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Transfer Learning-Based Classification of Radiation Induced Lung Injury in Breast Cancer Patients Using PET Images

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Abstract— **Radiation-induced lung injury (RILI) is a serious concern for patients affected by breast cancer. Preventing lung injury is impossible since radiotherapy is very effective for breast cancer when applied in the mammary glands close to lungs. Starting early treatment for preventing lung injury can improve the quality of life of the patients. This paper proposes artificial intelligence-based automation for classification of lung injury in retrospective patients. 1692 Position Emission Tomography images of injured lungs are taken and clustered with K-means clustering, since the data set is unlabeled. The entire dataset groups into two clusters-radiation pneumonitis and radiation fibrosis. Silhouette score is 0.1619 when applied on PET images of the lungs. VGG 16 based transfer learning is applied on the k-means clustering algorithm to improve the classification accuracy. The silhouette score is increased to 0.806836.**

I. Introduction

This Today, breast cancer is the leading cause of death in women. 1 in 28 women is likely to develop Breast Cancer in India. In the initial screening, many women present with stage III or IV cancer which requires extensive treatment [1]. If women are screened in their early stages radiotherapy improves survival in several women. Radiotherapy reduces mortality by a few percentages in a few categories of women depending on cancer characteristics. However, it can cause second cancer in the lungs decades later. Such effects occur as healthy cells are damaged due to radiation. Radiation treatment for breast cancer affects the lungs close to the radiation spot.

Radiotherapy affects the lung and hence causes radiation-induced lung disease/toxicity especially when the cancer is in the left breast [2]. The injury to lung occurs in various phases from pneumonitis to chronic fibrosis and sometimes even lung cancer. The risk of developing radiation-induced lung fibrosis (RILF) is very high in these patients [3].
Machine learning approaches are being applied extensively to problem-solving in healthcare, and there is no exception to radiation oncology. Algorithms are being developed for external beam radiation therapy; machine learning though tries to mimic conventional human-driven solutions, there is definitely an increased efficiency and consistency. But it has to be agreed that machine learning has limited utility since algorithms are trained using expert opinion as ground truth. There is a possibility that problems or ground truths are not well-defined. Because of this, a lot of research is happening in this area.

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Radiation-induced lung injury has been gaining attention since 2016, and with the COVID pandemic, a number of researchers are working in this area. Artificial Intelligence and Machine learning applications in this domain for limiting the complications are being proposed by the researchers, but due to the limitations, they are yet to be practiced in clinics.

AI-based machine learning algorithms to automatically diagnose lung toxicity will definitely limit the complications due to the treatment given to cancer patients. The COVID infection will not further disturb the quality of life, and the mortality rate of cancer patients due to COVID can be reduced.

This paper proposes transfer learning technique for classification of lung injury in retrospective patients. The dataset taken from Kaggle is unlabeled and hence initially k-means clustering is applied on the PET images of lungs. Since the classification accuracy is not good and when retrained the results were even worse. Transfer learning is applied for K-means with already trained VGG-16 architecture. The dataset is grouped into two classes and the accuracy of classification is improved with transfer learning.

II. Literature

Exposing the lungs is unavoidable, while irradiating the breast. Recent researches claim that recurrence of breast cancer significantly reduces when radiotherapy is applied to the regional lymph nodes, including the internal mammary chain (IMC). But these nodes are placed very close to the lungs. This will increase lung radiation exposure irradiating them. Lung injury is therefore unpreventable duringradiation.

A study published with the results of 40,781 women affected by breast cancer between 2010 and 2015 isanalyzed [4]. Women in this study are diagnosed forbreast cancer or ductal carcinoma. The study clearlyshows many of the women during the follow up after 10 years had lung injury.

When it comes to automation in diagnosis of lung injury, several papers are being published by researchers working in Artificial intelligence and machine learning.

VGG16, InceptionV3 as well as ResNet-50 are assessed for lung disease classification with transfer learning [5]. Pre-trained models with simple classifiers are capable of competing with complex systems.

Gaussian Bayes (GB), k-nearest neighbor (k-NN) and Support vector machines (SVM) algorithms are used in the classification of respiratory diseases [6]. When the number of features is large but sample size is limited, SVM and k-NN perform better when there are more than two classes. Gaussian Bayes gives the best output when there are only two classes.

400 lung CT images with various lung issues and normal images are taken for classification [7]. MLP, KNN and SVM classifier are used. Gray Level Co- occurrence Matrix (GLCM) is used for the selection of most relevant features. Classifier shows 99.2% for KNN and less for other two methods.

Another algorithm proposes classification of lung abnormalities from chest X-ray images [8]. Convolutional Neural Network is proposed for automatic extraction of features. Optimization is done using min-max scaling. The experimental results show that the accuracy of the model improves by 3.1% and at the same time computational complexity is reduced by 16.91%.

TL is a technique where a pre-trained model, typically trained on a large dataset, is used as a starting point for a new task or dataset. Each can be further divided into two subcategories; hence, four TL approaches are defined and surveyed in this paper.[9] These four approaches provide different levels of flexibility and complexity in utilizing pre-trained models for transfer learning. The choice of approach depends on factors such as the availability of data, similarity between the pre-training and target tasks, and the computational resources at hand.

The specific details and implementation of Truncated TL may vary depending on the paper or study you are referring to[10]. However, the general idea is to selectively reuse and fine-tune appropriate bottom layers while discarding the remaining layers, creating a more tailored transfer learning approach.

Differential TL" in the context of transfer learning (TL) for medical image classification (MIC) and segmentation. [11] It states that early work in this field, similar to developments in computer vision (CV), often utilized deep convolutional neural networks (DCNNs) pre-trained on CV tasks as feature extractors or initializers.

TRANSFER learning (TL) is a common practice for medical image classification (MIC), especially when training data are limited. [12]– [16] These studies have shown that leveraging pretrained DCNNs can significantly improve the performance of medical image classification tasks, especially when training data are limited.

III. Methodology

A. Data Acquisition and Augmentation:

Positron Emission Tomography (PET) images of the lungs injured due to radiation are taken from NIH database. The acquired images are of Ga-68 aerosol (Galligas) images, CT images and CT-Galligas fused images. These images are obtained from the exploratory study in patients with clinical diagnosis of injury. 1692 images are taken from the dataset. The size of each image is 400x400. Data augmentation is not carried out since each patient data has more than 100 views. Figure 1 shows CT lung and PET Galligas images taken during inspiration and affected by injury. Figure 2 shows the fused image.

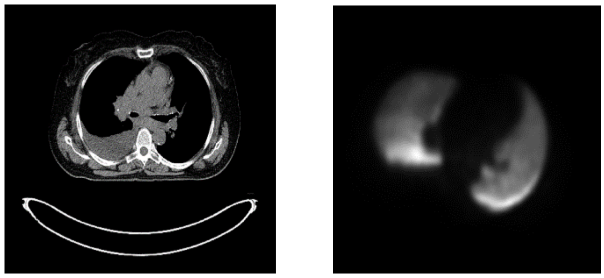

Figure 1: (a) CT-Lung (b) PET-Galligas

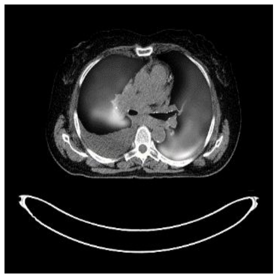

Figure 2: PET-CT-Lung (Fusion)

B. K-means Clustering:

Initially the entire data set is unlabeled and hence clustering algorithm is used for checking the possible levels in which the dataset can be grouped. K means clustering groups N observations into K predefined non-overlapping clusters. Every observation gets classified to one of the clusters.

In the given set of observations ($\mathbf{x}_1$, $\mathbf{x}_2$, ..., $\mathbf{x}_m$), in which every observation is a h-dimensional real vector, all the m observations are partitioned by the algorithm into k sets - k ($\leq m$) sets $\mathbf{S} = \{S_1, S_2, ..., S_k\}$ to minimize the variance. The goal is to measure the minimum variance as sum of squares with minimumdistance

$$\arg S_{\min} \sum_{i=1}^{k} \sum_{x \in S_i} ||x - \mu_i||^2 = \arg S_{\min} \sum_{i=1}^{k} |S_i| \operatorname{Var} S_i$$

where $\mu_i = \frac{1}{|S_i|}\sum_{x \epsilon S_i} x$, is the average of points S_i

$|S_i|$ is the size of S_i. And $\| . \|$ is the L^2 norm.

This is similar to reducing the pairwise squared deviations of points belonging to the same cluster

$$\arg S_{\min} \sum_{i=1}^{k} \frac{1}{|S_i|} \sum_{x,y \,\epsilon\, S_i} ||x-y||^2$$

The equivalence value may be derived from

$$|S_i| \sum_{x \epsilon S_i} ||x-\mu_i||^2 = \frac{1}{2} \sum_{x,y \epsilon S_i} ||x-y||^2$$

Total variance is always a constant.

Initially the Galligas images of the lungs are taken and k means is applied with 2 clusters. Each image is assigned to any of the clusters with minimum squared Euclidian distance.

$$S_i^{(t)} = \left\{ x_p : ||x_p - m_i^{(t)}||^2 \le ||x_p - m_j^{(t)}||^2 \forall\, j, 1 \le j \le k \right\},$$

where each x_p is assigned to exactly one cluster $S^{(t)}$ though there is a possibility that this could be assigned to both the clusters.

Since more images are not assigned to both the clusters the model is run again with three labels of clusters.

$$m_i^{(t+1)} = \frac{1}{|S_i^{(t)}|} \sum_{x_j \epsilon S_i^{(t)}} x_j$$

The algorithm is tried with varying number of clusters. It is seen that the silhouette score is very low for varying clusters with the optimal value obtained for 10 clusters. The optimal score obtained is 0.20740. This is also very low which shows that the k-means is not effective in clustering the data set.

Transfer Learning: Transfer Learning tries to utilize the knowledge gained in solving a problem to solve another related newer problem in less time with the help of the knowledge obtained while training the first model.

Algorithm

1. Preprocess the image as required by the transfer learning model

2. Convert every image into respective vector using the weights from the transfer learning model.

3. In every list, store all the image weights after flattening.

4. Form clusters after feeding the built list to k-means.

VGG 16 pretrained with ImageNet is used for classification with k-means. 65 feature vectors are derived from the pretrained model and from that clustering of the unlabeled dataset is done. Worked with different number of clusters but the silhouette score is high for two clusters.

IV. RESULTS AND DISCUSSION

The data set taken for analysis is unlabeled. The database actually has images of 20 subjects and dataset of each subject has 85 images approximately.

K means clustering gives very poor results with very less optimal silhouette score. Optimal value is obtained when number of clusters formed is 10. For clusters varying from 1 to 9 the silhouette score is very less ranging from 0.01 to 0.16.

When transfer learning is applied with VGG 16 pretrained model, the silhouette score improved with optimal value for two clusters. The silhouette score increased to 0.806836 from 0.16740. Figure 3 shows the silhouette score obtained for k-means clustering.

The results obtained have lot of variations as the dataset is unlabeled. VGG 16 is pretrained with ImageNet dataset. A pretrained model with medical image data set is not available. However, studies are already done for image classification in medical diagnosis by imparting the knowledge of CNN architectures pretrained with ImageNet data set with better accuracy. This model for classification of unlabeled data set started with this concept. However, the end results did not show any reliable classification both with k-means as well as transfer learning applied k-means.

To understand the possibility of applying k means and to understand where the model failed the data set is taken to the radiologist for labeling. The radiologist identified the data set had images of subjects with normal lung as well as affected lungs. The diseases in the affected lungs are classified as pneumonitis, pleural effusion, bronchitis and Carcinoma. This means there should be 6 clusters. But transfer learning provided optimal value with 2 clusters. This means the clustering is done based on 2 classes – (i) Normal and (ii) Affected. One cluster had 1352 images and the other cluster had 340 images. Based on the classification made by the radiologist, the clustering model developed with VGG16 gives optimal value for 2 clusters which matches the normal and affected classes.

Transfer Learning performs better in the clustering of unlabeled data set. However, the accuracy of the clustering algorithm is still questionable and can be better supported after proper labeling and classification of the same data set.

The authors are labeling the entire data set with the support of the radiologist in the team. After labeling, classification of the dataset will give better information on the accuracy of clustering algorithm. The labeled dataset sample images are shown in figure 3.

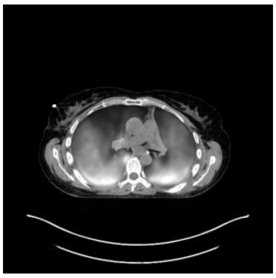

Figure 3(a)-Normal

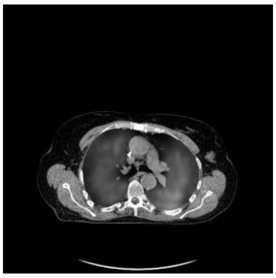

Figure 3(b)- Pneumonitis

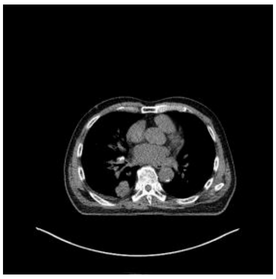

Figure 3(c)-Tuberculosis

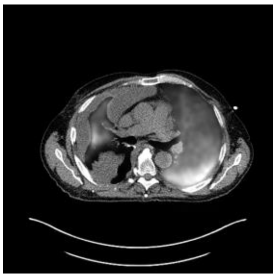

Figure 3(d)-Carcinoma

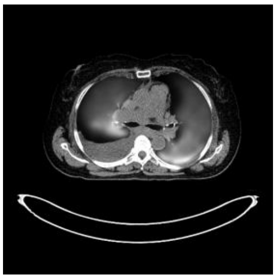

Figure 3(e)- Effusion

Figure3(f)- Infection

Figure 4 shows the silhouette score for clusters formed with simple k-means. It is seen from the graph that the highest silhouette score is 0.16 which means the reliability of the clustering model developed is very less. The silhouette score of transfer learning model shown in Figure 5 is highest with 0.8 for 2 clusters and hence better.

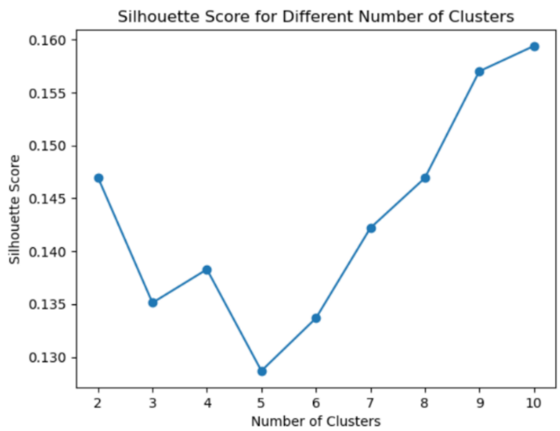

Figure 4: Silhouette score for K means with PET image

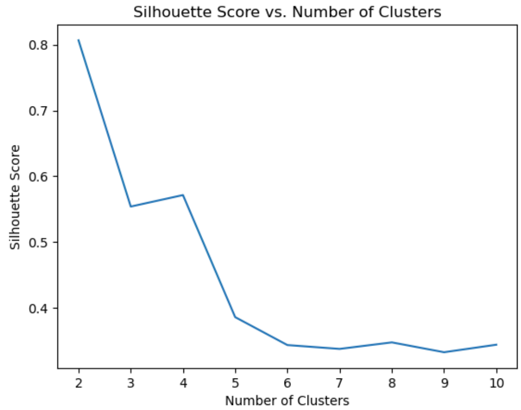

Figure 5: Silhouette score for Transfer Learning applied K means with PET images.

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