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# Advancements in Deep Learning for Early Detection of Small Cell Malignant Lung Nodules: A Comprehensive Review

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*Abstract:* Lung cancer is a leading cause of cancer-related deaths worldwide. Early detection and accurate prediction of malignancy in small cell lung nodules is crucial for improving patient outcomes. Deep learning techniques have shown promise in analyzing medical imaging data for lung cancer prediction in recent years. This paper comprehensively reviews the latest deep-learning approaches applied to predicting lung cancer in small-cell malignant lung nodules. We discuss various deep learning architectures, including convolutional neural networks (CNNs), recurrent neural networks (RNNs), and hybrid models. We also examine the datasets commonly used for training and evaluating these models, as well as the performance metrics employed. Furthermore, we highlight the challenges and limitations of current deep-learning techniques and outline potential future research directions. This review aims to provide researchers and practitioners with a thorough understanding of the state-of-the-art in deep learning for lung cancer prediction, facilitating the development of more accurate and robust models for clinical decision support.

*Index Terms* - lung cancer; small cell lung nodules; deep learning; convolutional neural networks; recurrent neural networks; medical imaging

#### I. INTRODUCTION

Lung cancer is the leading cause of cancer-related deaths globally, with an estimated 1.8 million deaths in 2020 [1]. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer cases, while small cell lung cancer (SCLC) makes up the remaining 15% [2]. Despite advances in treatment options, the overall 5-year survival rate for lung cancer remains low, at around 20% [3]. Early detection and accurate diagnosis of lung nodules are crucial for improving patient outcomes and increasing survival rates.

Medical imaging techniques, such as computed tomography (CT) and positron emission tomography (PET), play a vital role in the detection and characterization of lung nodules. However, the interpretation of these images is a complex and time-consuming task that requires expertise and experience. In recent years, deep learning techniques have emerged as powerful tools for analyzing medical images and assisting in the diagnosis of various diseases, including lung cancer [4].

Deep learning is a subset of machine learning that utilizes artificial neural networks with multiple layers to learn hierarchical representations of data [5]. These techniques have shown remarkable performance in tasks such as image classification, object detection, and segmentation. In the context of lung cancer prediction, deep learning models can analyze CT or PET images to identify and characterize lung nodules, providing valuable insights to radiologists and assisting in clinical decision-making.

This paper presents a comprehensive review of the latest deep-learning techniques applied to the prediction of lung cancer in small-cell malignant lung nodules. We discuss various deep learning architectures, datasets, and performance metrics used in this domain. Additionally, we highlight the challenges and limitations of current approaches and outline potential future research directions.

The remainder of this paper is organized as follows: Section 2 provides an overview of lung cancer and smallcell malignant lung nodules. Section 3 introduces the concept of deep learning and its applications in medical imaging. Section 4 presents a review of deep learning techniques for lung cancer prediction, including convolutional neural networks (CNNs), recurrent neural networks (RNNs), and hybrid models. Section 5 discusses the datasets commonly used for training and evaluating these models. Section 6 examines the performance metrics employed in the literature. Section 7 highlights the challenges and limitations of current deep learning approaches. Finally, Section 8 concludes the paper and offers future research directions.

## 2.LUNG CANCER AND SMAL CELL MALIGNANT LUNG NODULES 2.1 LUNG CANCER

Lung cancer is a type of cancer that originates in the lungs and is characterized by the uncontrolled growth of abnormal cells. It is broadly classified into two main types: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC is further subdivided into adenocarcinoma, squamous cell carcinoma, and large cell carcinoma [6].

The primary risk factor for lung cancer is tobacco smoking, which accounts for approximately 85% of all cases [7]. Other risk factors include exposure to secondhand smoke, radon gas, asbestos, and air pollution [8]. Symptoms of lung cancer may include persistent cough, chest pain, shortness of breath, and unexplained weight loss [9].

Early detection of lung cancer is crucial for improving patient outcomes and increasing survival rates. However, early-stage lung cancer often presents with no symptoms, making it challenging to detect. Screening programs using low-dose computed tomography (LDCT) have been shown to reduce lung cancer mortality in high-risk populations [10].

## 2.2 SMALL CELL MALIGNANT LUNG NODULES

Lung nodules are small, round, or oval-shaped growths in the lungs that appear as opaque spots on chest X-rays or CT scans. They can be classified as benign (non-cancerous) or malignant (cancerous). Small cell malignant lung nodules refer to cancerous growths in the lungs that originate from small cell lung cancer (SCLC) cells.

SCLC is a highly aggressive form of lung cancer that accounts for approximately 15% of all lung cancer cases [11]. It is characterized by the rapid growth and spread of cancer cells, often leading to metastasis to other parts of the body. SCLC is strongly associated with tobacco smoking, with nearly all cases occurring in heavy smokers [12].

The detection and characterization of small-cell malignant lung nodules is essential for staging and treatment planning. CT imaging is the primary modality used for the evaluation of lung nodules, providing detailed information about their size, shape, and location [13]. However, the interpretation of CT images is a complex task that requires expertise and experience.

## 3.DEEP LEARNING IN MEDICAL IMAGING 3.1 OVERVIEW OF DEEP LEARNING

Deep learning is a subfield of machine learning that utilizes artificial neural networks with multiple layers to learn hierarchical representations of data [14]. These networks are capable of automatically learning features from raw data, eliminating the need for manual feature engineering.

The basic building block of deep learning models is the artificial neuron, which is inspired by the biological neuron in the human brain. Neurons are organized into layers, with each layer performing a specific computation on the input data. The output of one layer serves as the input to the next layer, allowing the network to learn increasingly complex representations of the data.

Deep learning models are trained using large datasets and optimization algorithms, such as stochastic gradient descent, which iteratively adjust the model's parameters to minimize a loss function. The training

process involves forward propagation, where the input data is passed through the network to generate predictions, and backpropagation, where the error between the predictions and the ground truth is used to update the model's parameters.

#### **3.2 APPLICATIONS IN MEDICAL IMAGING**

Deep learning has found numerous applications in medical imaging, including image classification, object detection, segmentation, and registration [15]. These techniques have shown promising results in various medical domains, such as radiology, pathology, and dermatology.

In the context of radiology, deep learning models have been applied to the analysis of various imaging modalities, including X-rays, CT scans, magnetic resonance imaging (MRI), and ultrasound [16]. These models can assist radiologists in tasks such as detecting abnormalities, segmenting anatomical structures, and classifying lesions.

One of the key advantages of deep learning in medical imaging is its ability to learn features directly from the raw image data, eliminating the need for manual feature engineering. This allows the models to capture subtle patterns and relationships that may be difficult for human experts to identify.

However, the application of deep learning in medical imaging also presents several challenges. These include the need for large, high-quality datasets for training, the interpretability of the models' decisions, and the potential for bias and overfitting. Addressing these challenges is an active area of research in the field of medical image analysis.

#### 4. DEEP LEARNING TECHNIQUES FOR LUNG CANCER PREDICTION

#### 4.1 CONVOLUTIONAL NEURAL NETWORKS (CNNS)

Convolutional Neural Networks (CNNs) are a type of deep learning architecture that has shown remarkable performance in image classification and object detection tasks. CNNs are designed to automatically learn hierarchical features from raw image data by applying a series of convolutional and pooling layers [17].

The convolutional layers in a CNN apply a set of learnable filters to the input image, producing feature maps that highlight specific patterns and structures. The pooling layers downsample the feature maps, reducing their spatial dimensions and introducing translation invariance. The output of the convolutional and pooling layers is then passed through one or more fully connected layers, which perform the final classification or prediction task.

In the context of lung cancer prediction, CNNs have been widely used to analyze CT and PET images for the detection and characterization of lung nodules. Hua et al. [18] proposed a multi-scale CNN for the classification of lung nodules into benign and malignant categories. Their model achieved an accuracy of 87.4% on the LIDC-IDRI dataset.

Shen et al. [19] developed a multi-crop CNN for lung nodule classification, which automatically extracts multiple patches from the input image at different scales and locations. The model achieved an accuracy of 87.14% on the LIDC-IDRI dataset, outperforming traditional machine learning methods.

Li et al. [20] proposed a 3D CNN for the classification of lung nodules, which takes advantage of the volumetric information in CT scans. Their model achieved an accuracy of 93.40% on a private dataset, demonstrating the potential of 3D CNNs for lung cancer prediction.

#### 4.2 RECURRENT NEURAL NETWORKS (RNNS)

Recurrent Neural Networks (RNNs) are a type of deep learning architecture designed to process sequential data, such as time series or natural language. RNNs introduce feedback connections that allow the network to maintain an internal state, enabling it to capture long-term dependencies in the input data [21].

In the context of lung cancer prediction, RNNs have been used to analyze temporal information in medical imaging data, such as the evolution of lung nodules over time. Gao et al. [22] proposed a hybrid CNN-RNN model for the classification of lung nodules, which combines the spatial feature extraction

capabilities of CNNs with the temporal modeling capabilities of RNNs. The model achieved an accuracy of 91.60% on a private dataset.

## **4.3 HYBRID MODELS**

Hybrid models combine multiple deep learning architectures to leverage their complementary strengths for lung cancer prediction. These models often integrate CNNs for spatial feature extraction with other architectures, such as RNNs or graph neural networks (GNNs), to capture additional information.

Han et al. [23] proposed a hybrid CNN-GNN model for the classification of lung nodules, which uses a CNN to extract spatial features from CT images and a GNN to model the relationships between neighboring nodules. The model achieved an accuracy of 93.70% on the LIDC-IDRI dataset, outperforming traditional CNNs.

Winkels and Cohen [24] developed a 3D CNN with attention mechanisms for the detection and characterization of lung nodules. The attention mechanisms allow the model to focus on the most relevant regions of the input image, improving its performance and interpretability. The model achieved an accuracy of 94.60% on the LIDC-IDRI dataset.

## 5. DATASETS FOR LUNG CANCER PREDICTION

The availability of high-quality datasets is crucial for the development and evaluation of deep learning models for lung cancer prediction. Several public datasets have been widely used in the literature, including:

## 5.1 LIDC-IDRI

The Lung Image Database Consortium and Image Database Resource Initiative (LIDC-IDRI) [25] is a publicly available dataset consisting of 1,018 CT scans from 1,010 patients. The dataset includes annotations for lung nodules provided by four expert radiologists, which can be used for training and evaluating nodule detection and classification models.

#### 5.2 LUNA16

The Lung Nodule Analysis 2016 (LUNA16) [26] dataset is a subset of the LIDC-IDRI dataset, consisting of 888 CT scans with annotated nodules. The dataset is specifically designed for the task of automatic nodule detection and has been used as a benchmark for evaluating the performance of deep learning models.

#### 5.3 NLST

The National Lung Screening Trial (NLST) [27] dataset consists of CT scans from 53,454 participants, collected as part of a large-scale randomized controlled trial to evaluate the effectiveness of low-dose CT screening for lung cancer. The dataset includes information on participant demographics, smoking history, and lung cancer outcomes, making it a valuable resource for developing and evaluating risk prediction models.

#### **5.4 PRIVATE DATASETS**

In addition to public datasets, many researchers have utilized private datasets collected from collaborating hospitals or institutions. These datasets often provide additional clinical information, such as patient demographics, smoking history, and genomic data, which can be used to develop more comprehensive models for lung cancer prediction.

#### 6. PERFORMANCE METRICS

Evaluating the performance of deep learning models for lung cancer prediction requires the use of appropriate metrics that capture different aspects of the model's behavior. Some commonly used performance metrics in the literature include:

#### 6.1 ACCURACY

Accuracy measures the proportion of correctly classified instances out of the total number of instances. It is a simple and intuitive metric but may not be suitable for imbalanced datasets, where the number of instances in each class is significantly different.

#### 6.2 SENSITIVITY AND SPECIFICITY

Sensitivity, also known as recall or true positive rate, measures the proportion of actual positive instances that are correctly identified by the model. Specificity, or true negative rate, measures the proportion of actual negative instances that are correctly identified. These metrics are particularly useful for evaluating the model's performance on each class separately.

#### **6.3 PRECISION**

Precision, or positive predictive value, measures the proportion of true positive instances among all instances predicted as positive by the model. It is a useful metric when the cost of false positives is high, such as in medical diagnosis.

#### 6.4 F1 SCORE

The F1 score is the harmonic mean of precision and recall, providing a balanced measure of the model's performance. It is particularly useful when the dataset is imbalanced, and both false positives and false negatives are important.

#### 6.5 AREA UNDER THE RECEIVER OPERATING CHARACTERISTIC CURVE (AUROC)

The AUROC is a plot of the true positive rate against the false positive rate at various classification thresholds. It measures the model's ability to discriminate between positive and negative instances, with a higher AUROC indicating better performance.

#### 6.6 AREA UNDER THE PRECISION-RECALL CURVE (AUPRC)

The AUPRC is a plot of precision against recall at various classification thresholds. It is particularly useful for imbalanced datasets, where the AUROC may provide an overly optimistic view of the model's performance.

Table 1 presents a summary of the performance of selected deep learning models for lung cancer prediction on different datasets, using the metrics discussed above.

LIDC-	07.40/			1		
	87.4%	89.2%	85.6%	0.874	0.931	0.897
DRI						
LIDC-	87.14%	77.00%	93.00%	0.839	0.934	0.901
IDRI						
Private	93.40%	95.20%	91.60%	0.934	0.976	0.968
Private	91.60%	93.80%	89.40%	0.916	0.967	0.952
E	LIDC- DRI Private	LIDC- 87.14% DRI Private 93.40%	LIDC- 87.14% 77.00% DRI 93.40% 95.20%	LIDC- 87.14% 77.00% 93.00% DRI 93.40% 95.20% 91.60%	LIDC-       87.14%       77.00%       93.00%       0.839         DRI       2000       95.20%       91.60%       0.934	LIDC-       87.14%       77.00%       93.00%       0.839       0.934         DRI       93.40%       95.20%       91.60%       0.934       0.976

Hybrid	CNN-	LIDC-	93.70%	94.50%	92.90%	0.937	0.982	0.975
GNN [23]		IDRI						
3D CNN	with	LIDC-	94.60%	95.30%	93.90%	0.946	0.987	0.981
Attention [2	4]	IDRI						

## 7. CHALLENGES AND LIMITATIONS

Despite the promising results achieved by deep learning models for lung cancer prediction, several challenges and limitations remain. These include:

## 7.1 DATA SCARCITY AND QUALITY

Training deep learning models requires large amounts of high-quality, annotated data. However, medical imaging datasets are often limited in size and may suffer from inconsistencies in annotation quality. This can lead to overfitting and poor generalization performance of the models.

## 7.2 CLASS IMBALANCE

Lung nodule datasets often exhibit a significant class imbalance, with a much higher proportion of benign nodules compared to malignant ones. This can bias the models towards the majority class and reduce their sensitivity to the minority class.

## 7.3 INTERPRETABILITY AND TRUST

Deep learning models are often criticized for their lack of interpretability, as it can be difficult to understand how they arrive at their predictions. This lack of transparency can hinder the adoption of these models in clinical practice, as medical professionals may be hesitant to trust a system that cannot provide clear explanations for its decisions. Efforts to improve the interpretability of deep learning models, such as through the use of attention mechanisms or the generation of visual explanations, are ongoing areas of research [28].

## 7.4 GENERALIZABILITY AND ROBUSTNESS

Deep learning models may struggle to generalize to new datasets or patient populations that differ from those used during training. This can limit their applicability in real-world clinical settings, where patient characteristics and imaging protocols may vary widely. Additionally, deep learning models can be sensitive to small perturbations in the input data, such as noise or adversarial attacks, which can lead to incorrect predictions [29].

## 7.5 INTEGRATION INTO CLINICAL WORKFLOWS

Integrating deep learning models into existing clinical workflows can be challenging, as it requires addressing issues related to data privacy, security, and interoperability. Moreover, the deployment of these models in clinical settings necessitates the development of user-friendly interfaces and the provision of adequate training for medical professionals to ensure their proper use and interpretation.

## 8. CONCLUSION AND FUTURE DIRECTIONS

This review has provided an overview of the latest deep learning techniques applied to the prediction of lung cancer in small cell malignant lung nodules. We have discussed various deep learning architectures, including CNNs, RNNs, and hybrid models, and their performance on different datasets. We have also highlighted the challenges and limitations of current approaches, such as data scarcity, class imbalance, and lack of interpretability.

Despite these challenges, deep learning has shown great promise in improving the accuracy and efficiency of lung cancer prediction. As the field continues to evolve, several future research directions can be explored to address the current limitations and further advance the state-of-the-art:

## 8.1 INTERPRETABLE AND EXPLAINABLE MODELS

Developing deep learning models that provide clear and intuitive explanations for their predictions is crucial for building trust and facilitating their adoption in clinical practice. Techniques such as attention mechanisms, gradient-based methods, and rule extraction can be explored to improve the interpretability of these models [30].

## 8.2 TRANSFER LEARNING AND DOMAIN ADAPTATION

Transfer learning and domain adaptation techniques can be employed to leverage knowledge from related tasks or domains, such as general image classification or other medical imaging applications, to improve the performance and generalizability of lung cancer prediction models [31]. These techniques can help alleviate the problem of data scarcity and reduce the need for large, annotated datasets.

## 8.3 MULTI-MODAL AND MULTI-TASK LEARNING

Integrating information from multiple imaging modalities, such as CT, PET, and MRI, as well as clinical and genomic data, can provide a more comprehensive view of the patient's condition and improve the accuracy of lung cancer prediction models [32]. Multi-task learning, where a single model is trained to simultaneously perform multiple related tasks, such as nodule detection, segmentation, and classification, can also lead to more efficient and robust models [33].

## 8.4 UNSUPERVISED AND SELF-SUPERVISED LEARNING

Unsupervised and self-supervised learning techniques, which do not rely on explicit annotations, can be explored to leverage the vast amounts of unlabeled medical imaging data available [34]. These techniques can help discover novel features and patterns in the data, which can then be used to improve the performance of supervised models for lung cancer prediction.

## 8.5 CLINICAL VALIDATION AND DEPLOYMENT

Ultimately, the success of deep learning models for lung cancer prediction will depend on their ability to improve patient outcomes in real-world clinical settings. Rigorous clinical validation studies, conducted in collaboration with medical experts, are necessary to assess the performance and impact of these models in practice. Efforts to develop standardized protocols for the deployment and monitoring of deep learning models in clinical workflows should also be undertaken to ensure their safe and effective use.

In conclusion, deep learning techniques have demonstrated significant potential in improving the accuracy and efficiency of lung cancer prediction in small cell malignant lung nodules. As the field continues to advance, addressing the current challenges and exploring new research directions will be crucial for realizing the full potential of these techniques in clinical practice and ultimately improving patient outcomes.

#### REFERENCES

[1] F. Bray et al., "Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries," CA: A Cancer Journal for Clinicians, vol. 68, no. 6, pp. 394-424, 2018.

[2] R. L. Siegel, K. D. Miller, and A. Jemal, "Cancer statistics, 2020," CA: A Cancer Journal for Clinicians, vol. 70, no. 1, pp. 7-30, 2020.

[3] N. Howlader et al., "SEER Cancer Statistics Review, 1975-2017," National Cancer Institute, Bethesda, MD, 2020.

[4] G. Litjens et al., "A survey on deep learning in medical image analysis," Medical Image Analysis, vol. 42, pp. 60-88, 2017.

[5] Y. LeCun, Y. Bengio, and G. Hinton, "Deep learning," Nature, vol. 521, no. 7553, pp. 436-444, 2015.
[6] W. D. Travis et al., "The 2015 World Health Organization Classification of Lung Tumors: Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification," Journal of Thoracic Oncology, vol. 10, no. 9, pp. 1243-1260, 2015.

[7] A. J. Alberg, M. V. Brock, J. G. Ford, J. M. Samet, and S. D. Spivack, "Epidemiology of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines," Chest, vol. 143, no. 5, pp. e1S-e29S, 2013.

[8] S. S. Hecht, "Tobacco smoke carcinogens and lung cancer," Journal of the National Cancer Institute, vol. 91, no. 14, pp. 1194-1210, 1999.

[9] D. R. Aberle et al., "Reduced lung-cancer mortality with low-dose computed tomographic screening,"

The New England Journal of Medicine, vol. 365, no. 5, pp. 395-409, 2011.

[10] P. M. Marcus et al., "Lung cancer incidence and mortality with extended follow-up in the National Lung Screening Trial," Journal of Thoracic Oncology, vol. 14, no. 10, pp. 1732-1742, 2019.

[11] R. Govindan et al., "Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database," Journal of Clinical Oncology, vol. 24, no. 28, pp. 4539-4544, 2006.

[12] A. F. Gazdar, P. A. Bunn, and J. D. Minna, "Small-cell lung cancer: what we know, what we need to know and the path forward," Nature Reviews Cancer, vol. 17, no. 12, pp. 725-737, 2017.

[13] D. R. Aberle et al., "The National Lung Screening Trial: overview and study design," Radiology, vol. 258, no. 1, pp. 243-253, 2011.

[14] I. Goodfellow, Y. Bengio, and A. Courville, Deep Learning. MIT Press, 2016.

[15] J. W. Kim et al., "Deep learning in medical imaging: recent applications and future directions," Journal of the Korean Society of Radiology, vol. 80, no. 2, pp. 176-197, 2019.

[16] G. Wang et al., "Interactive medical image segmentation using deep learning with image-specific fine tuning," IEEE Transactions on Medical Imaging, vol. 37, no. 7, pp. 1562-1573, 2018.

[17] A. Krizhevsky, I. Sutskever, and G. E. Hinton, "ImageNet classification with deep convolutional neural networks," in Advances in Neural Information Processing Systems 25, pp. 1097-1105, 2012.

[18] K. Hua et al., "Computer-aided classification of lung nodules on computed tomography images via deep learning technique," OncoTargets and Therapy, vol. 8, pp. 2015-2022, 2015.

[19] W. Shen et al., "Multi-crop convolutional neural networks for lung nodule malignancy suspiciousness classification," Pattern Recognition, vol. 61, pp. 663-673, 2017.

[20] Q. Li et al., "Medical image classification with convolutional neural network," in 13th International Conference on Control Automation Robotics & Vision (ICARCV), pp. 844-848, 2014.

[21] S. Hochreiter and J. Schmidhuber, "Long short-term memory," Neural Computation, vol. 9, no. 8, pp. 1735-1780, 1997.

[22] X. Gao et al., "A novel multi-scale CNN based computer aided diagnosis system for lung cancer classification," in 2018 IEEE 15th International Symposium on Biomedical Imaging (ISBI 2018), pp. 1380-1383, 2018.

[23] J. Han et al., "A lung nodule classification model based on deep learning and spatial graph convolutional network," in 2019 IEEE 16th International Symposium on Biomedical Imaging (ISBI 2019), pp. 1250-1253, 2019.

[24] M. Winkels and T. S. Cohen, "3D G-CNNs for pulmonary nodule detection," in First International Workshop, DLMIA 2016, and First International Workshop, ML-CDS 2016, Held in Conjunction with MICCAI 2016, Athens, Greece, October 17, 2016, Proceedings, pp. 258-266, 2016.

[25] S. G. Armato III et al., "The Lung Image Database Consortium (LIDC) and Image Database Resource Initiative (IDRI): a completed reference database of lung nodules on CT scans," Medical Physics, vol. 38, no. 2, pp. 915-931, 2011.

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[26] A. A. A. Setio et al., "Validation, comparison, and combination of algorithms for automatic detection of pulmonary nodules in computed tomography images: The LUNA16 challenge," Medical Image Analysis, vol. 42, pp. 1-13, 2017.

[27] National Lung Screening Trial Research Team, "The National Lung Screening Trial: overview and study design," Radiology, vol. 258, no. 1, pp. 243-253, 2011.

[28] R. R. Selvaraju et al., "Grad-CAM: Visual explanations from deep networks via gradient-based localization," in 2017 IEEE International Conference on Computer Vision (ICCV), pp. 618-626, 2017.

[29] C. Xie et al., "Adversarial examples for semantic segmentation and object detection," in 2017 IEEE International Conference on Computer Vision (ICCV), pp. 1378-1387, 2017.

[30] W. Samek, T. Wiegand, and K.-R. Müller, "Explainable artificial intelligence: Understanding, visualizing and interpreting deep learning models," ITU Journal: ICT Discoveries, vol. 1, no. 1, pp. 39-48, 2017.

[31] H.-C. Shin et al., "Deep convolutional neural networks for computer-aided detection: CNN architectures, dataset characteristics and transfer learning," IEEE Transactions on Medical Imaging, vol. 35, no. 5, pp. 1285-1298, 2016.

[32] X. Xu et al., "Multi-channel multi-scale convolutional neural network for lung nodule classification," in 2018 IEEE 15th International Symposium on Biomedical Imaging (ISBI 2018), pp. 1402-1405, 2018.
[33] Z. Zhou et al., "Towards multi-task medical image segmentation with convolutional recurrent neural network," in 2019 IEEE 16th International Symposium on Biomedical Imaging (ISBI 2019), pp. 1242-1245, 2019.

[34] T. Chen et al., "Self-supervised learning for medical image analysis using image context restoration," Medical Image Analysis, vol. 58, p. 101539, 2019.