Feasibility of Simplifying Imaging-Based Personalized Dosimetry with Machine Learning

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Objectives: This work investigates the feasibility of utilizing machine learning (ML) to predict the optimal level of I-131 injected activity which could allow reducing the number of time points required for dosimetry calculation for the SIERRA phase III clinical trial.

Background: Personalized dosimetry in targeted radiopharmaceutical therapy provides a methodology to estimate the dose for each patient. Dosimetry can guide the amount of administered activity to patients maximizing the radiation dose to the tumor without causing toxicity in healthy organs. Currently, the methodology of the Committee on Medical Internal Radiation Dose (MIRD) to estimate the radiation dose involves imaging at multiple timepoints over a period of several days, which is not always feasible or practical.

The SIERRA trial uses an iodine-131 labelled antibody (Aramidamab, Iomab-B) to deliver high doses of radiation to leukemia cells of older patients (55 years and older) with relapsed or refractory acute myeloid leukemia. This is done as a conditioning regimen for bone marrow transplant.

Machine learning has become a powerful tool for predictive modelling within healthcare and nuclear medicine imaging. The availability of demographic, anatomic structural, and lab test information within the context of SIERRA opens the possibility to improve dosimetric prediction using machine learning.

Methods: 74 patients who received the Iomab-B treatment were retrospectively analyzed in this work. The therapeutic infused activity was personalized based on an initial dosimetric dose with a low activity (7-20 mCi) Iomab-B infusion followed by 3 gamma camera imaging acquisitions performed immediately after infusion is complete, at 24 h, and at 72-96 h post infusion. The biodistribution information at the different imaging timepoints was used to calculate the dose to the liver following the MIRD formalism.

212 features (organ uptake and volume from planar and CT images respectively, demographic information, blood, and marrow tests) were evaluated. Features with greater than 20% of entries missing were discarded. Other remaining missing values were replaced with the median. Interquartile range of features was scaled using the RobustScaler preprocessing method using Python’s scikit-learn library. A novel feature selection pipeline was designed and implemented using Python’s mlxtend library (SequentialFeatureSelector method). The LASSO linear regression method (α=0.3) was used to train and test the model (70/30 train/test split). The model was used in combination with a single timepoint image (first image) to predict the injected activity required to achieve a 24 Gy maximum dose to the liver.

Results: Liver mass, initial liver uptake, serum aspartate aminotransferase value (pre and post dosimetric infusion), body surface area (BSA), serum lactase dehydrogenase, lymphocyte count, and neutrophil count were robust features observed to account for variations in prescribed activity. The machine learning model had r²=0.71 and RMSE=179.8 mCi (mean prescribed activity=716.4 mCi). Error of less than 30% was reported in 63.6% of patients, which represents the fraction of patients within the uncertainty threshold of optimized gamma-camera imaging. SIERRA-specific constraints (maximum manufactured activity is 1030
mCi) led to further reduced model error within the clinical setting (RMSE=167.4 mCi). Our ML model outperformed conventional single-variable methods, such as those based on body or liver mass (RMSE=337.2 mCi or 278.3 mCi, respectively). Furthermore, the current method appears to significantly improve upon the predictive capability of liver dosimetry using the single initial time point (RMSE=331.8 mCi).

**Conclusion:** Our results suggest that with carefully selected features, it is feasible to train a ML model that reduces the number of images to predict a personalized I-131 injection for the SIERRA trial.