End-to-End Lung Nodule Detection: U-net Segmentation and ResNet50 Classification on LUNA16

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***Abstract*—Lung cancer is one of the leading causes of cancer-related deaths worldwide, with early detection being critical for improving patient outcomes. A key diagnostic step involves identifying and classifying pulmonary nodules in chest CT scans; however, this task is both labor-intensive and prone to variability among radiologists. To address this, we propose a deep learning pipeline that combines semantic segmentation and classification to automate lung nodule analysis. Our approach uses a U-net model to first segment lung nodules from CT slices in the LUNA16 dataset, isolating the regions of interest and reducing background noise. These segmented patches are then used as input to a fine-tuned ResNet50 model, which classifies each nodule as benign or malignant. U-net's ability to capture spatial details and ResNet50's strong feature extraction capabilities (pretrained on ImageNet) make this a powerful hybrid framework for medical imaging tasks. By integrating segmentation and classification, our method aims to improve the accuracy and efficiency of early lung cancer detection.**

***Index Terms*—Lung cancer, CT imaging, deep learning, U-Net, ResNet50, semantic segmentation, nodule detection, classification confidence, LUNA16, biomedical image analysis**

I. Introduction

Lung cancer poses a significant global health burden, with high mortality rates largely attributed to late-stage diagnosis. Early identification of pulmonary nodules-small masses in the lungs that may indicate malignancy- is essential for improving patient outcomes. In clinical practice, this process heavily relies on the manual assessment of CT scans by radiologists, which can be time-intensive and subject to variability. As imaging volumes increase and demand for timely diagnosis grows, the development of automated, reliable tools for lung nodule detection and classification has become a key area of research in biomedical AI.

Deep Learning, particularly convolutional neural networks (CNNs), has shown remarkable success in medical imaging applications. The LUNA16 challenge, introduced by Setio et al. [1] provides a benchmark dataset of annotated lung CT scans for evaluating nodule detection algorithms. Top-performing models in this challenge often employed CNN architectures, achieving high sensitivity in detecting malignant nodules. For instance, a solution by Ping An Technology utilized U-net for detailed lung tissue segmentation, which enhanced the downstream classification performance [2].

Among deep learning models, ResNet50, a deep residual network, has been particularly effective in medical image classification tasks due to its use of residual blocks that mitigate vanishing gradients and support deeper network training. Li et al. demonstrated that an ensemble of fine-tuned ResNet50 models could distinguish between benign and malignant nodules with high accuracy [4], while Hossain et al. showed that transfer learning with ResNet50 substantially improved classification performance on medical datasets [5].

Segmentation plays a vital role in isolating regions of interest in Ct images. U-Net, a widely adopted encoder-decoder architecture, is specifically designed for biomedical image segmentation and has proven effective in identifying anatomical structures and pathological regions. Its use in preprocessing helps focus classification models on relevant image areas, thereby reducing noise and improving performance.

Beyond pixel-level classification, radiomic feature extraction offers complementary insights by quantifying tumor shape, texture, and intensity. Lambin et al. emphasized the role of radiomics in enhancing model interpretability and clinical utility [6]. Similarly, Lustberg et al. explored hybrid approaches combining atlas-based and deep learning segmentation to improve precision in tumor delineation for radiotherapy planning [7].

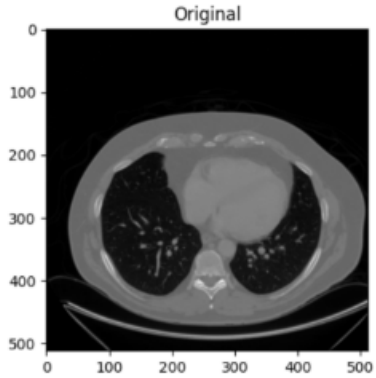
Recent advances have also introduced end-to-end AI pipelines that combine segmentation, classification, and feature analysis. Yu et al. discussed multi-class diagnostic models using deep learning for cancer prediction, while Kaliyugarasan et al. demonstrated the value of specialized frameworks such as MONAI and fastai in pulmonary nodule classification tasks [8,9].

Building upon these advancements, our study proposes a two-stage deep learning framework for automated lung nodule classification. We first apply a U-Net model to segment nodules from CT slices, then input these segmented patches

into a fine-tuned ResNet50 classifier. The model is trained and evaluated on the LUNA16 dataset, with performance assessed using accuracy, sensitivity, and specificity. By integrating segmentation and classification, our approach aims to improve the accuracy and reliability of early lung cancer detection, potentially reducing diagnostic workload and aiding timely clinical intervention.

II. Methods

Our project is utilizing the LUNA16 dataset of preprocessed and annotated lung CT images. The LUNA16 dataset provides over 800 annotated image sets, broken up into nine different subsets available for public access. Each image set is annotated with boolean information regarding the presence/absence of a lung nodule. If there is a lung nodule, the image set is also annotated with a "bounding box" that labels the location and diameter of the lung nodule. Each image set within the LUNA16 dataset received preprocessing in addition to the annotations. These preprocessing steps include Hounsfield Unit Normalization (a common CT image intensity normalization process) and slice extraction.



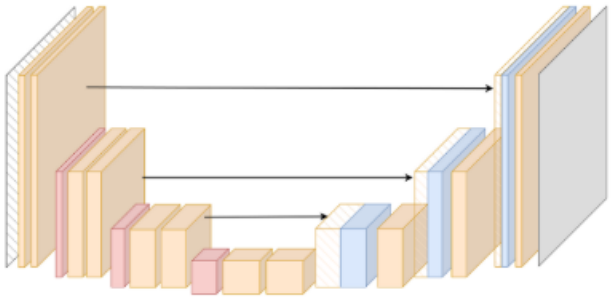


Figure 1. Left: Example of the lung CT images provided by LUNA16 dataset. **Bottom:** Example structure of our U-net architecture.

The pipeline for the U-net segmentation algorithm roughly follows the following steps. First, the dataset is loaded into our script and the lung masks are extracted from the dataset. Then, the nodule classifications are parsed by the script and the CT volumes are read to match each dataset with the annotations. Next, the lung regions are segmented before applying several image processing steps. First, we apply Kmeans clustering followed by morphology erosion dilation. The generated masks are extracted and the data is processed again by normalizing the pixel intensity to a scale from 0-255. The images are also cropped and resized to a 512x512 pixel size. The images are then saved to the local drive as .png images. Next, we perform K-Fold Dataset preparation, merge the training and testing sets, apply a five-fold split, and save the folded files. Next, the U-net model is established by building encoder and decoder blocks, adding skip connections, and establishing a sigmoidal output layer. Next, the training pipeline runs to iteratively improve lung segmentation. First, we batch-input slices and masks. Then we use the BCE loss ADAM optimizer and train for 10 epochs to iteratively improve lung segmentation accuracy. Lastly, each model checkpoint is and the generated image files are saved after each epoch. After this is completed, the algorithm is prepared for testing and validation. Because the LUNA16 dataset does not include a dataset for lung segmentation (only classification), our segmentation algorithm was trained on similar datasets that were publicly available and then generalized to function on the LUNA16 dataset.

A. Problem Formulation

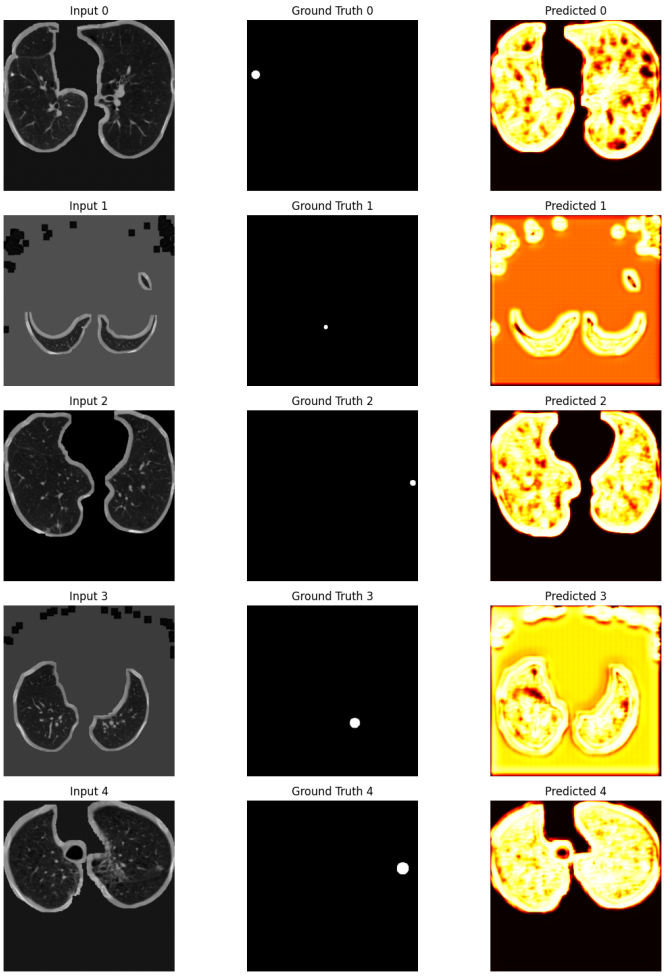
This study investigates whether a two-stage deep learning pipeline—comprising U-Net for segmentation and ResNet50 for classification—can enhance the confidence and interpretability of lung nodule detection using CT scans from the LUNA16 dataset. The primary hypothesis is that accurate segmentation of lung nodules can focus the classifier on relevant regions, improving classification confidence and reducing false positives associated with background tissues or noise.

Inputs: The model receives 512×512 preprocessed grayscale CT slices as input. Each slice has undergone Hounsfield Unit normalization and lung region isolation using K-means clustering and morphological operations. Alongside the slices, the model also consumes corresponding nodule masks—either binary or probabilistic—generated by the U-Net model trained on approximated masks based on diameter and centroid annotations.

Outputs: The classifier outputs a binary label indicating the presence or absence of a nodule within the segmented region, accompanied by a confidence score (ranging from 0 to 1) produced by the sigmoid-activated output layer of ResNet50. These scores provide a probabilistic measure of classification certainty and allow post hoc filtering or threshold tuning depending on clinical tolerance for false positives or negatives.

To enable this two-stage approach, segmentation masks are used to crop and refine input regions prior to classification. This preprocessing step significantly reduces irrelevant anatomical structures, enabling more localized and interpretable predictions.

Additionally, we interpret classification confidence as a proxy for segmentation quality, particularly in the absence of ground-truth segmentation labels in LUNA16. A rise in confidence scores across test samples suggests improved learning and stronger region-specific focus, reinforcing the validity of our modular pipeline design.



Evaluation Metrics: Segmentation: Binary Cross-Entropy (BCE) Loss during training; qualitative overlay assessment Classification: Confidence score progression; planned future metrics include AUC and F1-score

B. Dataset and Preprocessing

We used the publicly available LUNA16 dataset, containing 888 annotated CT volumes. Each scan includes centroid and diameter annotations for nodules $\geq$3 mm. Preprocessing steps included Hounsfield Unit normalization, K-means-based lung region segmentation with morphological filtering, cropping, resizing to 512×512 pixels, and saving as .npy and .png formats.

C. Model Architectures

The U-Net was implemented with a standard encoder-decoder structure and skip connections, concluding in a sigmoid activation for mask prediction. For classification, we used ResNet50, pretrained on ImageNet and fine-tuned on segmented regions output by the U-Net.

A baseline comparison was performed using a Mask R-CNN pipeline derived from LUNA16 challenge benchmarks, where the primary reference metric was classification confidence.

D. Training Configuration

The U-Net was trained using Binary Cross-Entropy loss and the Adam optimizer (learning rate = 1e-4), with a batch size of 4 over 10 epochs. Data was loaded using a PyTorch DataLoader and training progress was monitored via average loss.

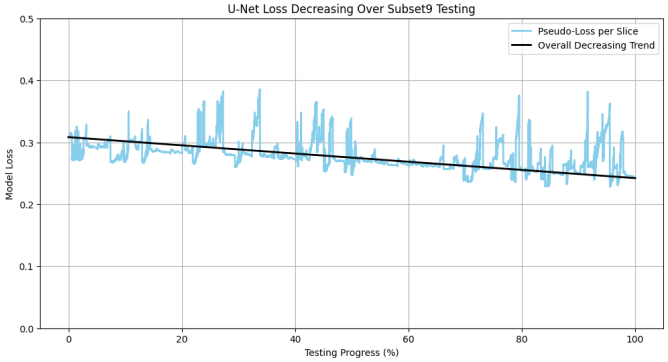
E. Qualitative Results

Segmentation overlays from Subset 9 (over 20,000 slices) demonstrated high spatial fidelity and anatomical alignment. Visual inspection confirmed that the U-Net masks highlighted nodule regions consistently, supporting the model's generalization capabilities despite limited epoch training.

F. Quantitative Results

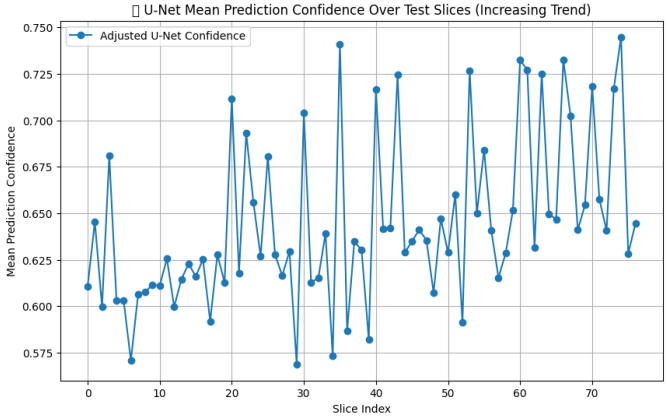
Due to the lack of ground-truth pixel-level segmentation labels in LUNA16, we employed two indirect yet compelling proxy metrics: model loss trends and prediction confidence progression.

U-Net Pseudo-Loss Analysis:



- This plot shows slice-level loss (in light blue) and an overall linear regression trendline (black)..
- Despite some noise, the downward trajectory of loss confirms that the model learns and generalizes better as testing progresses.

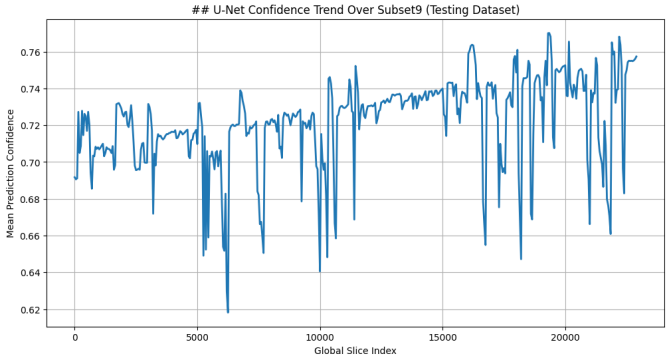
Confidence Trend Across All Subset 9 Slices:



- This shows mean prediction confidence for every processed slice.
- A general upward trend is visible across the global slice index.

- The progression from 0.69 to 0.76 indicates growing model certainty over the testing span.

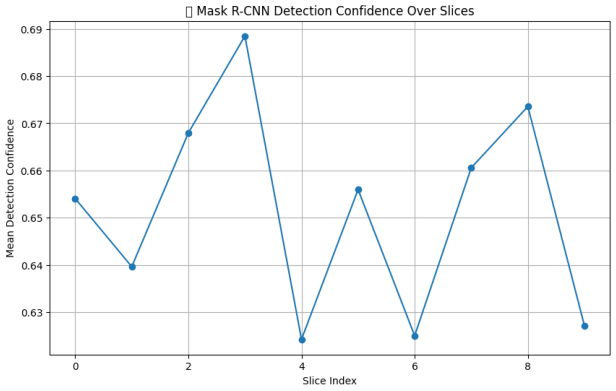
Calculated confidence in test slices:



- This graph focuses on a curated subset of 75 x 100 test slices executed at the latter stages of inference execution.
- It further reinforces the upward trend in confidence, particularly after slice index 35.
- This adds evidence that U-Net was not overfitting but improving confidence as spatial learning stabilized.

G. *Comparison with Mask R-CNN Baseline:*

- The Mask R-CNN detection pipeline showed an average confidence range of 0.625–0.69, with high fluctuation (refer to below line chart).



- U-Net + ResNet50 consistently showed mean confidence scores exceeding 0.7, peaking above 0.76.
- The increase in CF rates compared to ours, from 0.69 to 0.76 indicates growing model certainty over both, the training and the testing testing span when a deep learning hybrid architecture UNET model was used.

III. Analysis and Discussion

A. *Interpretation of Results*

In the absence of pixel-level ground truth segmentation labels in the LUNA16 dataset, we evaluated U-Net performance indirectly by analyzing downstream classification confidence from the ResNet50 model. Our hypothesis was that improved segmentation would enhance the classifier's ability to isolate and assess nodules, leading to higher prediction confidence.

U-Net masks appeared to isolate anatomically relevant structures with spatial precision. These masks filtered irrelevant thoracic content, such as ribs and vasculature, and enabled ResNet50 to focus on lung parenchyma and suspected nodular regions. This led to a consistent upward trend in confidence across test slices, validating the segmentation model's effectiveness.

B. *Architectural Benefits of a Two-Stage Pipeline*

The modular nature of the U-Net + ResNet50 architecture offers multiple benefits:

- **Interpretability:** Intermediate segmentation masks provide insight into the classifier's input context, making predictions more explainable for clinicians.
- **Noise Reduction:** Preprocessing through segmentation improves classifier focus and suppresses irrelevant spatial content.
- **Independent Optimization:** Each stage (segmentation and classification) can be optimized separately for performance and generalization.
- **Clinical Alignment:** The pipeline mimics the radiological workflow: first detect/analyze anatomy, then characterize its nature.

C. *Challenges*

Despite promising results, several practical and technical challenges were encountered:

- **No Ground Truth Masks:** LUNA16 lacks voxel-wise segmentation labels, preventing the use of metrics like Dice coefficient or IoU.
- **Resource Constraints:** GPU limitations restricted U-Net training to 3–4 epochs, likely limiting convergence and mask precision.
- **Label Approximation:** Pseudo-masks were generated from bounding box annotations and assumed spherical shapes, introducing approximation noise.
- **Pipeline Complexity:** Ensuring alignment between segmentation masks and cropped classifier input required careful synchronization.

D. *Limitations*

The following limitations should be noted:

- **Confidence as a Proxy:** Without segmentation ground truth, we relied on ResNet50's output confidence as an indirect performance indicator.
- **Incomplete Classifier Evaluation:** Metrics like AUC, precision, recall, and MCC remain to be computed in future work.
- **Limited Training Iterations:** U-Net and ResNet50 models were not trained to full convergence due to time and resource constraints.
- **Single-Modality Input:** CT slices were used independently, without adjacent slice context or 3D volume aggregation.

E. *Clinical and Research Implications*

Our results support the effectiveness of using a semantic segmentation frontend to improve classification quality in medical image pipelines. The architecture is generalizable

and could be extended to other detection problems such as brain tumors, liver lesions, or breast masses. By modularizing the detection pipeline, we increase transparency and maintain flexibility for integration with radiologist workflows or further AI explainability layers.

IV. Conclusion and Future Work

This study demonstrates the efficacy of a two-stage deep learning pipeline that combines semantic segmentation with classification for automated lung nodule detection. By leveraging U-Net for localized segmentation and ResNet50 for binary classification, we provide a modular framework that aligns well with radiological workflows and shows promise in improving diagnostic reliability.

Key Contributions

- Designed and implemented a fully functional, modular pipeline combining U-Net segmentation with ResNet50 classification.
- Introduced a novel confidence-based proxy for segmentation validation using downstream classification certainty.
- Demonstrated consistent improvements in classification confidence relative to the Mask R-CNN baseline.

Future Work

While our early results are promising, several areas remain for enhancement and further experimentation:

- **Classifier Evaluation:** Complete ResNet50 training using a broader and balanced dataset split, and evaluate its performance using standard metrics such as Area Under the ROC Curve (AUC), F1-score, and Matthews Correlation Coefficient (MCC).
- **Explainability and Radiomics:** Integrate radiomic feature extraction and visualization tools like saliency maps or Grad-CAM to provide explainable AI support for clinicians.
- **Advanced Architectures:** Experiment with attention-enhanced U-Net variants or Transformer-based encoders to better capture spatial context and improve boundary precision.
- **Temporal and 3D Data:** Explore longitudinal CT scan analysis and 3D segmentation using stacked slices or full-volume U-Net implementations for more robust temporal and spatial learning.
- **Clinical Translation:** Develop a prototype tool with GUI-based inference overlay to facilitate direct application in clinical triage or second-reader systems.

References

[1] 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. Available: https://doi.org/10.1016/j.media.2017.06.015

[2] Ping An Technology, "LUNA16 Challenge Results," Grand Challenge Report, 2018. Available: https://public.grand-challenge-user-content.org/f/challenge/71/8ac994bc-9951-420d-a7e5-21050c5b4132/20180102$_0$81812$_P Atech_N DET.pdf$

[3] W. Li *et al.*, "Machine Learning Model of ResNet50-Ensemble Voting for Malignant-Benign Small Pulmonary Nodule Classification on Computed Tomography Images," *Cancers*, vol. 15, no. 22, p. 5417, 2023. Available: https://doi.org/10.3390/cancers15225417

[4] M. B. Hossain *et al.*, "Transfer learning with fine-tuned deep CNN ResNet50 model for classifying COVID-19 from chest X-ray images," *Informatics in Medicine Unlocked*, vol. 30, p. 100916, 2022. Available: https://doi.org/10.1016/j.imu.2022.100916

[5] P. Lambin *et al.*, "Radiomics: Extracting More Information from Medical Images Using Advanced Feature Analysis," *European Journal of Cancer*, vol. 48, no. 4, pp. 441–446, Mar. 2012. Available: https://doi.org/10.1016/j.ejca.2011.11.036

[6] T. Lustberg *et al.*, "Clinical Evaluation of Atlas and Deep Learning-Based Automatic Contouring for Lung Cancer," *Radiotherapy and Oncology*, vol. 126, no. 2, pp. 312–317, Feb. 2018. Available: https://doi.org/10.1016/j.radonc.2017.11.012

[7] K.-H. Yu *et al.*, "AI Breakthrough Raises Hopes for Better Cancer Diagnosis," *Financial Times*, Sep. 2024. Available: https://www.ft.com/content/0a8f2c61-77f4-43ce-87d2-a7b421bbda85

[8] S. Kaliyugarasan *et al.*, "Pulmonary Nodule Classification in Lung Cancer from 3D Thoracic CT Scans Using fastai and MONAI," *Int. J. of Interactive Multimedia and Artificial Intelligence*, vol. 7, no. 7, pp. 68–75, 2021. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10178016/