**Introduction:**

By measuring changes in tumor microvascular properties, dynamic contrast-enhanced (DCE) MRI has been shown capable of providing early prediction of breast cancer response to neoadjuvant chemotherapy (NACT) [1-3]. Since heterogeneity is an important feature of malignant tumors, the utility of image texture analysis [4] has been increasingly investigated for cancer diagnosis and therapeutic monitoring. In this preliminary study, we sought to evaluate the individual potentials of thousands of 3D texture features, extracted from parametric maps of quantitative pharmacokinetic (PK) and semi-quantitative DCE-MRI parameters, for early prediction of breast cancer therapy response.

**Methods:**

Thirty-six breast cancer patients who underwent NACT consented to research DCE-MRI studies performed at visit 1 (V1, before NACT) and V2 (after the first cycle of a 6-8 cycles NACT regimen). 3D DCE-MRI data acquisition details are described in [3]. Tumor ROIs were drawn on post-contrast DCE image slices covering the spatial extent of the tumor. Voxel-by-voxel (within the ROI) DCE time-course data were subjected to both the Standard Tofts Model (SM) [5] and Shutter-Speed Model (SSM) [6] PK analyses to extract quantitative parameters of $K^{trans}$, $v_e$ , $k_{ep}$ ($=K^{trans}/v_e$), and $\tau_i$ (mean intracellular water lifetime, SSM-only parameter). The SSM accounts for the effects of transcytolemmal water exchange kinetics. The $dK^{trans}[=K^{trans}(SSM)-K^{trans}(SM)]$ parameter, a measure of the water exchange effects on $K^{trans}$ estimation, was also calculated. Additionally, five semi-quantitative metrics (voxel-based) were quantified [7-9]: IE (initial enhancement), SER (signal enhancement ratio), PIE (post initial enhancement), SlopeIn (wash-in slope), and iAUC [initial area under the curve (to 90 s after contrast injection)]. Pathologic response to NACT and residual cancer burden (RCB) for each tumor were determined by pathology analysis of post-NACT resection specimens [10], with RCB = 0 indicating pathologic complete response (pCR).

We extracted 1044 statistical features [11-14] to characterize the tumor texture (heterogeneity) from 3D tumor ROI parametric maps of each quantitative PK or semi-quantitative parameter. These features are direct texture measures as the moments, the local binary patterns (LBP, a non-parametric gray-scale invariant texture model which summarizes the local structure), the pattern spectrum (PS, granulometry based on mathematical morphology operators), or are extracted using an intermediate statistical matrix representation: Haralick features from the Co-Occurrences Matrix (a tabulation of how often different combinations of voxel values occur for a given offset), the Run Length Matrix (RLM, counting the run length with the same gray level in a given direction), the Size Zone Matrix (SZM, counting the number of connected zones of a given size and intensity), and finally a fuzzy version of SZM (Fuzzy-SZM) and RLM (Fuzzy-RLM). To capture the early NACT-induced changes in tumor heterogeneity as measured by DCE-MRI, we subtracted the texture feature values at V2 from those at V1 for each texture feature of each DCE-MRI metric. The predictive ability of each feature for RCB was then assessed using linear regression, and the validation was performed with the leave-one-out method (Fig. 1). Four correlations were used to confirm the results: Pearson (linear), Spearman (rank), Kendall's Tau (rank), and Goodman-Kruskall gamma (rank).

**Results:**

We found 535 features producing good correlations with RCB values with all four correlation coefficients > 0.7 (Fig. 2). Haralick features show good correlations with RCB most frequently, followed by SZM, RLM, and LBP. It is interesting to note that although the moments are often used to characterize tumors, these features perform poorly in this study for early prediction of NACT response. Fig. 3 shows how often several quantitative PK parameters and semi-quantitative metrics provided good texture features for early prediction of therapy response with coefficients of all four correlations with RCB > 0.7. It appears that the SSM maps of $K^{trans}$, $\tau_i$ and $k_{ep}$ are at least 50% more likely to provide a good feature for prediction of response than the SM PK parameters or the semi-quantitative metrics.

**Discussion:**

This preliminary study evaluates and compares 3D texture features of DCE-MRI parametric maps for early prediction of breast cancer NACT response through correlations with RCB values. The evaluated imaging metrics include quantitative PK parameters derived from the SM and SSM analyses, and semi-quantitative parameters. The results suggest that texture features of quantitative PK parameters are likely to be more useful than those of semi-quantitative metrics for prediction of therapy response. The superiority of the SSM PK parameter features over the SM features for prediction of therapy response may result from the SSM correction of SM underestimation of the PK parameters – and thus larger dynamic ranges for the SSM parameters [15], as well as the highly effective SSM-unique $\tau_i$ parameter.

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**References:**

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**Fig 1.** Overview of the texture features extraction algorithm.
**Fig 2.** Distribution of the 535 texture features producing good correlations with RCB values with all four correlation coefficients > 0.7.
**Fig 3.** Distribution of the likelihood of a DCE-MRI metric (quantitative PK or semi-quantitative parameter) to provide good texture features for early prediction of breast cancer therapy response.

Synopsis

36 breast cancer patients underwent research DCE-MRI before and after one cycle of neoadjuvant chemotherapy. 3D tumor imaging texture features were extracted from parametric maps of quantitative pharmacokinetic (PK) and semi-quantitative DCE-MRI parameters, and correlated with pathologically measured post-therapy residual cancer burden (RCB). Texture features from quantitative PK parameters were found to be more useful than those from semi-quantitative metrics for early prediction of therapy response, while the features from the SSM PK parameters were superior to the SM counterparts for prediction of response.

Title

## Texture Feature Analysis of Quantitative and Semi-Quantitative DCE-MRI Metrics for Early Prediction of Breast Cancer Therapy Response

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