Shutter-Speed Model Dynamic Contrast-Enhanced MRI to Reduce Unnecessary Surgeries of Atypical Breast Lesions: A Preliminary Study

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Introduction

The atypical breast lesions are high-risk benign lesions, mostly including pathologies such as atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), lobular carcinoma *in situ* (LCIS), and papillary lesions. Following core needle biopsies (CNBs), up to 87% of the patient population with atypical lesions are further referred for surgical excisions as standard care because of possible underestimation of malignancy by the CNB procedures (1,2). Recent studies show that surgical pathologies reveal malignancies in only 11-38% of such cases (1,2).

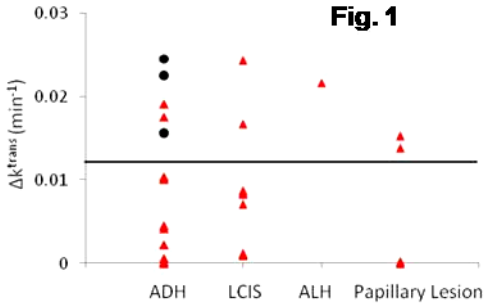
It has recently been shown that the quantitative Shutter-Speed Model (SSM) analysis of dynamic contrast-enhanced (DCE) breast MRI time-course data dramatically improves breast cancer diagnostic accuracy compared with the Standard Model (SM) DCE-MRI approach and current clinical MRI protocols (3-5). The SSM takes into account the finite transcytolemmal water exchange kinetics, while the SM assumes these to be effectively infinitely fast (3,4). Further, the newly discovered DCE-MRI biomarker, ΔK^{trans} [$\equiv K^{trans}$ (SSM) – K^{trans} (SM)], where K^{trans} is the capillary contrast agent extravasation rate constant, has higher diagnostic accuracy (near perfect specificity at 100% sensitivity) for breast cancer than K^{trans} itself (3,5). ΔK^{trans} is a measure of K^{trans} underestimation due to the SM's neglect of the finite water exchange kinetics (a shutter-speed effect) (3,4). Thus, the use of SSM DCE-MRI has the potential to reduce unnecessary breast biopsies that yield benign pathologies. In this study, we sought to investigate if SSM DCE-MRI can be used to potentially reduce unnecessary surgeries of CNB-proven atypical breast lesions.

Methods

In an ongoing IRB-approved SSM DCE-MRI study of patients with suspicious breast lesions (5), the research DCE-MRI data were acquired *prior to* clinically scheduled CNBs. The patients with CNB-proven atypical lesions (N = 28) further underwent surgical excisions as standard care. The SSM DCE-MRI results were correlated with the final surgical pathologies to determine if SSM DCE-MRI can differentiate with high accuracy these atypical lesions between those completely benign and those containing malignancies.

The research DCE-MRI data acquisitions were conducted at 1.5T and 3.0T using a body transmit and a four- or seven-channel phased-array bilateral breast receive RF coils. A 3D SPGR gradient echo pulse sequence was used to acquire 14-20 serial sagittal image volume sets continually, spatially covering the whole breast with the suspicious lesion to be biopsied. Other parameters included 10° flip angle, 2-5 ms TE, 6-9 ms TR, 3 mm section thickness, 20-24 cm FOV. Depending on the breast size, 16-40 image slices were acquired for each set, resulting in inter-sampling interval (temporal resolution) of 13-44 s. At the start of the second volume set acquisition, Gd contrast agent 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 (6), and averaged to generate a mean AIF. The tumor region-of-interest (ROI) and mean AIF signal time-courses were then subjected to both SM and SSM analyses to extract pharmacokinetic parameters. Lesion ROI ΔK^{trans} values were calculated and pixel-by-pixel ΔK^{trans} values were mapped. The DCE-MRI data analysis was blinded from both CNB and subsequent surgical pathologies.

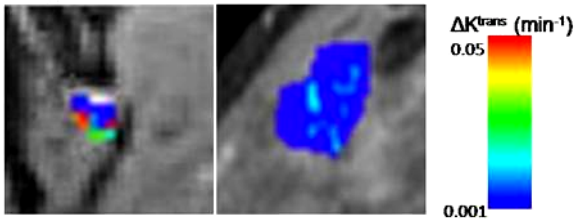
Fig. 1



Results

The studied 28 CNB-proven atypical lesions consisted of 13 ADH, 1 ALH, 9 LCIS, and 5 papillary lesions. Upon the final surgical pathology findings, only three of the CNB-proven ADH lesions were upgraded to malignant tumors (11%). **Fig. 1** shows the scatter plot of ROI ΔK^{trans} for the 28 atypical lesions. The black circles represent those upgraded to malignancies, while the red triangles indicate non-malignancies following surgeries. For the three atypical lesions with more than one instance, a cut-off line at 0.012 min^{-1} can be drawn to separate lesion clusters with larger and smaller ROI ΔK^{trans} values. The ΔK^{trans} values of the three lesions that were upgraded to malignancies are, indeed, all above the cut-off line, which represents 72% specificity and 100% sensitivity for cancer detection in this population. Had pre-CNB ROI ΔK^{trans} been considered in determining whether surgical excision was necessary, 18 patients (with ROI ΔK^{trans} below the cut-off line) out of 28 (64%) could have been spared the surgeries, and no cancer would have been missed.

Fig. 2



Eliminating partial-volume averaging effects, pixel-by-pixel SSM K^{trans} and/or ΔK^{trans} mapping can potentially further discriminate those lesions with ROI ΔK^{trans} values above the cut-off line, resulting in even greater reduction of unnecessary surgeries. **Fig. 2** shows the ΔK^{trans} maps of two CNB-proven ADH lesions: one (left panel) upgraded to invasive ductal carcinoma (IDC) following surgery, the other (right panel) remained benign. Both lesion ROI ΔK^{trans} values are above the Fig. 1 cut-off line. However, (red) ΔK^{trans} hot spots (> 0.05 min^{-1}) are seen in the lesion that was upgraded to IDC, while none is apparent in the other.

Discussion

The results from this preliminary study suggest that the SSM analyses of pre-CNB DCE-MRI data can potentially be used to spare probably the majority of atypical breast lesions from unnecessary surgeries, which are invasive and deforming. In current clinical settings, however, MRI examinations are not usually performed prior to CNB. We are currently investigating whether post-CNB-but-pre-surgery SSM DCE-MRI can achieve results similar to those of the pre-CNB studies despite possible imaging artifacts from the biopsy clips.

References **1.** Liberman L, *et al. Am J Roentgenol* 2007; 188: 684-690. **2.** Eby PR, *et al. Ann Surg Oncol* 2008; 15: 3232-3238. **3.** Huang W, *et al. Proc Natl Acad Sci* 2008; 105:17943-17948. **4.** Li X, *et al. Proc Natl Acad Sci* 2008; 105:17937-17942. **5.** Huang W *et al*. *Proc Int Soc Magn Reson Med* 2009;17:4240. **6.** Yankeelov TE, *et al. Magn Reson Med* 2003; 50:1151-1169.