Predicting treatment outcome after immunotherapy based on delta-radiomic model in metastatic melanoma

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INTRODUCTION

Melanoma is a malignant disease caused by melanocytes, and its incidence has been rising during the past decades. The recent studies showed that immunotherapy can significantly increase the patient survival rate and reduce the recurrence risk. However, it is very difficult to predict the immunotherapy response (progress or pseudoprogress). Since image features can capture more information in a non-invasive way, it may be used to predict the treatment outcome. Meanwhile, the recent studies shows that the delta-radiomics can be used to predict treatment response more accurately. As such, we developed an automated multi-objective delta-radiomic (Auto-MODR) model to predict immunotherapy response in metastatic melanoma. Auto-MODR not only takes advantages of the feature differences between the pre-treatment and one cycle post-treatment (known as delta-radiomic features), but also utilized all the generated Pareto-optimal models which are generated through multi-objective optimization. Besides, an evidential reasoning (ER) strategy was used to fuse the output probabilities of these generated Pareto-optimal models to obtain more reliable results.

AIM

To predict immunotherapy response (progress or pseudoprogress) in metastatic melanoma by developing a new reliable automated multi-objective delta-radiomic (Auto-MODR) model.

METHOD

Patients

Group 1		Group 2		Group 3
50 patients with metastatic melanoma	=	34 patients with anti-PD-18 immunotherapy	+	16 patients with CTLA-4 immunotherapy

Radiomic Features (497)

Intensity features(9)

Texture features(480)
12 features for each parameter,40 parameter groups in this study

Geometry features(8)

METHOD

Train stage

The training stage employs multi-objective optimization to get the Pareto-optimal model set. The aim is to maximize the sensitivity f_{sen} and specificity f_{spe} simultaneously, that is $f = max_{\alpha,\beta}(f_{sen}, f_{spe})$. We used iterative multi-objective immune algorithm (IMIA) to conduct feature selection and model training.

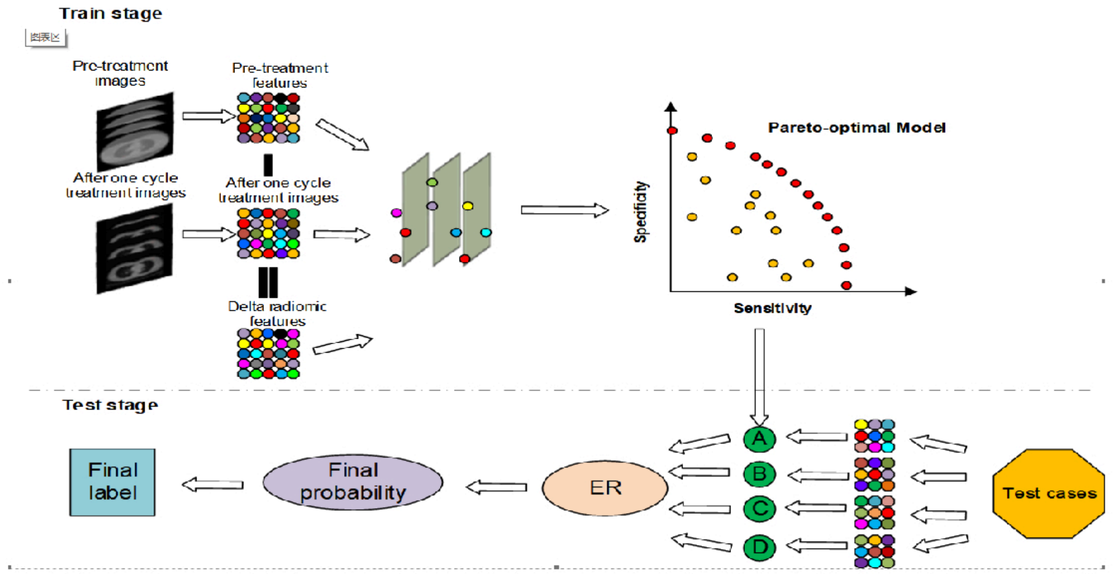

Figure 1. Auto-MODR workflow.

Test stage

The testing stage consists of weight calculation and ER based fusion. To obtain the balanced outcome, the model with non-zero weights represents a good balance between sensitivity and specificity, while a model with zero weight is extremely imbalanced (figure 2). Then the selected features feed into the models with non-zero weights. Finally, the output probability is obtained by using ER to combine the output probabilities of these models. The label with the maximal output probability is the final label.

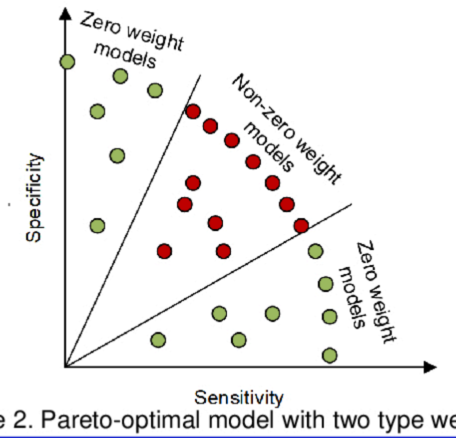

Figure 2. Pareto-optimal model with two type weights

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RESULTS

Figure 3 shows sensitivity, specificity, accuracy and area under the receiver operating characteristic curve (AUC) for different feature combinations. It can be seen that sensitivity, specificity, accuracy and AUC have increased a lot when combining the delta-radiomic features and traditional radiomic features. Particularly, the one-cycle post-treatment radiomic features coupled with delta-radiomic features achieved the best performance, with AUC of 0.829. However, the model that only used one-cycle post-treatment radiomic features yielded AUC of 0.728. Combining delta-radiomic features with traditional radiomic features, the experimental results shows that Auto-MODR can significantly improve the predictive performance.

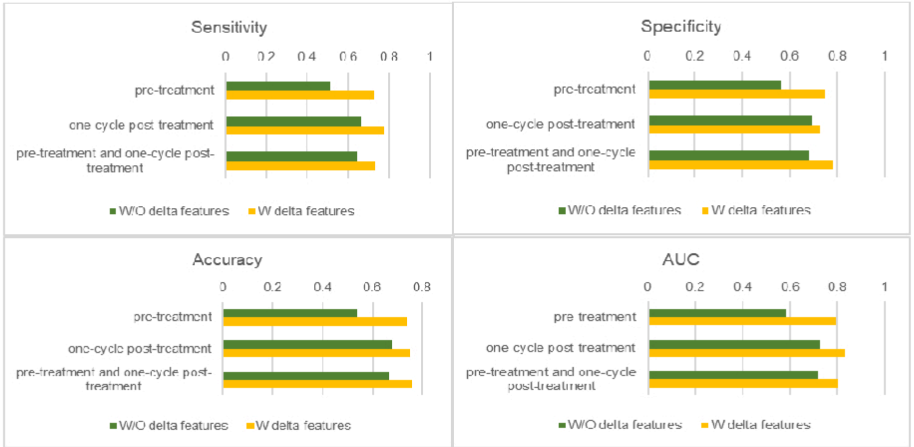

Figure 3. Results of using traditional features (non-delta) only versus traditional features combined with delta features.

Tables 1 compared Auto-MODR with traditional multi-objective model (MO) and traditional single-objective model (SO-AUC). Auto-MODR outperforms SO-AUC in higher AUC, accuracy and sensitivity. Meanwhile, Auto-MODR performs better than MO in all evaluation metrics.

Table 1. Result of different models for post-treatment features with delta features

Model	AUC	Accuracy	Sensitivity	Specificity	p-value
SO-AUC	0.749	0.683	0.606	0.75	<0.0001
MO	0.799	0.704	0.705	0.702	<0.0001
Auto-MODR	0.829	0.752	0.778	0.73	<0.0001

CONCLUSIONS

We developed a new automated multi-objective delta-radiomic (Auto-MODR) model for predicting immunotherapy response (progress or pseudoprogress) in metastatic melanoma. The experimental result demonstrated that the best performance can be obtained when combining the traditional radiomic features with delta-radiomic features.

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