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Machine Learning-Based Identification of Post-Radiation Dysphagia and Dysphagia-Related Organs at Risk in Patients with Oropharyngeal Carcinoma

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Abstract

Purpose: Dysphagia greatly impacts patients' quality of life after radiation therapy (RT) for oropharyngeal carcinoma (OPC). Traditional dose constraints for the pharyngeal constrictors and larynx are widely used during RT planning. However, post-RT dysphagia remains common, and its severity varies dramatically among patients. We hypothesize that other dysphagia-related organs at risk (DR-OARs) exist and may contribute to the prevalence and severity of post-radiation dysphagia, and that these DR-OARs can be identified using machine learning (ML) and RT dosimetric distribution.

Methods: We retrospective collected RT dose for 155 patients with human papilloma virus-related OPC treated with definitive Intensity Modulated Radiation Therapy at a single academic center from 2017 – 2021. Patients were classified as having no significant dysphagia (grade 0 or 1 by Common Terminology Criteria for Adverse Events V5) vs significant dysphagia (grade 2 and 3) at 6 months after RT. The dataset was partitioned into 125 training and 30 testing cases randomly. An ML classification model was developed using contrasted-CT from simulation and 3D dose distribution as inputs and the binary classification as output, with U-Net architecture followed by convolutional layers, dense layers and sigmoid activation. The final model was an ensemble bagging approach combining 3 sub-models. Following training, the model was employed to generate heatmaps of anatomic regions on the CT that had the highest influence on predicted dysphagia outcomes.

Results: Most patients had early-stage disease (67% T0-2, 73% N0-1 by AJCC 8th edition staging), 48% were never smokers, and 91% received concurrent chemotherapy. 58% received de-intensified RT to 60Gy and 42% to 70Gy. 82 patients had no significant post-RT dysphagia (N&#3f6 Grade 0, N&#3f76 Grade 1), and 73 had significant dysphagia (N&#3f59 Grade 2, N&#3f14 Grade 3). ML classification on the training set achieved an Area Under the Receiver Operating Characteristic Curve (AUC) of 0.96 with an independent t-test p< 0.001. The ML model on the test set yielded AUC=0.81 and p=0.002. To probe the model's discriminatory power beyond binary classification, we performed sensitivity analysis and tested the model's ability to distinguish different dysphagia grades in the test set: Grade 0-1 vs. Grade 2 (AUC=0.77, p=0.016), and Grade 0-2 vs. Grade 3 (AUC=0.81, p=0.033). Heatmaps identified the inferior pharyngeal constrictor (IPC) and Cricopharyngeus muscles as highly associated with dysphagia. The Cricopharyngeus posterior to the larynx had the highest impact on dysphagia.

Conclusion: We developed an ML classification model with high accuracy in identifying and classifying RT-induced late dysphagia in patients with OPC. The model identified the IPC and Cricopharyngeus as the most important DR-OARs. Prospective validation and further understanding of the dose response of the IPC and Cricopharyngeus muscles may facilitate the development of strategies to further reduce dysphagia and improve patient outcomes beyond RT dose reduction.