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Abstract
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Utilizing Unsupervised Machine Learning to Identify an Optimal Planning Target Volume Size Threshold for Online Adaptive Stereotactic Partial Breast Irradiation

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Abstract

Objectives:

With appropriate technique and patient selection, accelerated partial breast irradiation (APBI) confers similar oncologic outcomes and improved cosmesis compared to whole breast radiotherapy. Reduction in planning target volume (PTV) sizes correlates with reduced incidence of fat necrosis in APBI patients treated with 5 fraction stereotactic body radiotherapy. One such method to reduce treated volume is via daily online adaptive radiotherapy (OART). This technique accounts for daily alteration in lumpectomy cavity sizes and anatomical breast variations. However, daily replanning necessitates longer treatment times for the patient and is more resource intensive due to direct physicist and physician involvement. Thus, it is important to prospectively determine which patients optimally benefit from OART. This study seeks to utilize unsupervised machine learning to identify which simulation structure set and reference planning metrics correlate to optimal benefit from daily online adaption.

Methods:

In this retrospective, 343 treatment plans were analyzed, covering 30 patient treatment courses of 32 targets (due to two bilateral patients). Each patient was prescribed 30Gy in 5 fractions; they received one reference plan based on simulation, along with five standard-of-care (SOC) plans (reference plans recalculated onto daily CBCT anatomy) and five treated plans (physician's choice of either the SOC plan or adapted plan, which was optimized using daily anatomy). Nine plans were excluded due to data export issues. Twenty simulation metrics, including target and organ-at-risk (OAR) volumes, dose metrics, and distances between target and OAR surfaces and centroids, were collected. Additionally, 10 SOC and treated 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. The Wilcoxon paired, non-parametric test assessed the net improvement with adaptation by comparing the average treated plan metrics ((Treat_mean)) with both the average SOC plan metrics ((SOC_mean)) and the reference plan metrics. Adaptive benefits were then calculated using the difference between the reference dose metrics and average treated dose metrics (e.g., Δ_(Breast V30Gy) = Ref_BreastV30Gy - (Treat_mean_BreastV30Gy)). Spearman non-parametric correlation coefficients (r) were then calculated for each combination of 20 simulation metrics and 10 adaptive benefits, enabling identification of strong univariate predictors of adaptive benefit. Finally, the study utilized k-means clustering, an unsupervised machine learning algorithm which groups multivariate data without bias. Patients were partitioned along n-dimensions, where n was the number of simulation metrics with at least one strong univariate Spearman correlation of 0.5 or greater, providing a multivariate grouping of patients. To mitigate outlier effects, three clusters were utilized instead of two. The Mann-Whitney U unpaired, non-parametric test was then used to assess the difference in adaptive benefit between the resulting clusters.

Results:

Treated plans yielded significant improvements ($p \leq 0.05$) compared to SOC plans across all metrics besides Heart V1.5Gy and Skin D0.01cc, which showed no significant difference ($p > 0.05$). Treated plans exhibited significant improvements ($p \leq 0.05$) when compared to reference plans for all OAR objectives, except for Heart V1.5Gy ($p > 0.05$). There was no significant difference ($p > 0.05$) between the reference and treated CI, although the reference high-dose spillage was lower than treated plans ($p \leq 0.05$). Seven combinations of

simulation metrics and adaptive benefits resulted in a Spearman correlation greater than 0.5, indicating a strong correlation using Cohen's standard of effect size: V_PTV vs. ΔBreast V30Gy (r = 0.60), V_PTV/V_Breast vs. ΔBreast V30Gy (r = 0.63), Breast 30Gy vs. ΔBreast V30Gy (r = 0.70), Breast 15Gy vs. ΔBreast V30Gy (r = 0.67), Breast 15Gy vs. ΔBreast V15Gy (r = 0.54), Lung V9Gy vs. ΔLung V9Gy (r = 0.52), and Spillage vs. ΔSkin D0.01cc (r = -0.64). Three clusters were then obtained along the resulting six simulation metric dimensions (V_PTV, V_PTV/V_Breast, Breast 30Gy, ΔBreast V15Gy, Lung V9Gy, Spillage). Although patients were grouped along six dimensions, the resulting clusters were perfectly stratified along V_PTV, suggesting that V_PTV is the driving factor in patient grouping: cluster 1 (n=15) with V_PTV < 95cc, cluster 2 (n=13) with 95cc≤ V_PTV ≤200cc, and cluster 3 (n=4) with V_PTV >200cc. Patients in clusters 2-3 (V_PTV≥95cc) generally experienced greater adaptive benefit compared to those belonging to cluster 1 (V_PTV< 95cc), with significant improvements in adaptive benefit for the Breast V30Gy and Skin D0.01cc metrics in the larger volume cohort (p≤0.05). Importantly, the median percent reduction in V_PTV from simulation to treatment was identical for cluster 1 and clusters 2-3 (13.2%). Therefore, increased adaptive benefit for larger targets cannot be attributed to larger relative seroma volume shrinkage.

Conclusion(s):

The delivery of kV-CBCT OART for stereotactic APBI led to significantly improved or similar dosimetry and plan quality compared to both reference and SOC planning across all metrics, except for the reference high-dose spillage. Notably, delivering reference plans onto daily anatomy (i.e., SOC) resulted in a decrease in conformity and an increase in high dose spillage (p< 0.05), indicating that maintaining reference plan quality when accounting for anatomical changes becomes prohibitive without adaptive capabilities. The findings from this study clarify that specific simulation metrics can effectively predict univariate adaptive benefits in Breast V30Gy, Breast V15Gy, Lung V9Gy, and Skin D0.01cc. Additionally, our results show that, although smaller targets are typically preferred for SBRT, partitioning patients using a 95cc PTV volume threshold resulted in larger PTV volumes experiencing significantly improved adaptive benefits across multiple metrics. This suggests that the ideal candidates for daily adaptive APBI may be patients with large PTVs and reference plans that meet initial planning goals.