Knowledge based adoptive radiotherapy for head and neck cancer

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Significance:

According to WHO, Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020, or nearly one in six deaths. Among all the treatment modulities radiotherapy is used in approximately 67% of cancer treatment plans in Western countries, underscoring its critical role as a primary curative option for managing uncomplicated non-metastatic tumors [1]. By enabling quantitative analysis of treatment mechanisms, optimization of dosing regimens, and simulation of individualized therapeutic responses, computational models offer a promising avenue to refine and personalize treatment strategies beyond what murine model could provide [2]. Advances in experimental techniques and high-throughput omics technologies have generated large-scale biomolecular datasets, creating new opportunities for data-driven approaches in oncology. Machine learning (ML) has emerged as a powerful tool for transforming patient care by enabling risk assessment, diagnosis, prognosis, and prediction of therapy response [3, 4, 5]. These models are increasingly used to decipher complex tumor-related aberrations—including initiation, progression, and metastasis—by extracting meaningful insights from diverse and high-dimensional data [6].
In radiotherapy, ML-based clinical decision support systems have been employed to match new patients with historical treatment plans and adapt them based on response [7, 8, 9, 10, 11]. Platforms such as RadioGx integrate transcriptomic and genomic data to fit dose-response relationships using linear-quadratic models. These systems also simulate hypoxia-induced radioresistance and explore synergistic effects between radiation and pharmacological agents [8].

Innovation

Our innovation is to develop a machine learning framework that learns to personalize and adapt radiotherapy dose fractionation in real time, using patient-specific clinical, imaging, and biological data. Unlike traditional fixed protocols, our model aims to predict the optimal adaptive dosing schedule that maximizes tumor control while minimizing normal tissue toxicity.

Tumor Control Probability (TCP): TCP models estimate the probability of eradicating all clonogenic tumor cells with a given radiation dose, typically using formulations based on the linear-quadratic model of cell survival. For n fractions of dose:

$$\mathrm{SF} = e^{-n(\alpha d + \beta d^2)}$$

Where d is dose per fraction, n is number of fractions If T_{pot} is the potential doubling time of tumor cells with initial population N, typical Poisson-based TCP model is given by:

$$\mathrm{TCP} = e^{-N \cdot e^{-n(\alpha d + \beta d^2) - t \ln 2 / T_{\mathrm{pot}}}}$$

Normal Tissue Complication Probability (NTCP) The patients receiving radiation develop inflammation called pneumonitis (RP2) — a harmful lung inflammation. So, along the tumor control strategy the clinicians aim to reduce the normal tissue toxicity. NTCP models predict the probability

of radiation-induced complications in healthy tissues, often using dose-response curves such as the Lyman–Kutcher–Burman (LKB) model to quantify risk as a function of dose distribution.

$$NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{x} e^{-u^2/2}\, du$$

where

$$x = \frac{D - D_{50}}{m\, D_{50}}$$

with D_{50} as the dose yielding 50% complication probability and m shaping the slope of the dose-response curve.
Specific aim 1. Maximizing TCP.
Specific aim 2. Minimizing NTCP.
The overall aim is Knowledge-Based Response-Adapted Radiotherapy (KBR-ART) to optimize personalized RT treatment. $P = TCP \cdot (1 - NTCP)$

Study aim

To develop and evaluate a machine learning framework for real-time adaptive radiotherapy in [Head and Neck Cancer], predicting optimal dose adaptations at each fraction based on early treatment response. The model will use patient imaging and clinical data to recommend dose adjustments after the first fraction, assess applicability across patients, and compare predicted outcomes with actual post-therapy results across subsequent fractions.
We will consider one patient at a time for analyzing KBR-ART, then move on to next and so on.

Data sets

300 head-and-neck cancer patients from 4 Canadian centers (radiation or chemo-radiation). Includes clinical data, FDG-PET/CT imaging, and RT contours. 300 total; excluded those with recurrent/metastatic disease or on palliative treatment. Of these, 48 (16%) received radiation alone and 252 (84%) received curative chemo-radiation. Our study focuses on the 48 who received radiation only. Data are anonymized and available on TCIA: http://www.cancerimagingarchive.net.

Model Steps

1. Data to be used for KBR-ART:

   - Clinical
   - Radiomics
   - Dosimetry
   - Biological

   Then based on this data we will make the N samples of the patients receiving RT treatment only. The data matrices are the baseline, after 1st RT, after 2nd RT data of the above features.

$$\left\{ \begin{bmatrix} x_{11}^{(0)} & x_{12}^{(0)} & \dots & x_{1n}^{(0)} \\ x_{21}^{(0)} & x_{22}^{(0)} & \dots & x_{2n}^{(0)} \\ \vdots & \vdots & \ddots & \vdots \\ x_{N1}^{(0)} & x_{N2}^{(0)} & \dots & x_{Nn}^{(0)} \end{bmatrix} \middle| \begin{bmatrix} x_{11}^{(1)} & x_{12}^{(1)} & \dots & x_{1n}^{(1)} \\ x_{21}^{(1)} & x_{22}^{(1)} & \dots & x_{2n}^{(1)} \\ \vdots & \vdots & \ddots & \vdots \\ x_{N1}^{(1)} & x_{N2}^{(1)} & \dots & x_{Nn}^{(1)} \end{bmatrix} \middle| \begin{bmatrix} x_{11}^{(2)} & x_{12}^{(2)} & \dots & x_{1n}^{(2)} \\ x_{21}^{(2)} & x_{22}^{(2)} & \dots & x_{2n}^{(2)} \\ \vdots & \vdots & \ddots & \vdots \\ x_{N1}^{(2)} & x_{N2}^{(2)} & \dots & x_{Nn}^{(2)} \end{bmatrix} \right\}$$

2. In this step of estimation of RT outcomes we will use RadioGX to predict the radio-sensitivity based on the molecular features. It can identify genes or pathways correlation with radio-sensitivity of tumor tissue and normal tissue, based on which we can train a ML model to predict patient specific radio-sensitivity. Then to find NTCP we will find the correlation of RP2 with the genes expression using principal component and regression models. Based on these two we will maximize P to plan the next dose.

Collaborations

This project is a collaboration of Somiya Rauf (Graduate Student, Math and State department), Abdul-Malik Mohammed (Undergrad Student, CS department) and Joshua Pina (Undergrad Student, CS department)

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