Shutter-Speed Analysis of CR Bolus-Tracking Data Facilitates Discrimination of Benign and Malignant Breast Disease

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INTRODUCTION. The common benign fibroadenoma (FA) and malignant invasive ductal carcinoma (IDC) breast lesions can each give rise to positive mammography readings, and thus a significant number of false positive results. The time-courses of contrast reagent (CR) bolus-tracking (B-T) ^1H_2O MRI data are highly sensitive to breast abnormalities, and recent results are encouraging that their analysis will eventually provide results specific to the lesion nature (1). Here, we show that a refinement of the quantitative analysis of CR B-T data can improve the discrimination of IDC from FA.

The common monomeric Gd(III)-chelate CRs enter at most the extracellular space, while the majority of tissue water is intracellular (2). The standard pharmacokinetic model used to analyze T_1-weighted CR B-T ^1H_2O data assumes that equilibrium transcytolemmal water exchange (TCWX; necessary for intracellular water molecules to access CR molecules) appears always to have infinitely fast kinetics. However, recent theory and simulation (2), and analyses of animal (2,3) and human (4,5) data suggest that the MR "shutter-speed" for the equilibrium TCWX process can vary during the CR bolus passage, causing the exchange to "appear" to transiently slow down. Neglect of this effect can lead to significant underestimations of the pharmacokinetic parameters (2-5).

METHODS. Data were obtained with consent from four subjects with positive mammographic findings using a 1.5T instrument [Philips; Marconi Edge] (6). Subsequent biopsy and pathology confirmed IDC in two of these, and FA in the other two. Imaging employed body transmit and four-channel phased-array breast receive RF coils. The B-T portion of the protocol used a standard spoiled 3D GRASS sequence to obtain 20 pharmacokinetic frames of volumetric sagittal T_1-weighted images covering the entire breast with the suspicious lesion. The temporal resolutions ranged from 17.4 to 25.4 s, depending on the number (25-40) of image slices. Sequence parameters were: TR = 9.0 ms, TE = 3.8 ms, $\alpha = 30^o$, FOV = $(22\ cm)^2$, slice thickness = 1.5 mm, and matrix = 64 x 256 (phase x readout) zero-filled to 256^2. [Thus, the digital in-plane resolution is 0.86 mm; pixel area, 0.74 mm^2; and voxel volume, 1.1 μL.] Antecubital vein catheters delivered boli of 0.1 mmol/kg Gadodiamide (Omniscan) at 2 mL/s, followed by saline flushes. The injections began immediately after the first frame acquisitions and lasted ~15 s each. Quantitative analyses of the B-T data used the standard and shutter-speed approaches (2-5) to extract pharmacokinetic parameters.

RESULTS. Findings on single-slice data from one lesion of each of the four subjects are reported. Standard model analyses usually employ two-parameter simultaneous fittings of CR arterial input function (AIF) and tissue response B-T time-course pairs (2). [In this study, AIFs were estimated from CR B-T time-courses in axillary arteries.] One parameter measures the CR extravasation rate constant and the other the CR distribution volume. **Figure 1** presents a parametric space plot of results averaged for the pixels in ROIs largely encompassing each of the four lesions (four different symbols). The two horizontal axes measure the transendothelial CR transfer constant, K^{trans}, and the extracellular volume fraction, v_e (2-5). The standard model constrains the equilibrium TCWX system to the fast-exchange-limit [FXL] and thus to the plane. The results of such analyses are shown in Fig. 1 with open symbols. Though the IDC points (triangle and diamond) are somewhat separated from the FA points (hexagon and ellipse), they are clustered sufficiently near the origin to make their general discrimination problematic. However, it has been shown by theory and simulation, and with animal and human data, that the FXL-constrained analysis can significantly underestimate K^{trans} and v_e (2-5). This means that an alternative analysis of the same data with the shutter-speed model, which allows the TCWX system to transiently sortie into the fast-exchange-regime [FXR] (2-5), can cause the points to shift away from the origin, and thus increase the chances of IDC/FA discrimination. The gray-filled symbols in Fig. 1, which locate projections in the K^{trans}-v_e plane of points resulting from the FXR-allowed analyses, do indeed show this behavior. It is particularly the corrected K^{trans} parameter that suggests the possibility of distinguishing the malignant and benign pathologies. There are negligible K^{trans} changes for the benign FA lesions, but increases for each of the malignant IDC tumors (especially the factor of almost five for IDC2).

However, malignant lesions are generally heterogeneous (2-5), and analyses of ROI averages mask such details. Thus, in **Figure 2** we display color K^{trans} parametric maps, resulting from the two alternate analyses of the individual pixel data from the ROIs of each of the four lesions, in a 2 x 4 array. It is clear that the shutter-speed model (top row) renders the two benign lesions (FA1 and FA2) as homogeneous and blue but the IDC1 tumor as heterogeneous with green, yellow, and red regions - the latter representing vascular bed "hot spots." With the color-scale used in Fig. 2, IDC2 is "maxed-out." Other scales reveal that it too is heterogeneous, with a very hot "ridge" (>0.7 min^{-1}) having a superior/inferior orientation. For a sense of spatial scale in these maps, we give the ROI areas [IDC1, $(9.3\ mm)^2$; IDC2, $(5.3\ mm)^2$; FA1, $(6.0\ mm)^2$; FA2, $(6.2\ mm)^2$]. The results obtained so far suggest that in this context a K^{trans} value above ~0.3 min^{-1} should rouse suspicions of IDC.

Fig. 1

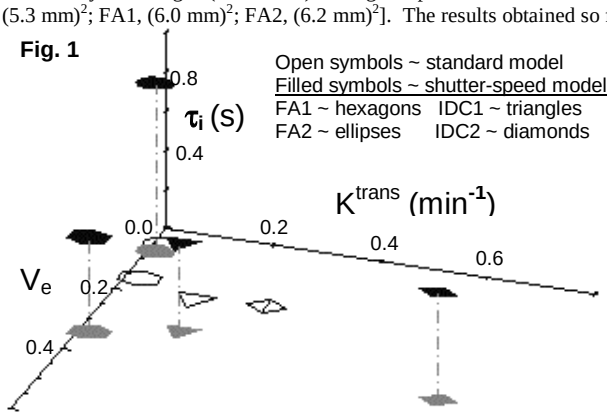
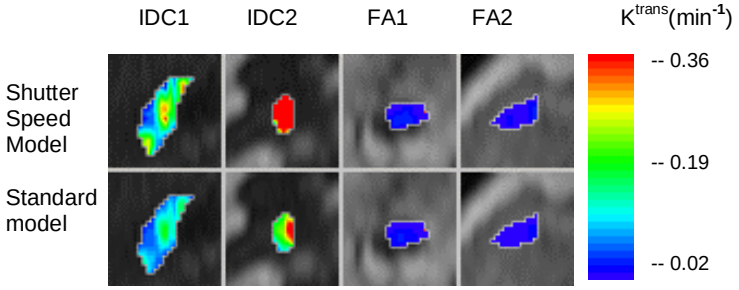


Fig. 2



DISCUSSION. These results are very encouraging. And, we have not yet even considered the third dimension afforded only by the shutter-speed model - the mean lifetime of water molecules in CR-inaccessible (mainly intracellular) spaces, τ_i (2). The black-filled Fig. 1 symbols mark the positions of the four lesion points in the 3D parametric space. The dimensionality increase is expected to only further improve IDC/FA discrimination. We are conducting analyses of additional lesions found in other breast image slices from these subjects, as well as expanding the study to a larger subject population.

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