Deep learning based representations for cardiac voxelised dosimetric data from childhood cancer therapy

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Abstract

Cardiac disease (CD) is among the most common side effects of childhood cancer therapy, and its early prediction can be lifesaving. A current research challenge consists in exploiting voxelised dosimetric data issued from dose reconstruction to assess the impact of the unavoidable irradiation of healthy tissues during radiotherapy in the occurrence of late effects. In this study, we investigate this very challenging problem by representing heart radiation doses using powerful 3D Convolutional Networks pre-trained on large scale medical data. After a dimensionality reduction, these representations were used to train different machine learning classifiers to predict the occurrence of a late treatment-induced CD for any childhood cancer survivor. Our preliminary results indicate the promising use of convolutional neural networks for dosimetric data representations to capture information related to the risk of late CD after radiation therapy.

Keywords: Transfer learning, radiation dose, late effects, childhood cancer

1. Introduction

Recent therapeutic advances now allow an average 5-year survival rate for childhood cancers over 85% (Siegel et al., 2022). However, survivors carry a significant risk of developing at least one treatment-associated life-threatening disease in adulthood (Hudson et al., 2021). Cardiac disease (CD), often fatal, is one of the most common known late effects of childhood cancer radiotherapy treatment. Early diagnosis can prove lifesaving. In this context, it is

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essential to better understand late events and their association with cancer treatments to improve therapeutic and follow-up protocols.

The French Childhood Cancers Survivors’ Study (FCCSS) provides a database of 7670 5-year survivors treated in France before the age of 21 for the most common childhood cancers (lymphomas, neuroblastoma, renal tumors, bone sarcoma and others). In this study, our goal is to provide solutions to identify early the patients who are at high risk of experiencing at least one CD, solely based on the radiation dose to the heart (Figure 1). Taking advantage of the availability, rare in this context, of whole-body voxel-scale dose reconstruction, we propose to use deep learning-based features to extract information from these 3D ‘images’ and train machine learning classifiers to predict the presence of a CD event. To the best of our knowledge, this is one of the first studies investigating the use of deep learning on this challenging problem.

2. Prediction of a late CD from cardiac dosimetric data

Methods. The numerous successful applications of deep learning methods to medical image analysis rely on their ability to learn powerful representations directly from the data, generating informative data manifolds. This study investigates their use in voxelised dosimetric data, evaluating them in the challenging task of CD event prediction. Convolutional neural networks were chosen to extract relevant information from volumetric dose distribution. We explore two different 3D-based ResNet architectures (ResNet10 and ResNet18), pre-trained on large publicly available medical datasets (Chen et al., 2019). A total of 5800 features are thus extracted from the volumetric 3D doses masked and cropped in the heart region. These features are then taken as inputs for the classification task of late event predictions (two classes: patients with reported CD or not). Given the high dimension of the problem, a pre-screening step is necessary, to eliminate the features not bearing any information. This dimension reduction is a two-step procedure: first, we eliminate the features with the lowest variance (threshold at the 1% quantile). Second, we select the 1000 features that have the highest F-values for the test comparing the respective means of the two patient classes. Using these selected features, we trained different machine learning classifiers, namely Random Forest, Support Vector Machines and Multi-layer Perceptrons.

Figure 1: Example of the dose to the heart of a patient treated for Hodgkin lymphoma, with a mean dose of 19.56 Gy. Doses vary from 3.33 Gy to 47.97 Gy.
**Data.** Our study is based on 3034 patients from FCCSS, treated with both radiotherapy and chemotherapy. Of them, 302 have experienced at least one cardiac event (CD) (the most frequent being heart failure, valvular heart disease, arrhythmia, pericardial disease and ischemic heart disease (Haddy et al., 2016)) between 2 and 40 years after their first cancer diagnosis. To train our classifiers we split our data in a stratified way into train and test sets (80%/20%). For the hyper-parameter selection, 5-fold cross validation is performed.

### 3. Results & Discussion

Our results are summarised in Table 1. The performance indicators are balanced accuracy (BA) and AUC-ROC for all the tested combinations. Overall, independently of the chosen architecture, our pipeline reports BA higher than 60% and AUC-ROC higher than 0.69 except for the multilayer perceptron model. Random forest and support vector machines seem to fit better our pipeline, and they show similar performances.

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**Table 1:** Results of the classification prediction with the extracted features over the testset. BA: balanced accuracy; AUC for area under the ROC curve.

Follow-up and treatment planning are constantly evolving, and studies like this keep providing evidence for the improvement of both. However, there is still room for improvement by exploring the interactions between the extracted dose-based features and clinical variables. Especially, the role of chemotherapy should be included, as it is a known risk factor of a subsequent CD. Finally, in the future, we are planning to implement end-to-end strategies for the training of more task-specific representations, integrating more variables to address this challenging problem, hopefully paving the way towards more personalized, less anxiogenic and safer follow-up protocols for cancer survivors.

### References


