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Evaluation of Hand-crafted Radiomics and Foundational Models to Predict Esophagitis in Patients with Locally Advanced Non-Small Cell Lung Cancer on the NRG Oncology Trial RTOG 0617

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ABSTRACT

Purpose:
We implemented a hand-crafted radiomics model and evaluated it against a foundational model, Med3D, a popular transfer network model pretrained on a large-scale medical imaging dataset, for prediction of radiation esophagitis (RE) in patients with locally advanced Non-Small Cell Lung Cancer (LA-NSCLC).

Methods and Materials:
The NRG Oncology/Radiation Therapy Oncology Group (RTOG) 0617 dataset was utilized for this study. We implemented handcrafted radiomics and a Med3D transfer network without fine-tuning to extract features from CT and 3D dose maps (dosiomics) using esophagus contours to predict for RE ≥ grade 2. Receiver operating characteristic (ROC) and correlation analyses were performed to identify significant predictors of toxicity. LASSO, Random Forest (RF), XGBoost and Support Vector Machine (SVM) were trained on 315 patients using 10-fold nested cross-validation (CV). Independent predictors were ranked on importance score, and stepwise-forward feature selection was used to select the subset that minimized validation error. The best performing model (highest AUC) was applied to 136 previously unseen test patients.

Results:
RE ≥ grade 2 occurred in ~40% of patients (n=178). Models based solely on clinical features did not demonstrate predictive performance. The highest performing model (LASSO) used a combination of handcrafted radiomics and dosiomics features with AUC of 0.70 for both validation and test datasets. The Med3D feature-based model (Random Forest) achieved an AUC of 0.75, 0.62 on the validation and test datasets, respectively suggesting an increased generalization error with this model.

Conclusion:
Results are suggestive that the Med3D foundational network combined with hand-crafted radiomics and dosiomics may serve as a signature for prediction of post-treatment RE. The increased generalization error with the Med3D model suggests that better training/fine-tuning of the contextual transfer learning with larger sample sizes is warranted.

INTRODUCTION

- Radiation esophagitis (RE) is a common adverse toxicity, symptomatically occurring in up to 40% of patients receiving treatment for lung, which can be crippling to a patient's health and quality-of-life [1].
- Acute RE can be of major concern, resulting in hospitalization, feeding-tube placement, treatment interruptions, and poorer clinical outcomes. Reducing this risk is therefore of significant clinical relevance [1].
- Hand-crafted radiomics and foundational model have been shown to serve as signatures of clinical endpoints such as overall survival, disease progression and tumor response [2,3].
- We investigated the predictive power of a hand-crafted radiomics and foundational model approach when applied to pre-treatment CT and post-treatment 3-dimensional (3D) dose distribution maps (dosiomics) to predict grade ≥ 2 RE.

CONCLUSIONS

- Results are suggestive that the Med3D foundational network combined with hand-crafted radiomics and dosiomics may serve as a signature for prediction of post-treatment RE.
- The increased generalization error with the Med3D model suggests that better training/fine-tuning of the contextual transfer learning with larger sample sizes is warranted.

METHODS AND MATERIALS

- The NRG Oncology/Radiation Therapy Oncology Group (ROTG) 0617 data from the National Clinical Trials Network was utilized [4,5,6]. Common-terminology-criteria-for-adverse-events (CTCAE) grade ≥ 2 esophagitis.
- RTOG 0617 patients (n=451) were included, the sample size was split as follows: n=315 (training 70%) and n=136 (testing 30%).
- A radiomics analysis pipeline was applied to pre-treatment CT and 3D dose maps (termed "dosiomics") to extract 174 hand-crafted and 9296 foundational features from esophagus contours (esophagus-CTV).
- Receiver operating characteristic (ROC) and correlation analyses were applied to identify predictive predictors of toxicity.
- Several distinct experimental setups were conducted, starting with the analysis of hand-crafted radiomics and dosimics, followed by the foundational model-based radiomics features.
- Predictive models, LASSO, Random Forest (RF), and Support Vector Machine (SVM) were trained on 315 patients using 5-repeat, 10-fold cross-validation and tested on 136 independent test patients [7].

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RESULTS

- From esophagus-GTV 39 hand-crafted radiomics feature and 43 dosiomics features were identified as independent predictors.
- Similarly, out of 9296 Med3D transfer network feature 119 form CT and 84 3D dose map features were also found to be both independent and significant.
- Models based on solely based on clinical features (PET staging, 60v70 Gy, AJCC stage, gender) were not predictive in the test set.
- LASSO Model based hand-crafted radiomics and dosiomics features from both esophagus achieved the highest an AUC of 0.70 (validation) and 0.70 (test).
- The model based on foundational model-based radiomics and dosiomics features from esophagus achieved an AUC of 0.75 (validation) and 0.62 (test) using the RF algorithm.

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Fig. 1. I. Summary of workflow: schematic steps include collection of clinical information and dose image, ML model construction and performance evaluation of the predictive models. II. Performance of models based on hand-crafted and foundational model features from CT and 3D dose to predict for RE ≥ grade 2.