Separation of benign and malignant breast lesions using pharmacokinetic analysis for a biopsy cohort

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INTRODUCTION: Dynamic contrast-enhanced (DCE) MRI is a high sensitivity tool for breast cancer screening and is currently recommended by the American Cancer Society for this indication in high-risk patients [1]. However, this technique suffers from a low and variable specificity (26-97%; Refs [2-4]), which leads to unnecessary biopsies. Clinical evaluation of the kinetic enhancement of indeterminate lesions relies on the signal intensity curves that also have significant overlap between benign and malignant lesions. Model-based pharmacokinetic analysis of contrast agent uptake curves in suspicious lesions is one method that has been applied to temporal DCE-MRI data in an attempt to improve its diagnostic accuracy. In this study, we investigate the utility of pharmacokinetic analysis of lesion kinetic data for patients that have been referred for biopsy. This is a uniquely problematic patient population since standard clinical analysis has already failed to separate benign and malignant lesions in this cohort.

METHODS: Patient Data. Unilateral DCE-MRI data were acquired at the NYU Cancer Center between November 2011 and October 2012 for 69 women undergoing MRI-guided biopsy of one or more lesions suspicious for breast cancer. The data were acquired on a 3T Tim Trio system (Siemens, Germany) using a dedicated 7 channel breast coil (In vivo). The DCE-MRI protocol used a 3D gradient-echo imaging sequence with fat-suppression and radial k-space sampling (radial VIBE; TR/TE=3.57/1.72 ms, FA=10 deg, FOV=280 mm, resolution 1.4 x 0.9 x 1.5 mm, 380 radial views/frame, 5-6 frames/scan) with a “stack-of-stars” scheme and golden-angle view ordering [5]. Contrast agent (Magnevist, Bayer) was administered approximately 60 seconds after the beginning of data acquisition. For each lesion, a core biopsy was obtained and the lesion type was determined via histology by a trained pathologist.

Data Analysis. High temporal resolution (5.5 sec) data were reconstructed using modified k-Space Weighted Image Contrast (KWIC) view-sharing [6] (10 subapertures, 38 spokes per subaperture) and regridding to a Cartesian grid. Regions-of-interest (ROIs) for each lesion as well as the internal mammary artery (IMA) were selected manually by a breast radiologist. The 25% most enhancing voxels in the manual ROIs for the lesion and the IMA were averaged to create the kinetic MR signal curves for both the lesion and arterial input function (AIF), respectively. MIR signal was converted to contrast agent concentration using the spoiled gradient-echo signal equation and assuming a linear relationship between the contrast agent concentration and the longitudinal relaxation rate [7]. The pre-contrast T1 relaxation values of the lesion and the AIF were assumed to be 1.5 s. The generalized kinetic model [8] with vascular volume fraction (GKM) was fitted to the MR signal curves for the lesion and background parenchymal tissue. For comparison with the pharmacokinetic model results, initial and delayed enhancement ratios (IER and DER) for each lesion were calculated from the clinical data (5 sec temporal resolution) by subtracting the pre-contrast MR signal from the MR signal for the third and fifth time points, respectively, and normalizing by the pre-contrast MR signal.

RESULTS: Eighty lesions were identified in 69 women. Forty-five were benign (56%), 14 were high-risk benign (18%), and 21 were malignant (26%). Initial and delayed enhancement ratios as well as the model parameters for the GKM model were calculated for each lesion type (benign, high-risk benign, and malignant). Fig. 1 shows the comparison of IER and DER for the lesion types. There is no significant difference between lesion types for these parameters. Breast images, lesion and AIF kinetic curves, and the pharmacokinetic model fit are shown in Fig. 2 for an example benign breast lesion. Fig. 3 shows a comparison of the fit parameters Ktrans, vP, and vE for the lesion types. There is no significant difference between the lesion types for any of the model parameters, however a promising trend is noted between all three lesion types for the parameter vP.

DISCUSSION: Patients referred for biopsy of breast lesions represent the most difficult cases since standard clinical analysis has already failed to separate benign and malignant lesions. Simple measures, such as IER and DER are inadequate for separation of lesion types in this population. Application of pharmacokinetic model techniques to this cohort shows that, although the results are not statistically significant, there are noticeable differences in median Ktrans and vP values between the lesion types. More detailed pharmacokinetic analysis may enhance these differences and provide a significant result. We will continue to accrue additional patient cases as well as expand the pharmacokinetic analysis to include more detailed models, such as the shutter-speed model, and T1 and T2 measurements. Methods appropriate for diagnosis of screening populations may not be adequate for discrimination of challenging cases as represented by the biopsy population considered in this study. More detailed analysis of these cases is necessary to reduce the number of biopsies performed in the clinic.