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Radiation Dose Prediction for Cervical Cancer Patients Using IMRT Technique with a Machine Learning Model Based on Support Vector Regression (SVR)

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ABSTRACT

Cervical cancer poses significant global health challenges, necessitating the need for innovative treatment approaches. This study addresses the gap in current radiotherapy methods by integrating Support Vector Regression (SVR) to predict radiation doses for cervical cancer treatment, thereby enhancing the precision of Intensity Modulated Radiation Therapy (IMRT). Using datasets from 102 and 173 cervical cancer cases, we developed and validated an SVR model to predict dose distributions based on radiomic and dosiomic features. The model demonstrated strong performance, achieving a Mean Absolute Error (MAE) of 0.069 for the testing data, with specific performance metrics as follows: bladder mean dose MAE of 0.0693, bowel mean dose MAE of 0.0926, and rectum mean dose MAE of 0.0779. These findings highlight the potential of machine learning to refine radiotherapy planning, reduce the workload on medical physicists, and improve patient outcomes. Future research should focus on expanding dataset sizes and enhancing model precision, particularly for anatomically challenging regions.

INTRODUCTION

Cervical cancer remains a formidable challenge in oncology, contributing to substantial morbidity and mortality worldwide [1,2]. According to data from the International Agency for Research on Cancer (IARC), Indonesia records approximately 348,809 new cancer cases annually, resulting in 207,210 deaths. Among these, cervical cancer accounts for 32,469 fatalities, representing 17.2 % of the total cases [3]. Effectively addressing this complex malignancy requires innovative treatment approaches, particularly in radiotherapy, where precision and efficacy are crucial [2,4]. Intensity Modulated Radiation Therapy (IMRT) stands out among radiotherapy techniques for its ability to deliver highly precise radiation doses to tumor targets, achieving an optimal balance between target volume coverage and minimizing exposure to surrounding healthy tissues and organs at risk (OAR) [5,6]. By utilizing advanced imaging modalities and computer-controlled linear accelerators, IMRT allows clinicians to shape radiation beams with remarkable accuracy to conform to the tumor's contours, enhancing therapeutic efficacy while reducing radiation-related toxicities. [5,7.8].

The integration of Artificial Intelligence (AI), specifically Machine Learning (ML), into radiotherapy planning marks the advent of a new era in personalized medicine [9]. By leveraging vast datasets of patient images, treatment parameters, and outcomes, AI algorithms can identify complex patterns and relationships, enhancing treatment planning and decision-making [10]. Machine Learning models, such as Support Vector Regression (SVR), have shown great potential in predicting dose distributions and optimizing treatment plans based on individual patient characteristics. SVR provides a robust framework for modeling complex dose-response

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relationships, accounting for the anatomical variability in cervical cancer cases, and enabling clinicians to customize treatment plans to each patient's unique profile. [11,12,13].

Radiomics and Dosiomics represent cutting-edge methodologies that delve into the quantitative analysis of medical images to extract clinically relevant information [14,15]. Radiomics allows for the characterization of tumor heterogeneity and the prediction of treatment responses by analyzing imaging data for features such as texture, shape, and intensity [16]. Dosiomics, in contrast, emphasizes the dosimetric aspects of radiotherapy, correlating dose distributions with clinical outcomes to guide treatment planning and optimization [17].

This study explores the intersection of technology and oncology, leveraging the combined potential of IMRT, AI-driven predictive modeling, and advanced radiomic and dosiomic analyses in the management of cervical cancer. By developing and validating an SVR model for dose prediction in IMRT, we aim to propel the paradigm shift towards personalized, data-driven radiotherapy planning, ultimately improving treatment efficacy and patient outcomes.

METHODOLOGY

Study location and participants

The research was conducted at the Integrated Radiation Oncology Service Installation of Dr. Cipto Mangunkusumo National Central General Hospital in Jakarta, Indonesia, and the Medical Physics and Biophysics Laboratory at the Department of Physics, Faculty of Mathematics and Natural Sciences, University of Indonesia, Depok, West Java, Indonesia. Two datasets were utilized: 102 planning cases of cervical cancer patients with stage I-III C1r, and 173 planning cases with random stages. Both datasets employed the IMRT technique with a 6 MV LINAC energy, provided in DICOM format and selected from the hospital's database. The study aimed to investigate whether stage uniformity or the size of the dataset would influence the performance of machine learning models. The research was conducted using a computer running Python software, with Google Colaboratory accessed through the Universitas Indonesia single sign-on network.

Study design

Efforts were made to ensure data validity and minimize discrepancies in machine learning research for dose prediction. The success of machine learning largely relies on the quality of the coding developed by researchers and the volume of data used. The core principle of machine learning is to learn patterns from input data, with larger datasets enabling more effective learning and yielding more accurate results.

Data collection

Data were collected from cervical cancer patients treated with IMRT at Dr. Cipto Mangunkusumo National Central General Hospital. The dataset consisted of patient images in DICOM format, including grayscale images (DICOM CT), dose distribution from treatment planning (DICOM dose), and contoured structures drawn by specialist doctors (DICOM Structure).

Data preprocessing

The first step involved preparing the dataset using 3D Slicer software to extract the dose distribution and structure. The selected structures included the target (PTV) and organs at risk (OAR) such as the bladder, bowel, femoral heads (right and left), and rectum.

Feature Extraction

Feature extraction converted the raw data into numeric features while preserving the original dataset's information. Radiomic features captured the organ shape information, while dosiomic features represented the dose distribution. The extracted features included D2 %, D50 %, D98 %, Dmean, and Dmax.

Data normalization

Dosiomic data were normalized to ensure consistency, scaling all values, between 0 and 1. Radiomic data, however, were not normalized, as doing so would distort the organ shape information.

Model training

Seventy percent of the data from both datasets was used as training data. The training process utilized machine learning algorithms in Python, leveraging modules such as pandas, scikit-learn, and numpy. Radiomic data served as the independent variable (X), while dosiomic data was the dependent variable (Y). The training was conducted in Google

Colaboratory, with the datasets converted into radiomic and dosiomic formats and saved as CSV files. The performance of the Support Vector Regression (SVR) model was influenced by three parameters: complexity capacity (C), epsilon (ε), and gamma (γ) [18]. The RBF kernel function was used, requiring parameters C and γ [19,20].

Grid Search with cross-validation was implemented to evaluate performance metrics and train multiple models [19,21,22]. The SVR model's performance was assessed using the Mean Absolute Error (MAE), which is calculated using Eq. (1):

$$MAE = \frac{1}{n}\sum_{i=1}^{n}|f_i - y_i| \quad (1)$$

The accuracy of the predictive results was evaluated based on the MAE value, with smaller MAE values indicating more accurate predictions.

Model testing

The remaining 30 % of the datasets were used as testing data to evaluate the performance of the trained SVR model on unseen data [23]. The predicted dose distribution values were compared to the actual dose distribution values, with performance assessed using MAE.

Evaluation

The gold standard in this study was based on clinical data that had undergone the complete treatment and patient recovery process. The predicted dataset from the SVR model was compared with clinically planned datasets, focusing on the dose to target and organs at risk. Dose distribution to the target was assessed using the Conformity Index (CI) value, indicating the degree of conformity between the dose received and the target volume (PTV). A CI value approaching 1 signifies ideal conformity. Following the guidelines in ICRU Report 62, the Conformity Index (CI) can be mathematically expressed in Eq. (2).

$$CI = \frac{V_{95}}{V_{PTV}} \quad (2)$$

Where V_{95} represents the volume of the PTV receiving 95 % of the prescribed dose, and V_{PTV} signifies the total volume of the PTV [24]. The homogeneity of dose distribution absorbed by the PTV was evaluated using the Homogeneity Index (HI), with smaller HI values indicating a more uniform dose distribution, as outlined in ICRU Report 83 in Eq. (3):

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \quad (3)$$

D2 %, D50 %, and D98 % represent the doses covering 2 %, 50 %, and 98 % of the PTV volume, respectively [25]. The dose administered to organs at risk (OARs) was evaluated based on the mean and maximum dose values across all OARs. Additionally, the statistical significance of differences between predicted and actual dose distributions was assessed using Wilcoxon signed-rank tests, with p-values less than 0.05 considered statistically significant.

Ethical considerations

This study was approved by the Ethical Review Board of Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta, Indonesia, with reference number 23-10-1776. All patient data used in this study was anonymized to protect patient privacy and confidentiality. To ensure data security, patient identifiers were removed, and data were stored in secure, encrypted databases accessible only to authorized personnel. During data processing and analysis, strict protocols were followed to maintain confidentiality and prevent unauthorized access. Additionally, data sharing with collaborators was conducted through secure channels to further protect patient information. These measures ensured that patient confidentiality and data security were maintained throughout the study.

Limitations

This study's limitations include the retrospective nature of data analysis, reliance on existing patient datasets, and the single-institution study setting. Additionally, patient variability, such as differences in tumor size, shape, and location, can impact the model's predictive accuracy. The generalizability of the model may be limited when applied to populations or institutions that differ significantly from the study sample. For example, variations in imaging protocols, treatment planning techniques, and patient demographics across different institutions could affect model performance. Future research could address these limitations by conducting prospective studies with larger and more diverse patient populations across multiple institutions. This approach would help validate the model's robustness and improve its generalizability.

RESULTS AND DISCUSSION

The dose prediction for all Organs at Risk (OAR), including the bladder, bowel, femoral heads (right and left), and rectum, as well as the Planning Target Volume (PTV), based on Fig. 1, for the dataset with various stages, and Fig. 2 for the dataset with the same stages, demonstrates a high degree of accuracy. Both the mean dose (D_mean) and the maximum dose (D_max) indicate the levels of radiation received by each OAR and PTV. This alignment suggests that the predictive model's dose closely matches the clinical measurements. Such precision is critical in radiotherapy, where accurate dose delivery can significantly improve treatment outcomes and minimize side effects.

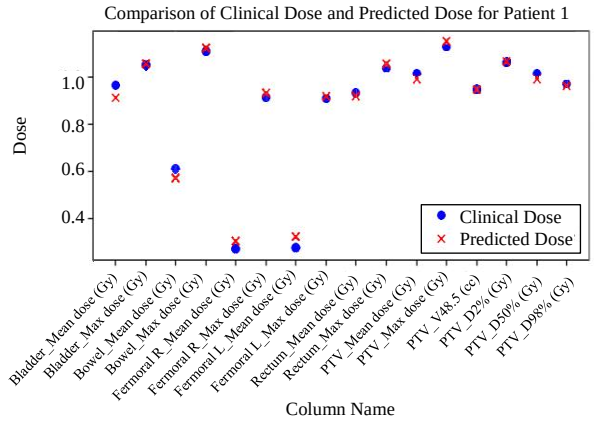

Fig. 1. Comparison of clinical dose and predicted dose of one patient for 173 patients dataset with various stages.

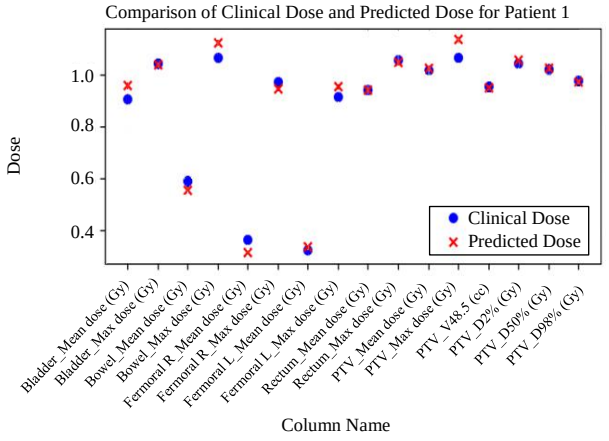

Fig. 2. Comparison of clinical dose and predicted dose of one patient for 102 patients dataset with the same cancer stages.

Upon reviewing the graphs in Fig. 1 and Fig. 2, it's evident that both exhibit a consistent level of accuracy across varying and identical stages. This consistency suggests that the data analysis process was reliable and produced trustworthy results. However, to fully understand the accuracy depicted in both figures, it is necessary to closely examine some key metrics. Specifically, analyzing the Mean Absolute Error (MAE) values, along with their mean, and p-values, will provide deeper insights into the predictive accuracy for each organ. By analyzing these metrics, researchers can better understand how consistent the predictions are across different anatomical structures.

Additionally, considering factors such as Homogeneity Index (HI) and Conformity Index (CI) will further enhance our understanding of accuracy in Fig. 1 and Fig. 2. These indices are critical for assessing how uniform and consistent the dose distribution is, which plays a vital role in evaluating the reliability of the data. While the visual representations suggest a high level of accuracy, detailed examination of MAE values, along with factors like HI and CI, is essential for a comprehensive evaluation of the findings. This approach is crucial for validating predictive modeling in medical research.

MAE analysis for model training and testing

During the training and testing phase of the Support Vector Regression (SVR) model, the Mean Absolute Error (MAE) is a key metric for evaluating the model's performance. The MAE measures the average magnitude of errors between the predicted and actual doses, with values closer to zero indicating higher accuracy. This metric is particularly important as it provides insight into the model's ability to generalize from the training data to new, unseen data.

Based on the observations in Table 1 and Table 2, the MAE values for both training and testing datasets, whether using various cancer stages or the same stage, fall within an acceptable range, highlighting the model's robustness and reliability.

Interestingly, the tables reveal that the MAE (Mean Absolute Error) values for training are generally larger than those for testing. This pattern is consistent with the typical behavior of machine learning models, which often exhibit higher training errors. During the training phase, the model is exposed to a wide range of data points and learns to generalize from them, incorporating an inherent margin of error as it refines its predictions. As a result, MAE values during training are usually higher, reflecting the model's effort to balance accuracy with generalization.

Table 1. MAE training and testing of each organ for the dataset with various stages.

Structure	Various Stages (173 Datasets)			
	MAE Training	MAE Testing	Best Parameter	
			C	Epsilon
Bladder Mean Dose	0.0648	0.0693	5.0	0.00125
Bladder Max Dose	0.0982	0.0992	2.0	0.125
Bowel Mean Dose	0.0552	0.0926	12.5	0.002
Bowel Max Dose	0.0933	0.1214	1.25	0.0875
Fem(R) Mean Dose	0.0674	0.0947	2.0	0.05
Fem(R) Max Dose	0.0894	0.0955	2.0	0.125
Fem(L) Mean Dose	0.0700	0.0917	1.625	0.05
Fem(L) Max Dose	0.0778	0.0990	2.0	0.0005
Rectum Mean Dose	0.0782	0.0779	2.0	0.02
Rectum Max Dose	0.0979	0.1035	2.0	0.125
PTV Mean Dose	0.0503	0.0699	20.0	0.002
PTV Max Dose	0.0941	0.1101	1.625	0.0875
PTV D2 %	0.0692	0.0864	8.75	0.01625
PTV D50 %	0.0498	0.0702	20.0	0.002
PTV D98 %	0.0481	0.0662	20.0	0.002

Table 2. MAE training and testing of each organ for the dataset with the same stages.

Structure	Various Stages (173 Datasets)			
	MAE Training	MAE Testing	Best Parameter	
			C	Epsilon
Bladder Mean Dose	0.0739	0.0627	5.0	0.0005
Bladder Max Dose	0.0815	0.1001	50.0	0.02
Bowel Mean Dose	0.0690	0.0841	1.25	0.0005
Bowel Max Dose	0.1038	0.1459	5.0	0.05
Fem(R) Mean Dose	0.0721	0.0947	5.0	0.0875
Fem(R) Max Dose	0.0890	0.0726	2.0	0.000875
Fem(L) Mean Dose	0.0762	0.0788	2.0	0.125
Fem(L) Max Dose	0.1033	0.1041	1.625	0.0005
Rectum Mean Dose	0.0778	0.0634	50.0	0.02
Rectum Max Dose	0.0917	0.1186	5.0	0.00125
PTV Mean Dose	0.0585	0.1034	5.0	0.002
PTV Max Dose	0.1040	0.1276	5.0	0.0005
PTV D2 %	0.0828	0.1102	5.0	0.0005
PTV D50 %	0.0572	0.1046	5.0	0.002
PTV D 98 %	0.0563	0.1085	5.0	0.00125

Conversely, when the model processes the testing dataset-comprising new, unseen data-the MAE tends to be lower. This reflects the model's improved ability to generalize from the training data, indicating enhanced performance and reduced error rates on the testing set. This discrepancy highlights the model's effectiveness in capturing underlying patterns during training, ultimately leading to superior performance on the testing data.

However, a notable exception is observed in the same stage section of Table 2, where some values are inconsistent, showing higher MAE values in testing than in training (e.g., bladder mean dose, rectum mean dose). This anomaly can likely be attributed to the smaller dataset size for the same-stage patients (103) compared to the dataset with various stages (173). The reduced data volume in the same stage dataset may have affected the model's training efficacy and its ability to generalize, contributing to these inconsistencies.

Both tables further illustrate the optimal hyperparameters used to achieve accurate predictions for each structure. This precision is achieved through the application of GridSearchCV within the SVR code, where it was applied individually to each structure. For each organ, a separate SVR model is trained, and the best hyperparameters are selected specifically for that organ based on the grid search.

The reason each structure has different hyperparameters is that SVR is highly sensitive to parameters like C and epsilon, and there is no exact mathematical procedure for deriving the optimal values [26,27,28,29]. Different features may require varying levels of regularization and tolerance for prediction errors. Unlike other machine learning models, such as Random Forest, which tend to be more robust to hyperparameter variations due to their ensemble nature (using multiple decision trees), SVR requires carefully tuned hyperparameters to optimize performance for each specific feature distribution.

Overall, these findings underscore the model's general reliability and highlight the importance of dataset size and diversity in achieving consistent and accurate predictive performance.

MAE analysis for model training and testing

The analysis for this section involves the mean dose for each structure (organ/tumor volume) across all patients, followed by a Wilcoxon signed-rank test to determine the statistical significance of the differences between clinical and predicted doses.

Based on Table 3, which examines the dataset with random cancer stages, the SVR model demonstrated remarkable accuracy across most dose metrics. Predictions for the Homogeneity Index (HI) and Conformity Index (CI) were nearly indistinguishable from clinical values, with p-values of 0.78 and 0.34, respectively, underscoring the model's robustness. Bladder dose predictions were notably precise for mean doses (clinical: 0.838, prediction: 0.836, $p = 0.28$). However, the max dose predictions for the bladder revealed a significant difference (clinical: 1.006, prediction: 0.985, $p = 0.03$), indicating a potential area for model improvement. Similarly, rectum max dose predictions exhibited a significant discrepancy (clinical: 0.982, prediction: 0.954, $p = 0.02$), suggesting the need for further refinement.

Table 3. Mean difference in average dose and maximum dose for organ at risk in the clinical plan and SVR, along with the p-value (various stages).

Structure	Various Stages (173 datasets)		
	D_{mean} (Clinical)	D_{mean} (Prediction)	P-value
HI	0.107	0.096	0.78
CI	0.954	0.952	0.34
Bladder Mean Dose	0.838	0.836	0.28
Bladder Max Dose	1.006	0.985	0.03
Bowel Mean Dose	0.485	0.465	0.07
Bowel Max Dose	1.050	1.038	0.44
Fem(R) Mean Dose	0.311	0.302	0.56
Fem(R) Max Dose	0.853	0.859	0.86
Fem(L) Mean Dose	0.320	0.292	0.09
Fem(L) Max Dose	0.863	0.878	0.71
Rectum Mean Dose	0.858	0.855	0.32
Rectum Max Dose	0.982	0.954	0.02
PTV Mean Dose	0.980	0.979	0.48
PTV Max Dose	1.075	1.064	0.94
PTV D2 %	1.039	1.025	0.76
PTV D50 %	0.977	0.979	0.73
PTV D 98 %	0.934	0.935	0.70

Table 4. Mean difference in average dose and maximum dose for organ at risk in the clinical plan and SVR, along with the p-value (same stages).

Structure	Same Stages (102 datasets)		
	D_{mean} (Clinical)	D_{mean} (Prediction)	P-value
HI	0.125	0.103	0.12
CI	0.951	0.953	0.20
Bladder Mean Dose	0.799	0.831	0.06
Bladder Max Dose	0.952	1.008	0.17
Bowel Mean Dose	0.464	0.458	0.29
Bowel Max Dose	0.967	1.064	0.04
Fem(R) Mean Dose	0.317	0.265	0.004
Fem(R) Max Dose	0.825	0.850	0.46
Fem(L) Mean Dose	0.317	0.273	0.01
Fem(L) Max Dose	0.817	0.863	0.85
Rectum Mean Dose	0.814	0.838	0.15
Rectum Max Dose	0.936	1.022	0.08
PTV Mean Dose	0.916	0.992	0.009
PTV Max Dose	1.008	1.089	0.05
PTV D2 %	0.977	1.045	0.56
PTV D50 %	0.915	0.995	0.004
PTV D 98 %	0.864	0.943	0.009

Predictions for bowel, femur, and Planning Target Volume (PTV) doses were generally in close agreement with clinical doses. Particularly, PTV dose metrics (mean, max, D2 %, D50 %, and D98 %) showed high p-values, affirming the model's efficacy in predicting these critical treatment parameters, which are essential for ensuring precise and effective radiotherapy.

Based on Table 4 for the dataset with the same cancer stage, the results were encouraging but revealed areas needing further improvement. The HI and CI predictions remained accurate, with non-significant differences from clinical values (p-values of 0.12 and 0.20, respectively). However, prediction for bladder and bowel max doses displayed significant differences (bladder max dose: $p = 0.17$, bowel max dose: $p = 0.04$), highlighting potential areas for model refinement.

Femur dose predictions, particularly for the mean doses of both right ($p = 0.004$) and left femur ($p = 0.01$), showed significant discrepancies, indicating that the model requires improvement in these areas. Additionally, PTV dose predictions, especially for mean and D50 %, exhibited significant differences (mean dose: $p = 0.009$, D50 %: $p = 0.004$), suggesting that further tuning is necessary.

The findings underscore the importance of dataset size and diversity in achieving consistent and accurate predictive performance. The larger dataset with random cancer stages yielded higher accuracy, indicating that a more extensive dataset enhances the model's ability to generalize and learn underlying patterns effectively. In contrast, the smaller dataset with consistent cancer stages showed more significant discrepancies, suggesting that while stage consistency helps standardize the data, the limited size restricts the model's learning capability.

Future research should focus on increasing dataset sizes and refining models, particularly for challenging areas such as the bladder and rectum. One approach to improving model performance is by carefully selecting radiomic features that are highly relevant to dosiomic results. Techniques like Recursive Feature Elimination (RFE) or Principal Component Analysis (PCA) should be employed to identify the most significant features, thereby reducing the risk of overfitting and enhancing predictive accuracy.

Additionally, enhanced data preprocessing methods, such as advanced normalization techniques, outlier detection, and data augmentation, can ensure high-quality input data and increase the variability of the training dataset. Further hyperparameter tuning and validation using cross-validation techniques will optimize the SVR model parameters. Incorporating additional performance metrics, such as the Area Under the Receiver Operating Characteristic Curve (AUC-ROC), will provide a comprehensive evaluation of model performance.

Incorporating clinical factors such as patient age, tumor histology, and prior treatment history into the predictive model can further enhance

its accuracy and applicability in clinical settings. These future research directions aim to refine the SVR model, making it more effective and reliable for radiotherapy dose prediction. Ultimately, this will benefit both clinicians and patients by improving treatment planning and outcomes.

The analysis was performed using Python version 3.8, with key libraries including scikit-learn (version 0.24.1) and pandas (version 1.2.3). The computer code used for this study is available upon request.

By leveraging advanced machine learning techniques, this study paves the way for more efficient and accurate treatment planning in radiotherapy. This has the potential to reduce the workload on medical physicists and improve patient outcomes. Further research and model refinement could enhance predictive accuracy, particularly for challenging regions such as the bladder, rectum, and femur.

CONCLUSION

This study demonstrates that SVR can effectively predict radiation doses for cervical cancer treatment, with larger datasets significantly enhancing predictive accuracy. The MAE values indicate acceptable performance, with training errors typically higher due to broader data exposure and testing errors lower, reflecting good generalization. Inconsistencies observed in smaller, same-stage datasets highlight the importance of dataset size for model reliability. Hyperparameter optimization for each organ using GridSearchCV further improves accuracy. The model's performance underscores the necessity of including a broad range of cancer stages and patient demographics to enhance generalizability.

Future work should focus on expanding data collection to incorporate diverse clinical scenarios and refine feature selection to enhance model precision. Specifically, identifying and leveraging the most relevant radiomic features can help minimize overfitting and boost predictive performance. Employing advanced techniques like Recursive Feature Elimination (RFE) and Principal Component Analysis (PCA) will be crucial in this process.

Moreover, improving data preprocessing strategies, such as normalization, outlier detection, and data augmentation, will further strengthen model robustness. Incorporating clinical variables such as patient age, tumor histology, and previous treatments can also significantly enhance the model's applicability in clinical settings.

Overall, this research paves the way for more personalized and accurate radiotherapy planning, promising better patient outcomes through improved treatment precision.

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AUTHOR CONTRIBUTION

R. F. Mushaddaq: Idea, writing, editing, corresponding author; D. S. K. Sihono: Idea expanding, supervision, verification; P. Prajitno: Idea expanding, co-advisor and verification.

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