Applications of 3D-CNN in Lung Cancer Patient Survival Prediction

School of Public Health
BROWN UNIVERSITY

David Moon[1], Ani Eloyan[1]
[1]Brown University, RI

Overview

In a dataset of lung cancer patients CT scans, we predicted the rate of death using deep learning methods that can account for spectral and spatial features of images. We follow a preprocessing framework for medical scans that eliminates the need for medical experts.

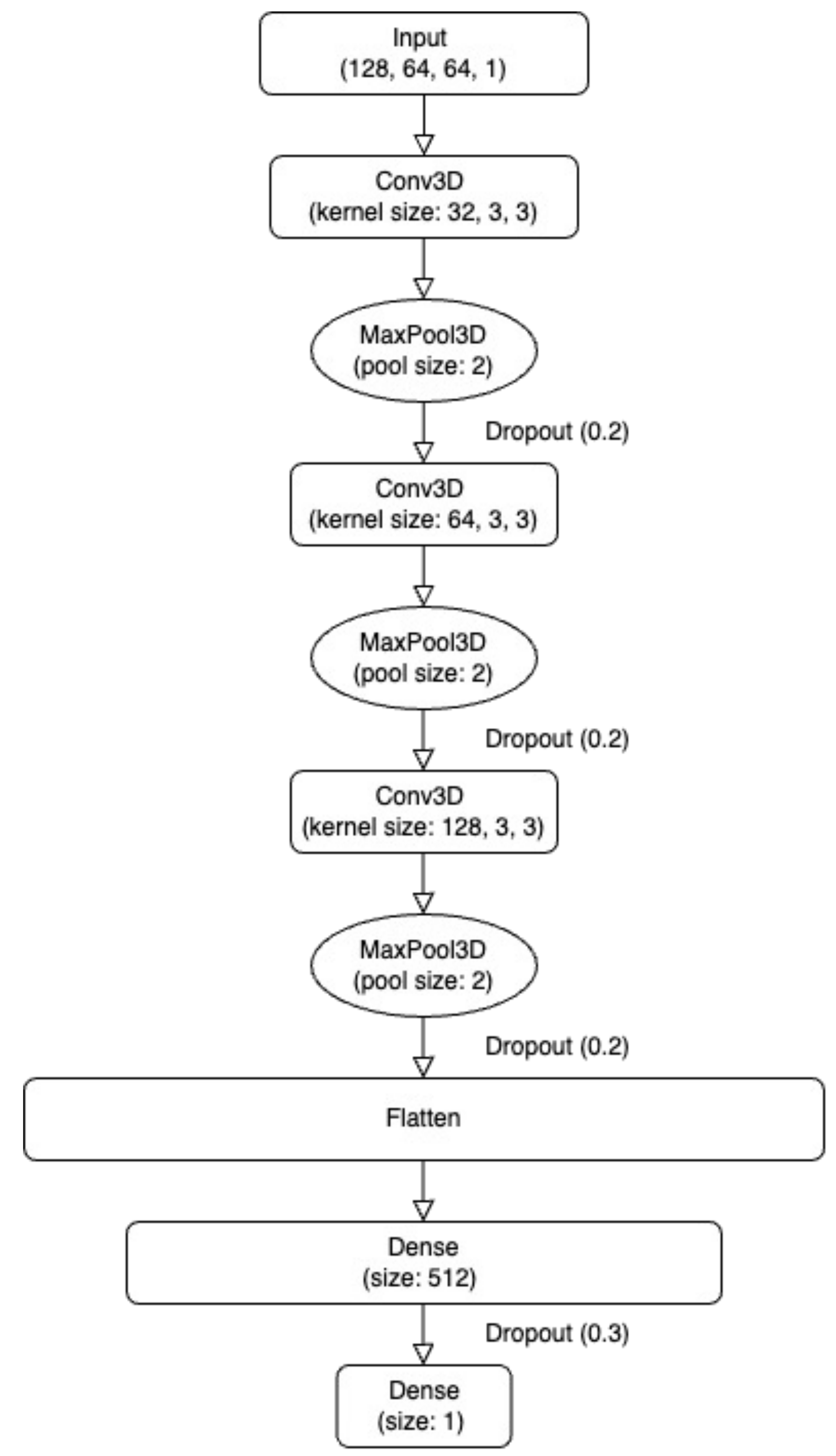
Background

- Computed Tomography (CT) is a widely used imaging procedure used to detect occurrences of lung cancer
- Lung cancer is the second most form of cancer worldwide; non-small cell lung cancer (NSCLC) accounts for 87% of all NSCLC cases
- Convolutional neural networks (CNN), a class of deep learning neural networks, have achieved performance rivaling medical professionals when applied to medical images (i.e. classification, segmentation, etc.)
- Current approaches to medical image analysis involve 2D CNNs that can extract spatial features; 3D CNNs can extract spectral and spatial features that are useful in analyzing volumetric data[1]
- The purpose of this research is to develop a 3D CNN approach to predict survival time (survival risk scores) of patients diagnosed with NSCLC

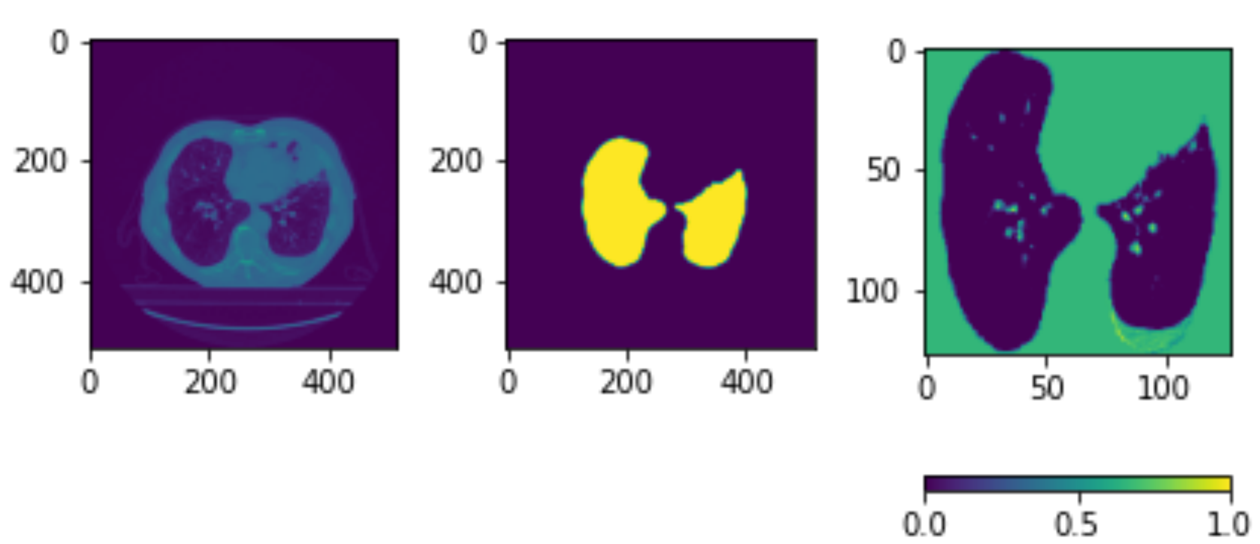
Methods

- Preprocessing
  - An existing CT lung segmentation implementation using trained U-net models[2] is applied to obtain masks of the lung area
  - Pixels are resampled to 1.0 x 1.0 x 1.0 mm^3 to ensure that each pixel represents a consistent volume[3]
  - Pixel values are standardized to Hounsfield Units (HU), windowed to enhance contrast of the lung structure, and normalized to the range (0,1)
  - Lung scans are cropped to remove noise and focus on the lung region
- Model implementation
  - Keras API is used to build a model with Conv3D, max-pooling, dropout, and dense layers
  - With a small dataset size (n=421), dropout layers following convolution layers add a regularization effect to reduce overfitting
  - Max pooling layers are implemented to avoid capturing unwanted background features and downsamples feature maps

Model Details



Model architecture. Rectified Linear Unit (ReLu) activation is applied after every layer except the last layer. The last layer applies L2 regularization (λ = 0.01). Updates are applied in mini-batch sizes of 20. The learning rate is 1e-4 with the adaptive moment estimation (Adam) optimizer.



Example of an axial slice from LUNG1-001 before (left) and after (right) preprocessing steps. The segmentation mask is shown in the middle.

Results

Model	3D-CNN	2D-CNN	COX + PCA (baseline)
Time-Dependent AUC, C^T	0.564	0.506	0.555

Time-dependent area under the ROC curve (AUC) is used as the primary evaluation metric. The time of interest is limited to the first three years of study. The evaluation of C^T is based on a 10-fold cross validation analysis. The 2D and 3D CNN models are trained for 10 epochs before evaluating on the test set. Model weights are updated by optimizing the Cox proportional hazards loss function.

The linear Cox proportional hazards model is a standard survival model that requires extensive feature engineering[5]. It is included as a baseline model with radiomic and clinical covariates. The model hyperparameters (i.e. learning rate, batch size, etc.) are manually tuned due to computational complexity – evaluation on the validation is used to determine optimal hyperparameters to prevent overfitting.

Conclusion

- **Performance of the 3D-CNN model yields a slight improvement over the baseline model**, the model can be adjusted in the following ways:
  - Pretrain weights using transfer learning, especially as more 3D-CNN pre-trained models become publicly available
  - Augment image pixel data with patient data (i.e. electronic health records) using data fusion strategies[6]
- **The size of the dataset is one of the biggest constraints**: data augmentation through random transformations of medical images should be explored
- **Computational complexity and excessive memory usage limit optimization strategies:** generic methods for hyperparameter tuning (i.e. grid search and randomized search) cannot be applied to 3D-CNN models

References

1. Singh, S. P., Wang, L., Gupta, S., Goli, H., Padmanabhan, P., & Gulyás, B. (2020). 3D Deep Learning on Medical Images: A Review. *Sensors (Basel, Switzerland)*, *20*(18), 5097.
2. Hofmanninger, J., Prayer, F., Pan, J., Röhrich, S., Prosch, H., & Langs, G. (2020, August 20). *Automatic Lung Segmentation in routine imaging is primarily a data diversity problem, not a methodology problem - European radiology experimental*. SpringerOpen.
3. Draelos, R. L., Dov, D., Mazurowski, M. A., Lo, J. Y., Henao, R., Rubin, G. D., & Carrin, L. (2020, October 9). *Machine-learning-based multiple abnormality prediction with large-scale chest computed tomography volumes*. Medical Image Analysis.
4. Park, S., & Kwak, N. (2016). Analysis on the Dropout Effect in Convolutional Neural Networks. *Asian Conference on Computer Vision*.
5. Katzman, J. L., Shaham, U., Cloninger, A., Bates, J., Jiang, T., & Kluger, Y. (2018). DeepSurv: personalized treatment recommender system using a Cox proportional hazards deep neural network. *BMC medical research methodology*, *18*(1), 1-12.
6. Huang, S. C., Pareek, A., Seyyedi, S., Banerjee, I., & Lungren, M. P. (2020). Fusion of medical imaging and electronic health records using deep learning: a systematic review and implementation guidelines. *NPJ digital medicine*, *3*(1), 136.