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JOINT AAPM | COMP MEETING

Deep Learning in a 3D Brain Cancer Digital Twin for Advancing Radioimmunotherapy Against Brain Cancers

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ABSTRACT

Purpose: Glioblastoma is the most prevalent and aggressive brain tumor in adults. The median survival of patients is 15 months, despite the current standard of care comprising surgery, radiotherapy, and chemotherapy. Hence, new therapeutic approaches are urgently needed. One new approach is the combination of radiotherapy with immunotherapy. Here, we move from 2D to 3D radioimmunotherapy (RIT) to better mimic the in vivo tumor environment. Furthermore, we develop a MATLAB-based digital twin model that, when given therapeutic signatures, will accurately predict cell survival after specific treatment.

Methods: A convolutional neural network (CNN) is designed in Deep Network Designer to define the structure and features of a cell spheroid. The CNN is trained using input therapeutic signatures extracted using our in-house developed Unsupervised Machine Learning (UML) algorithms. The model predicts the therapeutic outcomes after radioimmunotherapy treatment based on the feature data obtained by the CNN and optimizes treatment from therapeutic signatures.

Results: Our UML results involving RIT and 3D spheroid show dramatic demonstration of machine learning capability. At 24 hours post-treatment, brightfield morphology achieved near-perfect treatment separation: 95% of RIT spheroids clustered together, distinct from 100% of lenalidomide-only spheroids. These results provide therapeutic signatures for our CNN under development. New results of the model will be presented and hopefully demonstrate the ability to promptly predict therapeutic outcomes.

Conclusion: A deep learning-driven 3D twin model of glioblastoma cell spheroids is being developed for in vitro prognosis that will guide clinical trials in the short term and personalized therapy using patient samples in the long term.

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INTRODUCTION

Glioblastoma (GBM) is highly aggressive and the most prevalent brain tumor in adults. The median survival of patients is 15 months, despite the current standard of care comprising surgery, radiotherapy, and chemotherapy.

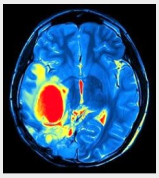


Figure 1 MRI shows a tumor located in the posterior left temporal lobe

Figure 2 Radiation therapy using mask-based gamma knife

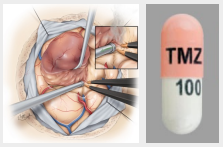
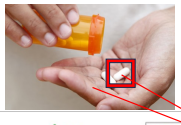


Figure 3 Current standard of care includes surgical resection of the tumor (left) and chemotherapy (right)

EXPERIMENTAL METHODS



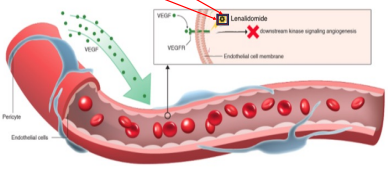


Figure 4 Lenalidomide Immunotherapeutic drug as an Angiogenesis Inhibitor. By blocking the VEGF signaling cascade, Lenalidomide inhibits the development of new blood vessels crucial for tumor growth and metastasis.

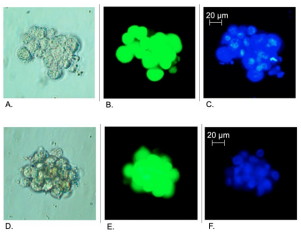


Figure 5 T98G 3D cell spheroids: A) phase contrast, B) Calcein-stained and C) Hoechst-stained images of the same 3D spheroid comprising of around 20 cells. The bottom panel is a different T98G 3D spheroid of around 18 cells with the same image characteristics: D) phase contrast, E) Calcein-stained and F) Hoechst-stained

COMPUTATIONAL METHODS

Unsupervised machine learning (UML) clusters morphological changes from imaging data to extract therapeutic signatures. UML methods allow for cell population identification

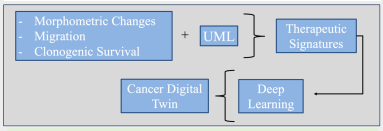


Figure 6 Computational flow chart from experimental data to input into the 3D Brain Cancer Digital Twin

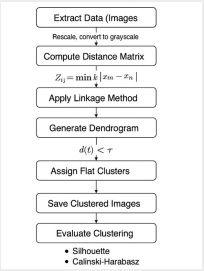


Figure 7 Flow chart detailing In-house developed UML workflow implemented in MATLAB

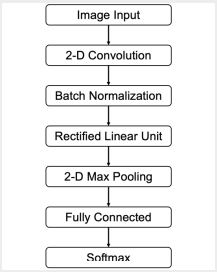


Figure 8 Flow chart detailing the general convolutional neural network layers in the in-progress architecture

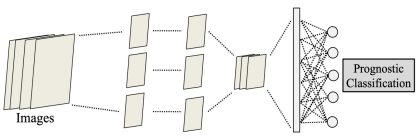


Figure 9 Convolutional Neural Network

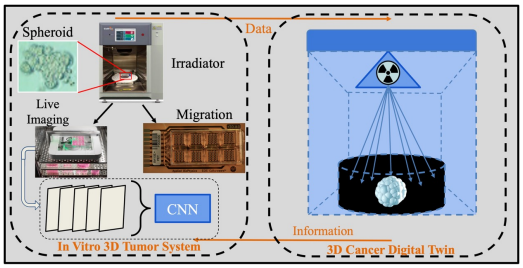


Figure 10 Data and information streamline from the *In Vitro* tumor system to the 3D Cancer Digital Twin

A convolutional neural network (CNN) will be trained using therapeutic signatures to define the structure and features of a spheroid. The CNN will transmit feature data to a 3D cancer digital twin (DT) modeled in MATLAB. The model predicts the therapeutic outcomes after radioimmunotherapy treatment based on the feature data obtained by the CNN and optimizes treatment from therapeutic signatures.

RESULTS

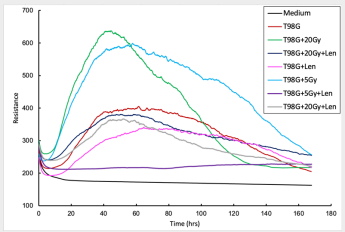


Figure 11 ECIS Migration of T98G cells after RIT treatment

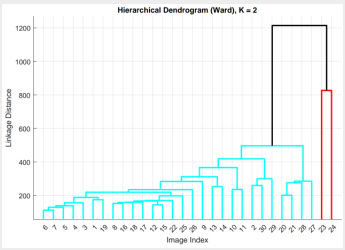


Figure 12 UML Dendrogram of clusters of T98G spheroids treated with 20 Gy and Lenalidomide

FUTURE DIRECTION

- Train the CNN to define features of spheroids based on clustering phenotypes defined in the UML, and transmit the data to the DT
- Design the DT model to predict outcomes of treatments based on known experimental data and compare for accuracy
- Optimize the model with supplemental therapeutic signature data

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NASA Nebraska Space Grant

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