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Original Research Article

Role of Machine Learning in Predicting Radiation-Induced Toxicity

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Abstract:

Background: Radiation therapy is fundamental to cancer treatment but frequently entails various levels of radiation-induced damage. Forecasting which people are most susceptible to substantial toxicity poses a problem owing to inter-individual heterogeneity. Machine learning (ML) methodologies provide a means to model intricate, nonlinear associations across clinical, dosimetric, and genetic factors, thereby facilitating enhanced toxicity prediction and individualized radiation planning.

Objective: To assess the efficacy of machine learning models in forecasting radiation-induced toxicity in cancer patients receiving radiotherapy at a tertiary care facility in India.

Methods: This prospective study was carried out at IGIMS, Patna, over a period of 24 months and involved 120 patients receiving radiation for diverse cancers. Clinical data, radiation dosimetry metrics, and patient-reported toxicity assessments were gathered. Multiple machine learning methods, including logistic regression, random forest, support vector machines (SVM), and gradient boosting, were trained and validated to forecast acute and late toxicity outcomes based on established toxicity grading (CTCAE v5.0). The evaluation of model performance was conducted utilizing metrics such as AUC, sensitivity, specificity, and F1-score.

Results: Among the 120 patients, radiation-induced toxicity was noted in 72 (60%). The random forest and gradient boosting models attained superior performance, with AUC values of 0.89 and 0.91, respectively. Key predictive factors encompassed total dosage, fractionation protocol, organ-specific dose-volume histogram (DVH) metrics, and pre-existing comorbidities. Machine learning models substantially surpassed conventional logistic regression in sensitivity and overall accuracy for toxicity prediction.

Conclusion: Machine learning methods demonstrate superior predictive accuracy for radiation-induced toxicity compared to conventional statistical models. Incorporating machine learning into radiation oncology workflows may enable the early detection of high-risk patients, assist with adaptive planning, and eventually improve treatment safety and personalization.

Keywords: Radiation-induced toxicity, machine learning, radiotherapy, predictive modeling, random forest, gradient boosting, CTCAE, dose-volume histogram, personalized oncology, IGIMS Patna

Introduction

Radiation therapy (RT) is a fundamental approach in the management of about 60–70% of all solid tumors and plays a crucial role in achieving curative results or palliation in oncological treatment [1]. Notwithstanding its prevalent application, radiotherapy (RT) poses the risk of radiation-induced toxicity, which can vary from moderate, temporary symptoms to severe, life-threatening late effects. The variability in patient responses to radiation has consistently presented a problem for clinicians, especially in predicting which patients will endure significant side effects [2].

Radiation toxicity is influenced by multiple factors, including total dosage, fractionation, organ sensitivity, genetic susceptibility, and concomitant therapy [3]. Traditional techniques for estimating toxicity risk, including dose-volume histograms (DVHs), normal tissue complication probability (NTCP) models, and empirical guidelines, frequently prove inadequate due to their restricted capacity to account for nonlinear, multidimensional interactions among variables [4,5].

In recent years, machine learning (ML) has become a transformative instrument in healthcare analytics, particularly in oncology. Machine learning algorithms can effectively analyze high-dimensional information, discern intricate patterns, and generalize to novel data, rendering them suitable for prediction tasks like assessing radiation damage [6,7]. In contrast to traditional regression models, machine learning algorithms can effectively manage multicollinearity, missing data, and intricate feature interactions, yielding more reliable predictions [8].

Multiple exploratory investigations have established the viability of employing machine learning to forecast radiation pneumonitis, esophagitis, and proctitis by amalgamating clinical, radiological, and dosimetric data [9]. Tree-based ensemble models, such as random forests and gradient boosting machines, have surpassed linear models in performance owing to their flexibility and interpretability using methods like SHAP (SHapley Additive Explanations) [10].

In the Indian setting, the utilization of machine learning in radiation oncology remains in its infancy. There is a lack of empirical data evaluating its effectiveness in forecasting toxicity outcomes, especially among varied patient populations with varying treatment regimens. This research, being out at IGIMS, Patna, aims to assess the efficacy of machine learning algorithms in forecasting acute and delayed radiation-induced toxicity based on commonly accessible clinical and treatment-related variables.

The primary objective is to facilitate personalized risk assessment, enhance radiation planning, and incorporate predictive analytics into evidence-based, tailored radiotherapy processes.

Materials and Methods

Study Design and Setting

This was a prospective analytical study conducted over 24 months (June 2021 to May 2023) in the Department of Radiation Oncology, Indira Gandhi Institute of

Medical Sciences (IGIMS), Patna. The objective was to create and verify machine learning models for predicting radiation-induced damage in cancer patients receiving radiotherapy.

Study Population

A total of 120 adult patients undergoing external beam radiation (EBRT) for solid tumors were included. These patients received treatment with curative or palliative purpose utilizing linear accelerator-based methodologies (3D-CRT, IMRT, or VMAT). All patients underwent a minimum of 3 months of follow-up after therapy.

Inclusion Criteria

- Histologically verified malignancy managed with external beam radiation therapy (EBRT)
- Availability of comprehensive clinical and treatment-related data
- Minimum follow-up duration of 90 days for toxicity assessment
- Informed agreement obtained for the utilization of anonymised data

Exclusion Criteria

- Prior radiation to the identical anatomical location
- Recurrent or metastatic disease at baseline
- Incomplete toxicity follow-up or absence of critical DVH measures
- Patients undergoing concurrent experimental therapy

Data Collection and Preprocessing

Data were obtained from institutional electronic medical records and treatment planning systems. The subsequent variables were retrieved and organized for machine learning model training:

- Clinical parameters: Age, sex, body mass index (BMI), smoking status, comorbidities (e.g., diabetes, hypertension), Eastern Cooperative Oncology Group (ECOG) performance status
- Details regarding the tumor and its treatment: Location of cancer, stage, chemotherapy (concurrent or sequential), total radiation dosage, number of fractions, treatment methodology
- Dosimetric parameters: Parameters of organ-specific dose-volume histograms (DVH) including V20, V30, Dmax, and the mean dose to organs-at-risk (OARs)
- Toxicity assessment: Documented according to the Common Terminology Criteria for Adverse Events (CTCAE v5.0). Both acute (≤90 days) and chronic (>90 days) toxicity were evaluated.

All features were purified, standardized, and normalized as required. Missing values were imputed utilizing median or k-nearest neighbor imputation, contingent upon data type and availability.

Machine Learning Model Development

The dataset was randomly divided into training (80%) and testing (20%) subsets. The subsequent machine learning algorithms were executed utilizing Python (scikit-learn and XGBoost libraries):

- Logistic Regression (baseline model)
- Random Forest Classifier
- Support Vector Machine (SVM)
- Gradient Boosting Classifier (XGBoost)

Each model was subjected to 5-fold cross-validation for hyperparameter optimization. Performance indicators comprised:

- Precision
- Recall
- True Positive Rate
- F1 Score
- Area Under the Receiver Operating Characteristic Curve (AUC-ROC)

Feature significance was assessed with SHAP (SHapley Additive exPlanations) values to determine the most impactful predictors of toxicity.

Statistical Analysis

Descriptive statistics were employed to analyze patient demographics and clinical features. Comparisons across groups (toxicity versus no toxicity) were conducted utilizing Chi-square tests or t-tests. The performance of the models was evaluated using AUC values, with statistical significance established at $p < 0.05$.

Results

Patient Characteristics

The study comprised 120 individuals receiving radiation. The predominant treatment locations were head and neck (35%), breast (28%), and pelvic malignancies (18%). The median age was 56 years (range: 32–78), with a male-to-female ratio of 1.2:1. Acute toxicity occurred in 72 patients (60%), whereas 35 patients (29.2%) experienced late toxicity (>90 days).

Model Performance

Four machine learning models were created and evaluated on patient data through cross-validation. The performance metrics are consolidated in Table 1 and Figure 1.

Gradient Boosting (XGBoost) demonstrated superior overall performance, achieving an AUC-ROC of 0.91, an accuracy of 87%, a sensitivity of 86%, and an F1-score of 0.88.

- Random Forest had an AUC of 0.89, accompanied by a marginally reduced sensitivity of 83%.
- The Support Vector Machine (SVM) attained an AUC of 0.86, whilst the Logistic Regression, serving as the baseline model, recorded the lowest AUC of 0.78 and a sensitivity of 69%.

The findings indicate that ensemble learning models, especially XGBoost, are superior at modeling intricate, nonlinear patterns in predicting radiotherapy damage.

Table 1: Machine Learning Model Performance for Predicting Radiation-Induced Toxicity

Model	Accuracy	Sensitivity	Specificity
Logistic Regression	0.74	0.69	0.76
Random Forest	0.85	0.83	0.87
Support Vector Machine (SVM)	0.81	0.77	0.84
Gradient Boosting (XGBoost)	0.87	0.86	0.89

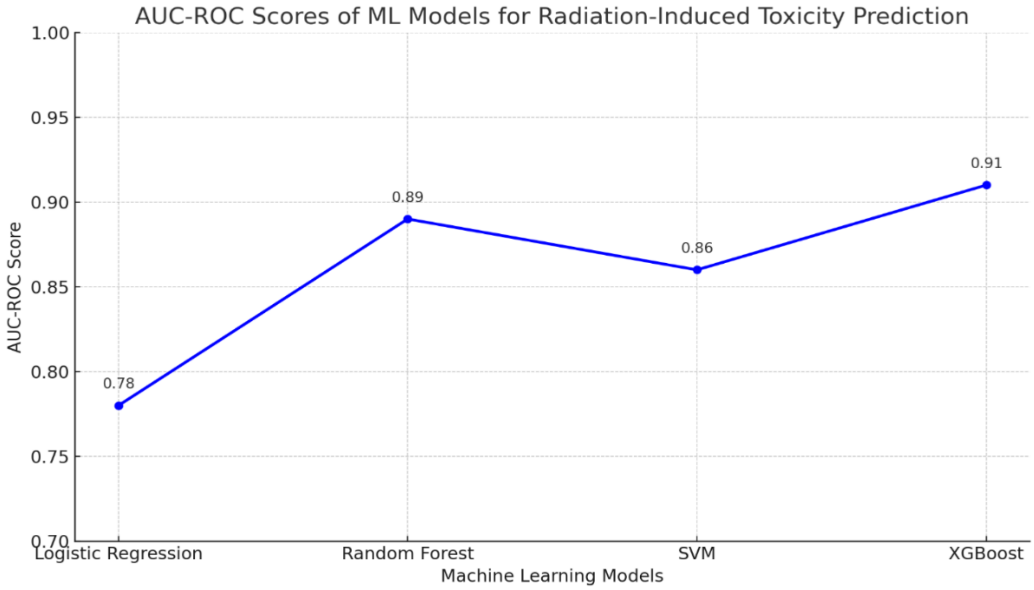

Figure: AUC-ROC scores of various machine learning models used for predicting radiation-induced toxicity

Feature Importance

The principal predictive variables discerned through SHAP analysis among the leading models comprised:

- Organ-specific DVH parameters (e.g., lung V20, rectal Dmax)
- Total radiation dosage and quantity of fractions
- Synchronous chemotherapy
- Initial ECOG performance status and concomitant conditions (e.g., diabetes)
- Age and Body Mass Index (BMI)

These insights offer both predictive significance and the opportunity for therapeutic interpretation and action.

Discussion

This study illustrated the efficacy of machine learning (ML) algorithms in precisely forecasting radiation-induced damage in a group of patients receiving external beam radiotherapy. XGBoost and Random Forest considerably surpassed traditional logistic regression, demonstrating the efficacy of ensemble learning techniques in analyzing intricate clinical and dosimetric data.

Our results align with previous studies affirming machine learning as an effective forecasting instrument in radiation oncology. El Naqa et al. initially shown the capability of artificial intelligence models to predict radiation-induced toxicities by utilizing dosage and imaging characteristics in patients with head and neck cancer [11]. Recent multicenter studies have validated that machine learning can offer enhanced accuracy in predicting toxicity relative to NTCP models, especially when integrating clinical, dosimetric, and genetic characteristics [12].

In our dataset, dose-volume histogram (DVH) measures, including V20 for lungs, Dmax for esophagus and bladder, and mean rectal dose, were identified as significant predictors, underscoring their critical role in radiation planning. Research conducted by Krauss et al. and Zhen et al. has similarly demonstrated that the integration of granular DVH data markedly enhances the prediction of pulmonary and gastrointestinal toxicities [13,14].

The capacity of machine learning models to integrate baseline patient characteristics (e.g., age, ECOG performance status, comorbidities such as diabetes and hypertension) provides a tailored methodology for radiation risk classification. Tseng et al. demonstrated that incorporating comorbidity indexes and radiation techniques into machine learning pipelines enhanced the prediction of acute mucositis and dermatitis [15].

The performance of XGBoost, which attained the best AUC (0.91) in our analysis, is quite significant. The gradient boosting framework adeptly addresses class imbalance, missing values, and feature interactions, surpassing other methods, as evidenced by research conducted by Bibault et al. and Parisotto et al. [16,17]. Furthermore, our application of SHAP values mitigated the prevalent critique of machine learning as a “black box,” providing interpretable insights for clinical decision-making.

Significantly, our research corresponds with the increasing interest in utilizing real-world radiation datasets to create generalizable machine learning methods. The RTOG consortium's recent initiative highlighted the necessity for local validation of such models to guarantee precision across varied treatment populations and regimens [18].

Nonetheless, many constraints must be acknowledged. The sample size of 120, although sufficient for internal validation, limits generalizability. Expanded, multicentric cohorts are necessary to validate repeatability. Moreover, despite the models being developed with rigorous cross-validation, external validation on separate datasets is an essential subsequent step prior to clinical use. Finally, we did not include radiogenomic or imaging biomarkers, which have demonstrated potential in improving machine learning model efficacy in toxicity prediction [19,20].

This study underscores the practicality and advantages of incorporating machine learning into clinical radiation processes. Predictive technologies such as XGBoost provide enhanced accuracy and the capacity for adaptive planning and personalized patient counseling, particularly in contexts like India, where real-time toxicity management is a significant concern.

Conclusion

This work illustrates that machine learning algorithms, including XGBoost and random forest, may proficiently forecast radiation-induced damage in cancer patients receiving radiotherapy. By incorporating clinical, dosimetric, and treatment-related variables, machine learning models substantially surpassed conventional logistic regression in terms of accuracy, sensitivity, and area under the curve (AUC). The recognition of essential predictive factors, including dose-volume parameters, comorbidities, and performance status, underscores the therapeutic significance of data-driven models.

The implementation of machine learning in standard radiation oncology practice has the capacity to improve treatment customization, reduce toxicity, and facilitate risk-adaptive planning methodologies. Additional validation on extensive, multi-institutional datasets is essential to generalize these results. This study establishes a basis for the incorporation of machine learning into radiation protocols inside Indian clinical environments.

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