axillary artery produced the tumor signal intensity and arterial input function (AIF) time-courses, respectively. Three reliable individual AIFs were measured, interpolated with an empirical expression (4), and averaged to generate a mean AIF. The tumor ROI and mean AIF signal time-courses were then subjected to both SM and SSM analyses, which were blinded from the subsequent pathology results (2,3).

Each DCE time-course was then re-sampled to simulate inter-sampling intervals of 3x the original interval (temporal resolution 3x poorer). Each new time point was generated by averaging with two adjacent points to yield a degraded time resolution (*i.e.*, contiguous three-point sets were averaged to give a sampling rate 1/3 that of the original acquisition) (6), but preserving the signal-to-noise ratio. The baseline was preserved by inserting data points at the beginning of the time series equal to the average of all actual baseline data points. The resulting low temporal-resolution time-courses were subjected to the same SM and SSM analyses. To mimic the 60-120 s clinical DCE temporal resolution, only the data with original temporal resolutions 20-40 s were selected for this analysis. These constitute data from a total of 66 lesions.

Receiver-operating-characteristic (ROC) curves were used to evaluate pharmacokinetic parameter diagnostic accuracies, and the areas under the curve (AUCs) were compared using a Bootstrap nonparametric test.

Fig. 1a

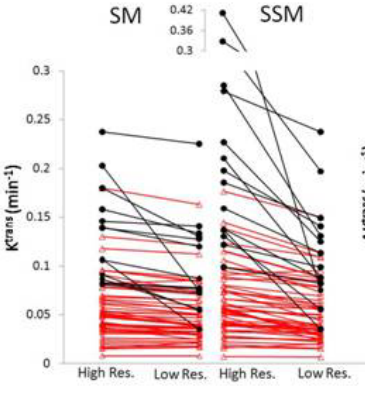
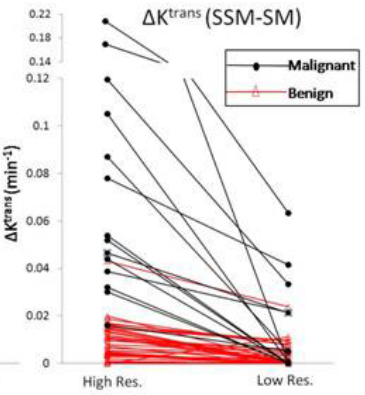


Fig. 1b



Results Upon pathology, only 14 of the 66 lesions were found malignant and the other 52 benign. The positive predictive value (PPV) of the clinical MRI protocol is only 21%. **Fig. 1** shows scatter plots of ROI SM and SSM K^{trans} (a), and ΔK^{trans} (b) obtained from the high (original data) and low (averaged data) temporal resolution data. All benign lesions are marked with red, and all malignant with black, symbols. The lines connect data points from the same patient. There are clear trends of decreasing K^{trans} and ΔK^{trans} from high to low temporal resolution, more so for the malignant lesions, resulting in greater overlap of the malignant and benign lesions at lower temporal resolution. The **Table** lists mean ± SD values for the SM and SSM K^{trans}, and ΔK^{trans} of the 66 lesions derived at high and low temporal resolutions. Paired t-tests reveal that the decreases of SM and SSM K^{trans}, and ΔK^{trans} at lower temporal resolution are statistically significant. The greater overlap of the malignant and benign lesion K^{trans} and ΔK^{trans} values at lower resolution leads to poorer diagnostic accuracy. The ROC curve analyses show that AUCs at lower temporal resolution are smaller than those at higher resolution and the decreases in diagnostic accuracy are statistically significant: (a) K^{trans} (SM), 0.93 (AUC at high resolution) *vs.* 0.84 (AUC at low resolution), $p < 0.05$; (b) K^{trans} (SSM), 0.97 *vs.* 0.87, $p < 0.02$; (c) ΔK^{trans}, 0.99 *vs.* 0.73, $p < 0.0005$. At higher temporal resolution, ΔK^{trans} possesses the highest diagnostic accuracy (2,3). At 100% sensitivity, from high to low temporal resolution, the diagnostic specificity decreases from 79% to 34% for K^{trans} (SM), 88% to 34% for K^{trans} (SSM), and 88% to 38% for ΔK^{trans}.

	K^{trans}				ΔK^{trans}	
	SM		SSM			
	High Res	Low Res	High Res	Low Res	High Res	Low Res
M	0.131±0.048	0.102±0.052[a]	0.208±0.090	0.116±0.054[b]	0.209±0.090	0.116±0.054[e]
B	0.055±0.030	0.050±0.031[c]	0.062±0.033	0.052±0.033[d]	0.062±0.033	0.052±0.033[f]

M = Malignant; B=Benign. Pair t-test (high *vs.* low temporal resolution)**: a**, P<0.01; **b**, P<0.0010; **c**, P<0.00001; **d**, P<0.00001; **e**, P<0.0005; **f**, P<0.000001

v_e is significantly increased for the benign lesion group going from high to low temporal resolution, but not significantly altered for the malignant group. However, v_e and Δv_e are not good diagnostic markers at either resolution, as their ROC AUCs range from 0.5 to 0.6.

Discussion The results suggest that, if quantitative pharmacokinetic analysis is employed for breast DCE-MRI, high temporal resolution for data acquisition is necessary, not only for accurate derivation of the pharmacokinetic parameters, but also for superior discrimination of benign and malignant lesions. The typical clinical DCE-MRI temporal resolution is clearly not adequate for either purpose. Improved acquisition schemes with alternative k-space sampling strategy in combination with parallel imaging acceleration are desirable for quantitative breast DCE-MRI analysis to be adopted in clinical practice, while not sacrificing high spatial resolution. However, there is no question that quantitative DCE-MRI for breast cancer diagnosis is already eminently feasible (2,3).

References **1.** Jansen SA, *et al. AJR* 2009;193:832-839. **2.** Huang W, *et al. Proc Natl Acad Sci* 2008; 105:17943-17948. **3.** Huang W, *et al. Proc Int Soc Magn Reson Med* 2009;17:4240. **4.** Yankeelov TE, *et al. Magn Reson Med* 2003; 50:1151-1169. **5.** Tofts PS, *et al. JMRI* 1999; 10:223-232. **6.** Tagge I, *et al. Proc Int Soc Magn Reson Med* 2009;17:2092.