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Unlocking the Adaptive Advantage: Leveraging Supervised Machine Learning to Classify Optimal Candidates for Online Adaptive Stereotactic Partial Breast Irradiation

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Abstract

Objectives:

Accelerated partial breast irradiation (APBI) offers similar rates of recurrence and cosmetic outcomes versus whole breast radiation therapy (RT) when patients and treatment techniques are appropriately selected. The use of stereotactic body radiation therapy (SBRT) for APBI is gaining popularity in the treatment of early-stage breast cancer due to reduced treatment volume and minimized dose to healthy tissue. KV-cone beam computed tomography (CBCT)-guided online adaptive RT (OART), which can account for inter-fractional anatomical variations, may be employed to further enhance target coverage while reducing normal tissue dose. OART is specifically advantageous during short course APBI because lumpectomy cavity seromas often change in size and shape However, OART stereotactic planning and treatment processes are also more resource-intensive than traditional APBI workflows. In particular, appointment times are longer which can lengthen the treatment day and require greater staffing, and both a physician and physicist are generally required at each fraction to generate and evaluate the adjusted contours and plan. Hence, it is imperative for clinics to effectively identify those patients who are most likely to receive significant benefits from OART. In this study, a machine learning model is built for predicting which stereotactic APBI patients receiving would benefit the most from OART, for the purpose of informing a resource-limited clinic which patients to treat adaptively.

Methods:

In this retrospective, single-institution study, 188 treatment plans were analyzed, covering 30 patient treatment courses of 32 targets (two patients with bilateral disease). Each patient was prescribed 30Gy in 5 fractions, and they received one reference plan based on simulation as well as five treated plans (four treated plans were excluded due to data export issues). During each treatment fraction, the physician and physicist chose to treat patients with either a standard-of-care (SOC) plan (reference plan recalculated onto daily CBCT anatomy) or an adaptive plan (plan optimized based on daily CBCT anatomy) based on quantitative and qualitative criteria. Twenty simulation structure set and plan metrics, including target and organ-at-risk (OAR) volumes, dose metrics, and distances between target and OAR surfaces and centroids, were collected. Additionally, 10 treated plan metrics were considered: volume of the planning target volume (V_PTV), PTV V100%, Breast V30Gy, Breast V15Gy, Heart V1.5Gy, Lung V9Gy, Skin D0.01cc, Rib D0.01cc, conformity index (CI), and high-dose spillage. Adaptive benefit was defined as the difference between the treated and reference plan dose metrics (e.g., Δ_BreastV30Gy=Ref_BreastV30Gy-Treat_BreastV30Gy). To verify that adaptive plans correlate to greater adaptive benefit compared to SOC plans, differences in SOC and adapted plan dose metrics were compared using the Mann-Whitney U unpaired, non-parametric test. Next, recursive feature elimination allowed for identification of key model features from the list of simulation metrics. A machine learning logistic regression model was then assembled to predict which patients would receive all five adaptive fractions, with stratified 4-fold cross validation and tuning of probability threshold and hyperparameters. To account for stochasticity due to the random fold patient assignments, this process was bootstrapped ten times. The average model accuracy, area under the curve (AUC) of the receiver operating characteristic (ROC) curve, and confusion matrix were then obtained from the resulting model validation results.

Results:

Adaptively treated fractions had greater PTV volume reduction compared to SOC plans ($p < 0.05$), and resulted in significantly greater adaptive benefit for the PTV V100%, Breast V30Gy, Breast V15Gy, conformity index (CI), and high-dose spillage metrics ($p < 0.05$). The majority of patients (62.5%) were treated with adaptive plans for every fraction. The features selected in the final model were PTV volume (cc), Breast volume (cc), gradient index (GI), high-dose spillage, distance between heart and PTV centroids, and distance between the nearest surfaces of the heart and PTV. Upon ten-fold bootstrapping, the model validation cohort performed with 75.9±2.0% accuracy (defined as correct patient class prediction), indicating the model correctly assigned patient class at a higher rate than either random chance or choosing to treat all patients adaptively. More importantly, the model was trained to prefer false positives over false negatives, with rates of 19.4% and 4.7%, respectively. Therefore, of the 37.5% of patients assigned to the SOC class (negative), only 4.7% were identified incorrectly (false negative). These validation results suggest that the proposed model would correctly move patients from adaptive to non-adaptive therapy with 87.5% accuracy, if implemented in a resource-limited clinic. Lastly, the mean AUC of the validation ROC curve was 0.80±0.01, exhibiting good class discrimination across all probability thresholds.

Conclusion(s):

Adaptively treated stereotactic partial breast treatments show significant improvements over SOC fractions, relative to initial reference planning for five of nine investigated plan metrics. As proof of concept, we constructed a supervised machine learning logistic regression model for predicting whether patients would be treated entirely adaptively, or receive at least one SOC treatment. While the overall accuracy of the model can be further improved, the rate of true negatives to false negatives was quite high (7:1). So although some low-benefit patients would be treated adaptively using this model, the majority of patients identified by the model as low-benefit were correctly classified, saving clinical resources. These results support utilization of machine learning models for bifurcating adaptive and non-adaptive patient pipelines in resource limited clinics.