Comparing the Predictive Accuracy of Deep Learning Models for Radiation Sensitivity Prediction Using Gene Expression Profiling

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Purpose: Predicting *in vitro* radiation sensitivity of cancer cell lines based on high-throughput genomics data using deep learning is promising to be applied in various fields such as radiotherapy or radiological protection. In a previous study, the feasibility of *in vitro* radiation sensitivity prediction model with reasonable predicting performance was presented using a convolutional neural network (CNN), which worked properly with acceptable accuracy and computation resources. However, there are various types of deep learning models in practice, and these models can even be modified under the user's preferences. Therefore, not only the CNN model presented previously, but also a wide range of different types of deep learning models can be used for *in vitro* radiation sensitivity prediction. Therefore, this study compared the prediction performance of various types of deep learning models to investigate the most suitable types of deep learning models for predicting *in vitro* radiation sensitivity.

Materials and Methods: Gene expression data of Gene Expression Omnibus database and clonogenic cell survival fraction at 2Gy (SF2) values of National Cancer Institute-60 panel were obtained from previous publications to compare the performance of prediction models. In this dataset, 174 triplicated samples of 59 tumor cell lines were included. Seven types of *in vitro* radiation sensitivity prediction models: multi-layer perceptron (MLP) with three layers ended with 128 nodes ("shallow1"), MLP with three layers ended with 32 nodes ("shallow2"), deep MLP with 9 layers ("MLP"), 5 convolution layers with 3 shallow fully connected (FC) network ("CNN with shallow FC"), shallow CNN with 3 convolution and 5 FC layers ("shallow CNN"), and finally deep CNN composed of 5 convolution and FC layers ("deep CNN") were compared to evaluate the prediction performance. A 6-fold cross-validation approach was applied to train and validate the model. The model was evaluated and trained with the Nvidia TITAN RTX and the TensorFlow 1.14.0 framework based on Python version 3.6.8. The accuracy of the model was defined as a percentage of samples that met the criteria: if either the absolute error between the measured and predicted SF2 of the sample is less than 0.01 or the relative error is less than 10%. One-way ANOVA based on the absolute prediction error was used to determine whether the results of each models were statistically significantly different. All statistical analysis was performed with GraphPad Prism version 7.03.

Results: In terms of the predictive accuracy, models (shallow1, shallow2, MLP, CNN with shallow FC, shallow CNN, deep CNN) showed the accuracy of 0.0%, 86.2%, 89.7%, 92.0%, 97.1%, and 97.7%, respectively. As a result of multiple comparison of one-way ANOVA, shallow CNN and deep CNN model were found to show significantly different absolute prediction error. Both shallow CNN and deep CNN showed adjusted P value of under 0.0001 compared with any other types of model, except when compared CNN with shallow FC and shallow CNN, adjusted P value = 0.0017. When the training time per epoch of shallow model is set to 1, the relative training time was 4.2 for MLP and 10.5 for CNN based models, respectively. The early convergence time for each models were not that different, around 20000 epochs with batch size 29.

Conclusions: In this study, we compared various types of deep learning models for predicting *in vitro* radiation sensitivity from gene expression profiling data. Since transfer learning is mainly used as a training method in deep learning field, the result of this study suggests that CNN with a moderate depth of FC layer seems to be sufficient to predict *in vitro* radiation sensitivity from gene expression profiling, unless the short training time is essential.

Keywords: Radiation sensitivity; Deep learning; Gene expression; Survival fraction at 2Gy; Model comparison

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