INTRODUCTION

Tumor response to neoadjuvant chemotherapy is currently monitored by changes in tumor size as measured by physical exam, ultrasound, or conventional MRI. However, these methods often do not correlate with pathologic findings at surgery. Dynamic contrast enhanced MRI (DCE-MRI) offers information related to tumor perfusion and permeability ($K_{\text{trans}}$), vascular volume ($v_p$), extravascular extracellular volume fraction ($v_e$), and the intracellular water lifetime of a water molecule ($\tau_i$). In this study, we attempted to determine the optimal analysis method for assessing if changes in these parameters after one cycle of therapy could separate pathologic complete responders (pCR) from non-responders (NR; i.e., patients with residual disease).

METHODS

22 patients with Stage II/III breast cancer were enrolled in an IRB-approved clinical trial where serial breast MRI scans were acquired pre-therapy ($t_1$) and after one cycle of therapy ($t_2$). Imaging was performed on a 3.0 T Achieva MR scanner (Philips Healthcare, Best, The Netherlands). The DCE-MRI acquisition employed a 3D spoiled gradient echo sequence with TR\/TE\/$\alpha$ = 7.9ms/1.3ms/20°. The acquisition matrix was 192×192×20 over a sagittal (22 cm)$^3$ FOV with a slice thickness of 5 mm. Each 20-slice set was collected in 16.5 seconds at 25 time points and 0.1 mmol/kg of Magnevist was injected at 2 ml s$^{-1}$ after three baseline dynamic scans. Eleven patients were pCR and the other 11 patients were NR.

Three pharmacokinetic models were used to estimate physiological parameters: the Tofts-Kety (TK), the Extended Tofts-Kety (ETK), and the fast exchange regime (FXR). For each model, eight DCE-MRI parameters were estimated to predict treatment response: the change in mean, median, mean of top 15%, and standard deviation (STD) from $t_1$ to $t_2$, the mean at $t_1$ and $t_2$, respectively, and the STD at $t_1$ and $t_2$, respectively. A Wilcoxon rank sum test was then used to determine if there was a significant difference between the pCR and NR groups.

RESULTS

The table displays the ability of $K_{\text{trans}}$ and $v_p$ to statistically separate pCR from NR patients. $K_{\text{trans}}$ (as estimated by the TK and ETK models) and $v_p$ (as estimated by the ETK model) lead to the most significant results. In particular, the TK estimates of the change of mean, change of the mean of the top 15%, the change in the STD, and the STD at $t_2$ of $K_{\text{trans}}$ are the most sensitive variables, achieving significance at the $p<0.01$ level. Nearly all $p$ values of $v_e$ and $\tau_i$ are not significant. It is very important to note that there was not a significant difference in enhancing tumor volume between the two groups ($p=0.24$), indicating that $K_{\text{trans}}$ and $v_p$ outperform tumor volume changes.

CONCLUSIONS

$K_{\text{trans}}$ as estimated by the TK and ETK models, as well as $v_p$, can separate complete responders from non-responders after a single cycle of neoadjuvant chemotherapy. These data contribute to a developing literature on quantitative DCE-MRI in the neoadjuvant setting. For example, Padhani et al. [1] showed that both tumor size and change in $K_{\text{trans}}$ range (similar to our STD measurement) were equally able to predict response, and Ah-See et al. [2] reported that changes in $K_{\text{trans}}$ were the best predictor of non-response. Our study, combined with those data, may ultimately allow clinicians to tailor therapy on an individual basis for this patient population.

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REFERENCES