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Personalized RadioSensitivity Assessment Based on Telomere Dynamics

Using Machine Learning

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Abstract : Being able to foresee how a patient with cancer will react to radiotherapy and their likelihood of experiencing negative long-term health effects can improve customized treatment strategies. Telomeres serve as a crucial indicator of an individual's sensitivity to radiation, correlating with the late effects caused by it. The length of telomeres was tracked in men with prostate cancer who were undergoing intensity-modulated radiation therapy (IMRT) using Telo-FISH. Changes in chromosomes were evaluated through dGH to anticipate the risk of developing additional malignancies. By incorporating individual telomere data into an XGBoost model, we could forecast the outcomes after radiotherapy, aiding in the evaluation of sensitivity to radiation and the risk of late effects.

Index Terms **- Telomeres, TeloFish,genomic instability, chromosomal rearrangements, prostate carcinoma, intensity-modulated radiation therapy, Machine Learning, individual radiation sensitivity,Linear Regression, XG Boost.**

I. INTRODUCTION:

The potential to forecast a cancer patient's reaction to radiotherapy and the risk of developing detrimental late health effects holds promise for refining personalized treatment strategies and optimizing individual outcomes. Telomeres serve as a compelling biomarker of individual radiosensitivity and susceptibility, as their dysfunction can mirror various radiation-induced late effects, spanning from degenerative conditions like fibrosis and cardiovascular disease to proliferative pathologies like cancer. In this study, we longitudinally evaluated telomere length in a cohort of fifteen prostate cancer patients undergoing Intensity Modulated Radiation Therapy (IMRT) using Telomere Fluorescence in situ Hybridization (Telo-FISH). Additionally, we employed directional Genomic Hybridization (dGH) to assess chromosome aberrations for high-resolution inversion detection, aiming to enhance predictions of individual patient risk for secondary malignancies. Notably, we introduced a novel approach by incorporating individual telomere length data into a machine learning model, XGBoost, trained on baseline and in vitro exposed telomere length measurements, to predict post-radiotherapy telomeric outcomes. This integrated analysis of telomere dynamics and chromosomal instability provides valuable insights into individual radiosensitivity and the risk of radiation-induced late effects.

II. RESEARCH OBJECTIVE

The main aim of this study is to explore the potential of telomere length dynamics and chromosomal instability as predictive factors for individual sensitivity to radiation and the likelihood of developing late effects from radiation exposure in cancer patients undergoing a specific type of radiation therapy known as Intensity Modulated Radiation Therapy (IMRT). Through the use of advanced molecular techniques such as Telomere Fluorescence in situ Hybridization (Telo-FISH) and directional Genomic Hybridization (dGH), the research intends to investigate how changes in telomere length and chromosomal aberrations can serve as indicators of an individual's reaction to radiation treatment.

Moreover, the study aims to employ machine learning algorithms, specifically XGBoost, to incorporate individual telomere length data and make accurate predictions regarding the outcomes of telomeres post-IMRT. By training the model on baseline telomere measurements and telomere lengths after exposure to radiation in a laboratory setting, the goal is to establish a method for personalized risk assessment and treatment planning based on an individual's genetic response to radiation therapy. This approach not only enhances our comprehension of individual sensitivity to radiation but also lays the groundwork for improving the prediction of late effects from radiation and the potential development of secondary cancers in cancer patients undergoing radiotherapy.

III. LITERATURE REVIEW

In 2023, Jency, Hu Yunfei and Nguyen Huong [1] proposed a Clinical assessment of a novel machine-learning automated

contouring tool for radiotherapy planning favored AI-Radover manual contouring. Rad was concluded to be a promising automated contour-ing solution that generated clinically acceptable contours and achieved time savings.

In 2023, Jiaming Zhang, Huijun Zhu, Jue Wang, Yulu Chen [2] identified about machine learning in NSCLC(in non-small cell lung cancer radiotherapy) radiotherapy was mainly related to the radiotherapy planning of NSCLC and the prediction of treatment effects and adverse events in NSCLC patients.

In 2022, Zhandong Li, Wei Guo, ShiJian Ding, Kai-Yan Feng [3] studied 2052 childhood cancer survivors, a machine learning approach identified key DNA methylation alterations associated with region-specific radiotherapy. The computational workflow, involving methods .

In 2022, Li Yang, Zhiyuan Xu, Hao Yu, Linlang Guo[4] developed and validated a comprehensive model integrating clinical and dosimetric parameters by machine learning method,which performed well in predicting G4 lymphopenia during pelvic RT for cervical cancer and will facilitate physicians to identify patients at high risk of G4 lymphopenia who might benefit from modified treatment approaches like Boruta and incremental feature selection, revealed crucial methylation signatures and rules.

In 2021,Jared J. Luxton, Miles J. McKenna, Aidan M. Lewis, Lynn E. Taylor,S.G. Jhavar [5] Implemented a individual telomere length data in a machine learning model, XGBoost, trained on pre- radiotherapy (baseline) and in vitro exposed (4 Gy γ-rays) telomere length measurements,to predict post radiotherapy telomeric outcomes.It accurately calculated outcomes.

In 2021, Bartłomiej Sadowski, Karolina Milewska, J. Ginter[6] explored the application of quantum physics and deep machine learning in ART to efficiently calculate treatment parameters, adapt to geometrical changes with uncertainty mitigation, and understand the relationship between patient characteristics and outcomes.

In 2020, Mengmeng Yan, Weidong Wang[7] developed a support vector machine classifier with 2 radiomic features (flatness and coefficient of variation) achieved an area under the receiver operating characteristic curve (AUC) of 0.91 on the test set. The 2 radiomic features, flatness, and coefficient of variation, from the volume of interest of lung tumor, can be the biomarkers for predicting tumor.

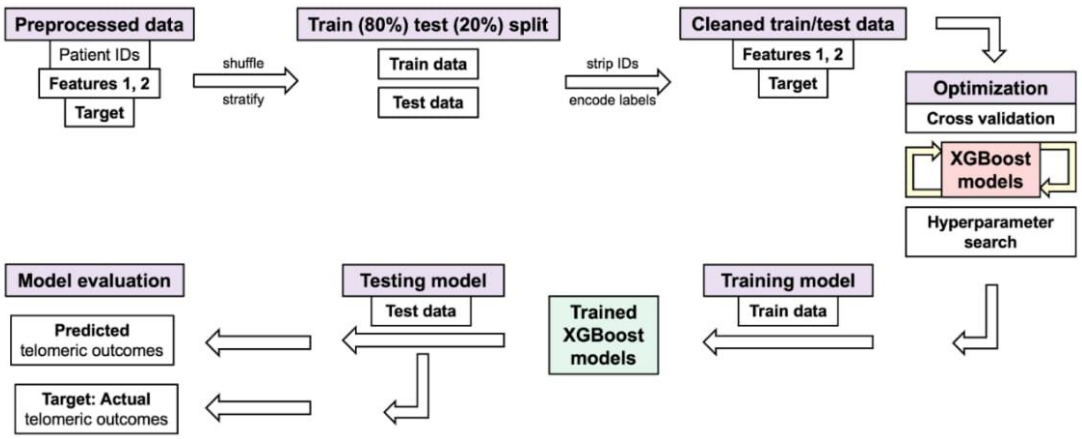
In 2020, Maria K. Y. Chan, A. Witztum, Gilmer[8] Valdes made a significant improvements seen in more recent models as machine learning techniques in radiotherapy QA matured. This grew from simple Poisson regressions to deep learning classification models, and then to complex hybrid models which improved accuracy.

In 2019, Paul Giraud, Philippe Giraud, Anne Gasnier, Radouane El Ayachy, Sarah E[9] investigated how advanced imaging analysis methods, such as radiomics, coupled with machine learning algorithms, can be utilized to extract quantitative features from medical images (such as CT scans or MRI images) of head and neck cancer patients. These features can then be used to develop predictive models to assess treatment response, predict outcomes, and personalize treatment strategies for patients undergoing radiotherapy.

In 2018, Huan-Hsin Tseng, Yi Luo, Randall K. Ten Haken, Issam El Naqa[10] analyzed the characteristics and types of features in clinical data as effective choice of data for feeding knowledge into KBR-ART. Second, in Section 3, we visited a few promising and powerful techniques of modern machine learning development, such as DNNs, CNNs, RNNs as well as the classical linear regression-type models

In 2016, Alexandra M Poos, André Maicher, Anna K. Dieckmann, MarcusOswald, Roland Eils[11] Integrated Mixed Integer Linear Programming models into a comparative machine learning based approach to identify regulatory interactions that best explain thediscrepancy of telomerase transcript levels in yeastmutants with deleted regulatorsshowing aberrant telomere length.

IV. PROPOSED SYSTEM:



a. proposed System

1. Preprocess data: Prepare the raw data by cleaning, transforming, and organizing it to make it suitable for analysis.

2. Divide train, test: Split the preprocessed data into two sets, one for training the model and the other for testing its performance.

3. Clean the train test data: Handle missing values, outliers, and other inconsistencies in the training and testing datasets to ensure data quality.

4. Optimization: Fine-tune model parameters and hyper parameters to improve its performance and efficiency.

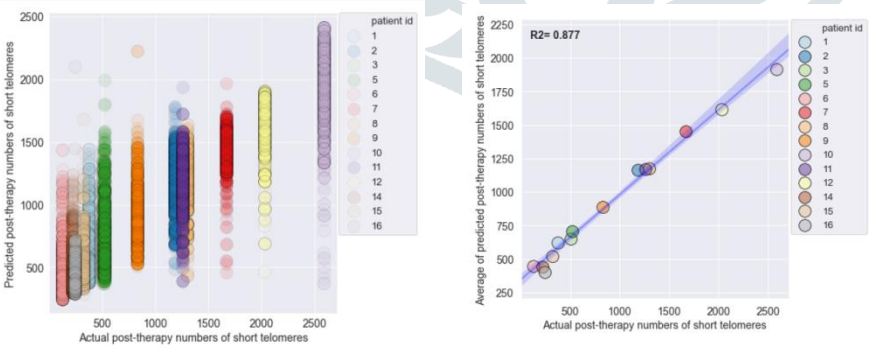
5. XGBoost model: Implement the XGBoost algorithm, a powerful gradient boosting technique, for building predictive models.

6. Train the model: Use the training dataset to teach the XGBoost model to recognize patterns and make predictions.

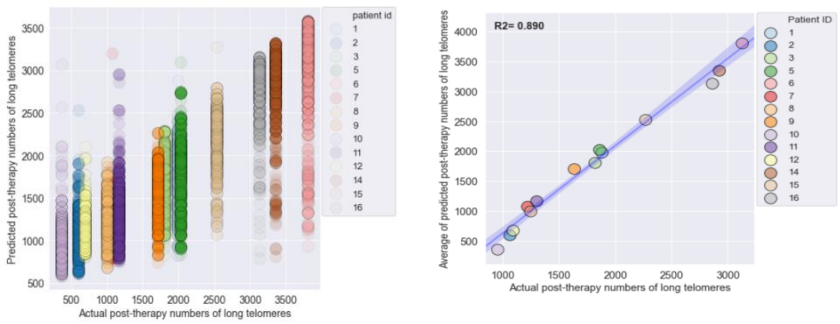
7. Test the Model: Assess the model's performance on the separate testing dataset to evaluate its accuracy and generalization ability.

8. Model Evaluation: Analyze the model's performance metrics, such as accuracy, precision, recall, and F1 score, to determine its effectiveness in predicting personalized radiosensitivity based on telomere dynamics.

. V. RESULTS AND CONCLUSIONS

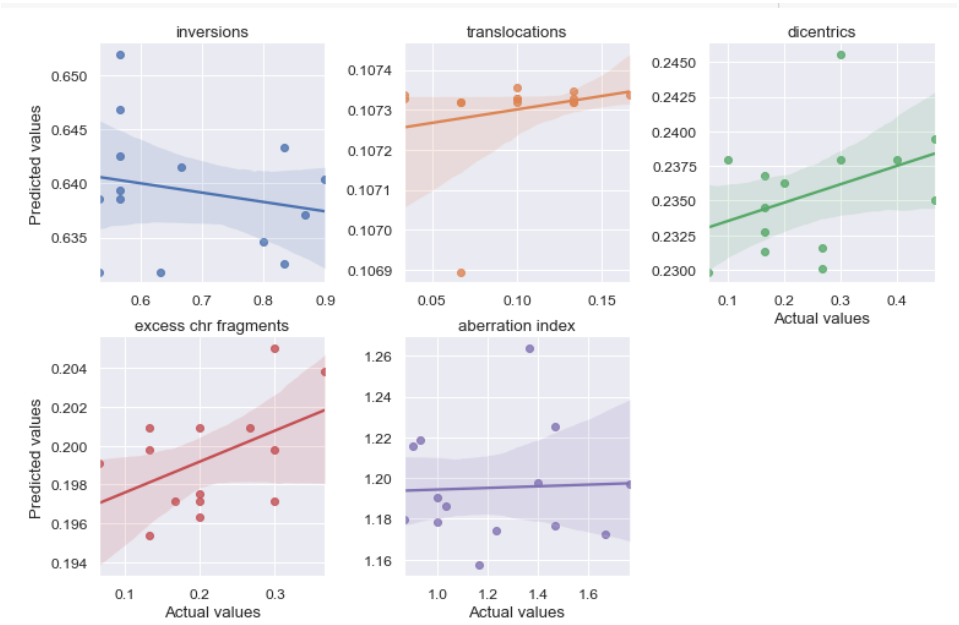


b. R2 score when predicting # of long telomeres post-therapy (4 C)

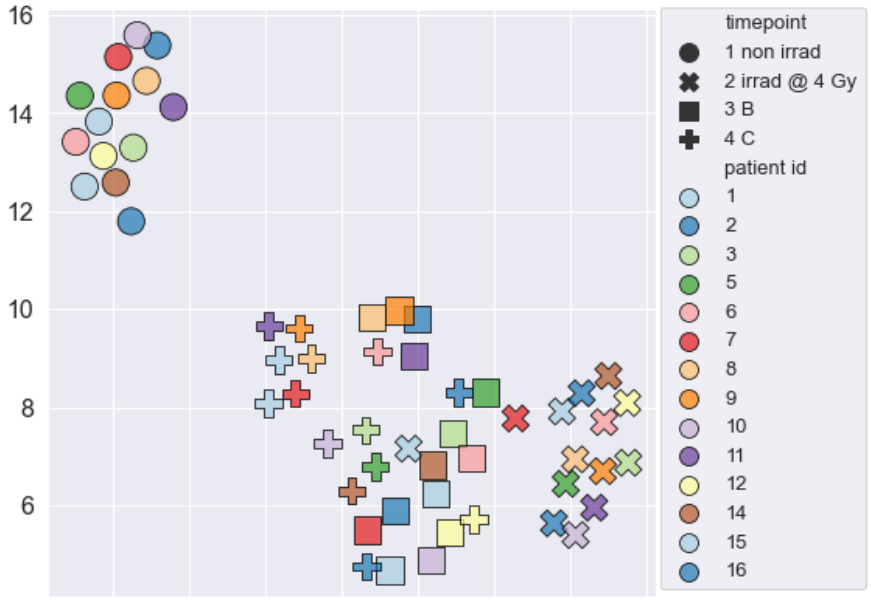


c.R2 score when predicting # of long telomeres post-therapy (4 C)

Linear regression nor XGBoost models successfully predicted post-IMRT chromosome aberration (CA) frequencies. Ordinary least squares linear regression models were made using pre-IMRT average CA frequencies from the non-irradiated (0 Gy) or in vitro irradiated (4 Gy) samples to predict 3-month post-IMRT average CA frequencies. Models were made for (A) inversions, (B) translocations, (C) dicentrics, (D) excess chromosome fragments (deletions), and (E) aberration index, which was created by summing all CA per cell. The model for dicentrics performed best, with an R 2 = 0.514.



d.pre-IMRT average CA frequencies :(A) inversions, (B) translocations, (C) dicentrics, (D) excess chromosome fragments(deletions), and (E) *(E)* aberration index



e. clustering the Telomere Data

In conclusion, the telomere-based radiosensitivity assessment using machine learning represents a promising approach in predicting individual responses to radiotherapy. By leveraging telomere data and advanced machine learning techniques, this method offers a personalized approach to cancer treatment, potentially improving outcomes and minimizing adverse effects. As research in this field continues to evolve, integrating telomere-based radiosensitivity assessment into clinical practice could revolutionize cancer treatment strategies, leading to more effective and tailored therapies for patients

VI. REFERENCES

[1] Hu Yunfei Nguyen Huong, Smith Claire- Clinical assessment of a novel machine-learning automated contouring tool for radiotherapy planning [Journal of Applied Clinical Medical Physics] 3 February 2023.

[2] Jiaming Zhang, Huijun Zhu, Jue Wang, Yulu Chen Machine learning in non-small cell lung cancer radiotherapy: A bibliometric analysis [Frontiers in Oncology] 17 March 2023.

[3] Zhandong Li, Wei Guo, ShiJian Ding, Kai-Yan Feng- Detecting Blood Methylation Signatures in Response to Childhood Cancer Radiotherapy via Machine Learning Methods [Biology] 2022.

[4] Li Yang, Zhiyuan Xu, Hao Yu, Linlang Guo- A machine learning model for grade 4 lymphopenia prediction during pelvic radiotherapy in patients with cervical cancer.

[5] Jared J. Luxton, Miles J. McKenna, Aidan M. Lewis, Lynn E. Taylor,S.G. Jhavar- Telomere Length Dynamics and Chromosomal Instability for Predicting Individual Radiosensitivity and Risk via Machine Learning [Journal Of Personalized Medicine] 8th March 2021.

[6] Bartłomiej Sadowski, Karolina Milewska, J. Ginter- Quantum Inspired Machine Learning Algorithms for Adaptive Radiotherapy [Applied Physics] 2021.

[7] Mengmeng Yan, Weidong Wang - Radiomic Analysis of CT Predicts Tumor Response in Human Lung Cancer with Radiotherapy [Journal of Digital Imaging] 2022.

[8] Maria K. Y. Chan, A. Witztum, Gilmer Valdes- Integration of AI and Machine Learning in Radiotherapy QA [Frontiers In Artificial Intelligence] 29 September 2020.

[9] Paul Giraud, Philippe Giraud, Anne Gasnier, Radouane El Ayachy, Sarah E- Radiomics and Machine Learning for Radiotherapy in Head and Neck Cancers [Frontiers in Oncology] 27 March 2019.

[10] Huan-Hsin Tseng, Yi Luo, Randall K. Ten Haken, Issam El Naqa- The Role of Machine Learning in Knowledge-Based Response-Adapted Radiotherapy [Frontiers in Oncology] 27 July 2018

[11] Alexandra M Poos, André Maicher, Anna K. Dieckmann, Marcus Oswald, Roland Eils, Martin Kupiec, Brian Luke, Rainer König- Mixed Integer Linear Programming based machine learning approach identifies regulators of telomerase in yeast[Nucleic Acids Research] 22nd Feb 2016