Multivariate Analysis of DCE-MRI for Early Prediction of Breast Tumor Response Using Machine Learning

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INTRODUCTION Dynamic contrast enhanced MRI (DCE-MRI) can offer information related to tumor perfusion and permeability (K^{trans}), vascular volume (v_p), extravascular extracellular volume fraction (v_e), and the intracellular water lifetime of a water molecule (τ_i). There have been many efforts employing DCE-MRI as a surrogate biomarker for assessing and predicting the response of breast tumors to neoadjuvant chemotherapy. However, most studies perform univariate analysis on these parameters. In this study, we perform multivariate analysis, using machine learning methods, to predict the response of breast cancer to neoadjuvant chemotherapy after a single cycle of therapy.

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 neoadjuvant chemotherapy (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\α =7.9ms\1.3ms\20^o. The acquisition matrix was 192×192×20 over a sagittal (22 cm)^2 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 the third dynamic scan. Responders (n=11) were defined as those patients who had a pathologic complete response at time of surgery, while non responders (n=11) were defined as patients with residual invasive cancer at the primary tumor site.

Three pharmacokinetic models were used to estimate physiological parameters: the Tofts-Kety model (TK) [1], the extended Tofts-Kety model (ETK) [1], and the fast exchange regime model (FXR) [2]. 12 parameters were computed for each model to assess treatment response: mean and standard deviation (STD) of K^{trans}, v_e, and v_p at t_2, and the change in the region of interest mean and STD of K^{trans}, v_e, and v_p from t_1 to t_2, respectively. For a given model, each variable was first considered by itself, and then in combination with the estimate obtained by all three models as inputs into Logistic Regression (LR) and Support Vector machine (SVM). The leave-one-out method, which used one patient as the test set and all other patients as the training set, was employed to compute the accuracy, precision, sensitivity, and specificity.

RESULTS Table 1 lists the best accuracy, prediction, sensitivity, and specificity obtained by LR and SVM with linear, quadratic, and Gaussian Radial Basis Function (RBF) kernels, respectively. The parameters leading to the best results are also shown in the table. Note that different parameters could lead to same results. For example, the change in mean K^{trans} estimated by TK or ETK, or the combination of this parameter as estimated by all three models yielded the best results using LR. Both K^{trans} and v_p led to better results than v_e and τ_i. In particular, the change from t_1 to t_2, in the mean of K^{trans} estimated by TK and the change in the mean of v_p estimated by ETK, are the most sensitive predictors. It is also interesting to note that, in this preliminary study, the combination of parameters did not significantly improve the results.

	Parameters used in analysis	**Accuracy**	**Precision**	**Sensitivity**	**Specificity**
LR	ΔK^{trans} (TK) / ΔK^{trans} (ETK)/ ΔK^{trans}(all 3 models)	73%	78%	64%	82%
SVM, linear	ΔK^{trans} (TK)/ ΔK^{trans}(all 3 models)/ Δv_p(ETK) /STD v_p(ETK)	77%	100%	55%	100%
SVM, quadratic	Δv_p(ETK)	77%	80%	73%	82%
SVM, RBF	ΔK^{trans} (TK)	77%	100%	55%	100%

Table 1: The accuracy, precision, sensitivity, and specificity using different classification methods and corresponding parameters.

CONCLUSION The preliminary results demonstrate the feasibility of using DCE-MRI data and machine learning for predicting the response of breast tumors to a single cycle of neoadjuvant chemotherapy. Also, it appears that the SVM with different kernels perform differently in this application. As research on selection of the appropriate kernel functions is very active, future efforts will include optimizing kernel functions and parameters in machine learning.

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