Detection of Lung Cancer on Computed Tomography Using Artificial Intelligence Applications Developed By Deep Learning Methods and The Contribution of Deep Learning to The Classification Of Lung Carcinoma

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Abstract: Background: Every year, lung cancer contributes to a high percentage deaths in the world. Early detection of lung cancer is important for its effective treatment, and non-invasive rapid methods are usually used for diagnosis.

Introduction: In this study, we aimed to detect lung cancer using deep learning methods and determine the contribution of deep learning to the classification of lung carcinoma using a convolutional neural network (CNN).

Methods: A total of 301 patients diagnosed with lung carcinoma pathologies in our hospital were included in the study. In the thorax, computed tomography (CT) was performed for diagnostic purposes prior to the treatment. After tagging the section images, tumor detection, small and non-small cell lung carcinoma differentiation, adenocarcinoma-squamous cell lung carcinoma differentiation, and adenocarcinoma-squamous cell-small cell lung carcinoma differentiation were sequentially performed using deep CNN methods.

Results: In total, 301 lung carcinoma images were used to detect tumors, and the model obtained with the deep CNN system exhibited 0.93 sensitivity, 0.82 precision, and 0.87 F1 score in detecting lung carcinoma. In the differentiation of small cell-non-small cell lung carcinoma, the sensitivity, precision and F1 score of the CNN model at the test stage were 0.92, 0.65, and 0.76, respectively. In the adenocarcinoma-squamous cancer differentiation, the sensitivity, precision, and F1 score were 0.95, 0.80, and 0.86, respectively. The patients were finally grouped as small cell lung carcinoma, adenocarcinoma, and squamous cell lung carcinoma, and the CNN model was used to determine whether it could differentiate these groups. The sensitivity, specificity, and F1 score of this model were 0.90, 0.44, and 0.59, respectively, in this differentiation.

Conclusion: In this study, we successfully detected tumors and differentiated between adenocarcinoma-squamous cell carcinoma groups with the deep learning method using the CNN model. Due to their non-invasive nature and the success of the deep learning methods, they should be integrated into radiology to diagnose lung carcinoma.

Keywords: Lung cancer, adenocarcinoma, deep learning, convolutional neural network, algorithm, computed tomography.

1. INTRODUCTION

A significant number of deaths occur in the world every year due to lung cancer [1]. Thus, early detection of lung cancer is important for its effective treatment [2]. Lung cancer is primarily divided into small and non-small cell lung carcinoma based on the pathology, and then non-small lung carcinoma is generally further classified as adenocarcinoma, squamous cell carcinoma, and large cell lung carcinoma. Squamous cell carcinoma (SCC) and adenocarcinoma are the most common types of non-small cell lung carcinoma. Non-small cell lung carcinoma is observed at a rate of approximately 85%, whereas small cell lung carcinoma occurs at 10-15% [3, 4]. Low-dose computed tomography (CT) is used for the screening of populations at high risk for lung
cancer. Annual low-dose CT scans have reduced lung cancer-related deaths by approximately 20% compared to chest radiographs [5]. The treatment of lung cancer varies according to the subtypes of the disease [6]. In lung cancer, the stage at the time of diagnosis is also very important. While the five-year survival rate is 5% in advanced metastatic lung cancer, it reaches 77.9% in the stage I non-small cell lung carcinoma [7]. Therefore, it is important to detect lung cancer at an early stage. A biopsy is performed to diagnose lesions observed on CT; however, it is an invasive method with various complications [8]. For this reason, there is a need for rapid methods to guide non-invasive diagnosis. Deep learning (DL) is a subgroup of artificial intelligence [9]; it is a multi-layer neural network algorithm divided into two, a convolutional neural network (CNN) and a deep belief network according to the use of tagged and untagged datasets [10]. In this study, we aimed to detect lung cancer using a deep learning method and determine the contribution of deep learning to the classification of lung carcinoma using CNN.

2. MATERIALS AND METHODS

A total of 301 patients that presented to Eskişehir OsmanGazi Medical Faculty and were pathologically diagnosed with lung cancer between 2016 and 2018 were included in the study after obtaining the approval of the local ethics committee. Using the thorax CT undertaken prior to the treatment for diagnostic purposes, the sections where the lung mass was the widest were evaluated. CT scans were performed using 128-section (GE, Revolution) and 64-section (Toshiba, Aquillion) devices, and the section thicknesses of the scans varied between 0.625 mm and 0.5 mm. The images were obtained in the mediastinum window with a width of 400 and a height of 40, and the scans were performed at a kV value of 120 and an mA value of 199. The sections taken in the mediastinum window were converted to the png format, and tumors were first detected in the axial plane images of 301 lung cancer cases. Then, lung cancer cases were divided into two groups as small (n = 52) and non-small cell lung carcinoma (n = 249), and the deep learning method was applied to determine the groups. In the adenocarcinoma-SCC differentiation, the images of 115 patients with adenocarcinoma and 134 with SCC were evaluated. Finally, for the differentiation of adenocarcinoma, SCC and small cell lung carcinoma by deep learning methods, 115, 134 and 52 cases, respectively, were included in the evaluation. Of the datasets, 80% were allocated to training, 10% to testing, and 10% to validation. The confusion matrix was used to calculate the success of the model. This matrix is a useful table that compares the predicted situation with the actual situation (Table 1).

Table 1. Confusion Matrix.

<table>
<thead>
<tr>
<th>Predicted Situation</th>
<th>Actual Situation</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>True Positive(TP)</td>
<td>False Negative(FN)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>False Positive(FP)</td>
<td>True Negative(TN)</td>
<td></td>
</tr>
</tbody>
</table>

The test dataset was used to calculate the diagnostic and predictive accuracy [ACC = (TP + TN) / (P + N)], sensitivity [TPR = TP / (TP + FN)], specificity [SPC = TN / (FP + TN)], negative predictive value [NPV = TN / (TN + FN)], positive predictive value [PPV = TP / (TP + FP)], and confusion matrix using the deep CNN algorithm based on a Tensorflow framework in Python.

3. RESULTS

In the diagnosis of lung cancer, a total of 301 images were taken into consideration, and after training on 239 axial sections, 31 sections were allocated to validation, and 31 sections to testing. In cancer detection, 29 sections were accurately detected, two were false negatives, and six were false positives (Fig. 1). The precision-recall (sensitivity) curve for tumor detection is given in Figure 2.

In the small cell-non-small cell lung cancer differentiation, a total of 301 images were evaluated, and 199 images for non-small cell lung carcinoma and 38 for small cell lung carcinoma were used in training. Seven images each were allocated to validation and testing for small cell lung carcinoma, while 25 images each were used for validation and testing in non-small cell lung carcinoma. The diagnosis was correct in 23 of the images in the test dataset, whereas 12 were found to be false positives and two were false negatives.

In the adenocarcinoma-SCC differentiation, a total of 249 images were evaluated, of which 115 had a diagnosis of adenocarcinoma and 134 had a diagnosis of SCC. For training, 93 adenocarcinoma and 108 SCC section images were used. Eleven images each were allocated to validation and testing in adenocarcinoma, and 13 images each were used for training and testing purposes in squamous cell carcinoma. Twenty of the tested images had an accurate diagnosis, while there were five false positives and one false negative.

A total of 301 images were evaluated in the adenocarcinoma-SCC-small cell lung carcinoma differentiation, with 93 adenocarcinoma, 108 SCC, and 38 small cell lung carcinoma section images being allocated to training. The number of images used for validation and testing was 11 each for adenocarcinoma, 13 each for SCC, and seven each for small cell lung carcinoma. While 19 of the tested images had an accurate diagnosis, 24 were found to be false positives and two were false negatives. The true positive, false positive and false negative values in all test groups are detailed in Table 2, and the sensitivity, precision, and F1 score in the test groups are shown in Table 3.

The deep CNN system was successful in the detection of tumors with the sensitivity, precision and F-1 score values of 0.95, 0.81 and 0.87, respectively. The CNN system was also successful in the differentiation of adenocarcinoma and SCC, with the sensitivity, precision and F-1 score values of 0.95, 0.80 and 0.86, respectively (Tables 2 and 3).

4. DISCUSSION

Early diagnosis is essential for the treatment and survival in lung cancer. Histopathology and molecular biology
Fig. (1). Flow chart of the datasets.

Fig. (2). Precision-recall (sensitivity) curve in tumor detection.

Table 2. Tumor detection in the test group, and true positive, false positive and false negative values in the differentiation of small and non-small lung carcinoma, adenocarcinoma-SCC, and adenocarcinoma-SCC-small cell lung carcinoma.

<table>
<thead>
<tr>
<th>-</th>
<th>Tumor</th>
<th>Small and Non-Small Cell Carcinoma</th>
<th>Adenocarcinoma-Squamous Cell Carcinoma</th>
<th>Adenocarcinoma – Squamous Cell Carcinoma – Small Cell Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positives</td>
<td>29</td>
<td>23</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>False positives</td>
<td>6</td>
<td>12</td>
<td>5</td>
<td>24</td>
</tr>
<tr>
<td>False negatives</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
are important at the stage of diagnosis. An invasive biopsy is required for these methods [11, 12]. There are various complications of the biopsy procedure, and sometimes the diagnosis can only be achieved after several attempts [8]. During this process, the stage of the disease can change. For this reason, non-invasive methods may be needed to make a diagnosis. In recent years, there has been growing interest in artificial intelligence methods. Deep learning is an important part of artificial intelligence [9], and various studies have been conducted on deep learning to detect lesions in the lung [13, 14].

In this study, we attempted to detect lung masses on thorax CT using deep learning methods. In total, 301 lung cancer images were used to detect tumors, and the model obtained with the deep CNN system had 0.93 sensitivity, 0.82 precision and 0.87 F1 score in detecting lung cancer. Zhang et al. used a three-dimensional CNN in their study and compared it to manual evaluation. In that study, 84.4% sensitivity and 83.0% specificity were obtained in detecting lesions. In our study, the sensitivity value was higher. We used two-dimensional images obtained from the axial section. Furthermore, in contrast to Zhang et al., who also included lesions below 10 mm [15], all of the lesions evaluated in the current study were over 2 cm.

Table 3. Sensitivity, precision and F1 score of the test groups.

<table>
<thead>
<tr>
<th>-</th>
<th>Sensitivity</th>
<th>Precision</th>
<th>F1 Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor detection</td>
<td>0.93</td>
<td>0.82</td>
<td>0.87</td>
</tr>
<tr>
<td>Small and Non-Small Cell Carcinoma</td>
<td>0.92</td>
<td>0.65</td>
<td>0.76</td>
</tr>
<tr>
<td>Adenocarcinoma-Squamous Cell Carcinoma</td>
<td>0.95</td>
<td>0.80</td>
<td>0.86</td>
</tr>
<tr>
<td>Adenocarcinoma-Squamous Cell Carcinoma-Small Cell Carcinoma</td>
<td>0.90</td>
<td>0.44</td>
<td>0.59</td>
</tr>
</tbody>
</table>

After detecting lung cancer with the CNN model, we divided the tumor group into small cell and non-small cell lung carcinoma according to the pathological diagnoses to evaluate the contribution of CNN to the classification of lung cancer. Fifty-three images were tagged as small cell lung carcinoma, and 248 as non-small lung carcinoma. After the training-validation stage, the sensitivity, precision and F1 score of the CNN model at the test stage were 0.92, 0.65, and 0.76, respectively. Thus, this model was not sufficiently successful in differentiation between small cell and non-small cell lung carcinoma. Non-small cell lung carcinoma is seen at a rate of approximately 85%, while small cell lung carcinoma has an incidence of around 10-15% [3], which is consistent with the numbers in our patient groups. Therefore, we had a smaller number of patients diagnosed with small cell lung carcinoma than with non-small cell lung carcinoma, which, we consider, had an effect on the success of the CNN model for the small-non-small cell lung carcinoma differentiation. Chen et al. used a multilayer artificial neural network to differentiate small cell lung carcinoma and non-small cell lung carcinoma in the lung periphery, and they reported the area under curve (AUC) value as 0.93, sensitivity as 0.85, and specificity as 0.85 [16]. Unlike our study, the authors did not take tumor heterogeneity into account.

In this study, after the small and non-small cell lung carcinoma differentiation, the images of the patients were grouped and tagged as those with a diagnosis of adenocarcinoma and those diagnosed with squamous cell carcinoma to determine the ability of deep learning to differentiate between these two groups. A total of 249 images obtained from 115 patients diagnosed with adenocarcinoma and 134 with squamous cell lung carcinoma were included in this CNN model. Following the training-validation stage, the sensitivity, precision and F1 score of the CNN model at the test stage were calculated as 0.95, 0.80, and 0.86, respectively. The CNN model was as successful in the adenocarcinoma-squamous cell lung carcinoma differentiation as tumor detection. Moitra et al. aimed to identify the best deep learning model by tagging non-small cell lung carcinoma cases as adenocarcinoma, squamous cell carcinoma, and not otherwise specified (NOS). Among the models tested, they reported the precision, recall and F1 score of the CNN model as 0.90, 0.90, and 0.90, respectively [17], which indicated a higher success rate of this model compared to our study; this can be attributed to the authors using positron emission tomography-computed tomography(PET-CT) in addition to CT images and their total number of data being much higher than ours.

Lastly, we grouped the patients as those diagnosed with small cell lung carcinoma, adenocarcinoma, and squamous cell lung carcinoma, and investigated the ability of the CNN model to differentiate between these subgroups of lung cancer. For this differentiation, the CNN model had a sensitivity of 0.90, a specificity of 0.44, and F1 score of 0.509, which indicated that the model was not successful. In their deep learning study, Wang et al. used 2,054 tagged images obtained from patients diagnosed with lung cancer in training and 168 images in testing. They achieved an 85.71% accuracy rate in their study. These authors included patients diagnosed with squamous, small cell, adenocarcinoma in situ, and invasive adenocarcinoma, and they also had a much higher number of images compared to our data set, which can explain the success of their model. Furthermore, unlike our study, a residual neural network was used in that previous study [18].

Since deep learning methods are a current issue, many studies have been conducted on lung cancer. However, the classification for tumor detection, classification based on deep learning for small-nonsmall lung cancer, squamous cancer and adenocarcinoma were not performed in the same study. We think our study is important in this respect.

The limitation of our study was that the number of patients diagnosed with small cell lung carcinoma was less than those of the other lung cancer groups.
CONCLUSION

In conclusion, in this study, we successfully detected tumors and differentiated adenocarcinoma-squamous cell carcinoma groups with the deep learning method using CNN. As non-invasive methods, deep learning models provide support for radiology clinics by assisting in the detection of lung cancer on CT. In addition to tumor detection, these models can offer benefits for clinicians in the differentiation of adenocarcinoma-squamous cell lung carcinoma. Thus, deep learning methods should be integrated into radiology practice to diagnose lung cancer, and CNN methods can guide the determination of lung cancer subgroups in a non-invasive manner.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethics committee permission for this study was approved by Eskişehir Osmangazi University Non-Interventional Clinical Research Ethics Committee.

HUMAN AND ANIMAL RIGHTS

No animals were used in this study. The reported experiments on humans were followed in accordance with the ethical standards of the committee responsible for human experimentation (institutional national) and with the Helsinki Declaration of 1975, as revised in 2008 (http://www.wma.net/).

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

The author is very thankful to all the associated personnel in any reference that contributed to the purpose of this research.

REFERENCES


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