# Use of a Deep Learning Artificial Intelligence Model for Differentiating Alveolar/Bronchiolar Adenomas and Carcinomas of the Lung in B6C3F1 Mice


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## Background

- Toxicologic pathology is rapidly transitioning to digitalization. The use of digital pathology (DP) combined with novel technologies such as artificial intelligence (AI) platforms, particularly deep learning (DL) (a subclass of AI), to assist pathologists in diagnosing lesions on pathology slides is increasing.
- Standard diagnostic toxicologic pathology is an expensive, time-consuming, labor-intensive process and hence there has been a growing need to develop faster, automated processes that would reduce costs and improve diagnostic accuracy and consistency to facilitate more efficient workflows.
- Development and use of automated DL/AI algorithms designed to objectively detect and classify proliferative lesions may be useful in assisting with decisional support in performing diagnostic toxicologic pathology.

## Objective

- Explore the use of AI/DL for routine diagnostic purposes in toxicologic pathology.
- Develop and train a computer-assisted, automated AI model/algorithm using convoluted neural network (CNN) to assist with diagnosis of mouse lung tumors in digital whole-slide image (WSI) scans of lung tissue sections.
- Apply the trained AI algorithm retrospectively to pathologist peer reviewed alveolar/bronchiolar (A/B) adenoma and carcinoma diagnoses to test the neural network's concordance with the peer reviewed diagnoses.

## Methods

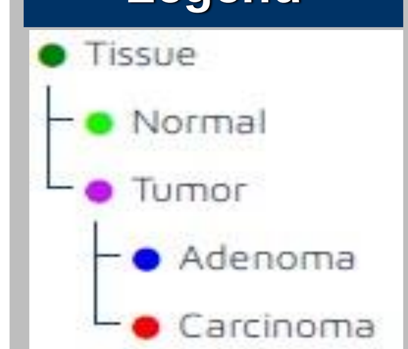
- Hematoxylin & Eosin-stained sections of B6C3F1 mouse lung tumors mounted on glass slides from US National Toxicology Program studies were scanned at 40X using a NanoZoomer S60 Digital WSI scanner.
- The digitized WSI (resolution = 0.2473 µm per pixel) were uploaded to the Aiforia™ Cloud Version 5.1.1 image processing and management platform (Aiforia Inc., Cambridge, United States) for processing with DL/CNNs and supervised learning.
- Using hand-drawn annotations on the digitized images, a supervised, multi-layered, CNN algorithm was created and trained to detect and recognize normal and tumor tissue, and the histological features/patterns that distinguish A/B adenoma from A/B carcinoma.
- The AI algorithm was trained on a diverse and representative data set of 27 WSI of mouse lung tumors to create a generalizable deep learning model.
- Known tissue artifacts were identified and trained into the AI model to exclude them from the analysis as background.
- Finally, the trained AI model was applied to WSI data set of 70 lung tumors (17 A/B adenomas; 53 A/B carcinomas) with known, NTP peer-reviewed diagnoses uploaded to the Aiforia™ Cloud platform.

**https://cloud.aiforia.com/Public/NIH_NIEHS_Herbert/uM3y-F5ftP_YhpUrSag3rz-QNWEHrg0SWuQBbPiUI2g0**

**Scan the code with your smart phone camera to view the results**

1. Click on a photo
2. Select "% Analyze" on the right side of the screen
3. Press "LungTumor_Tissue1Ki_FOV500_noaug"
4. View the results

## Legend




## Methods

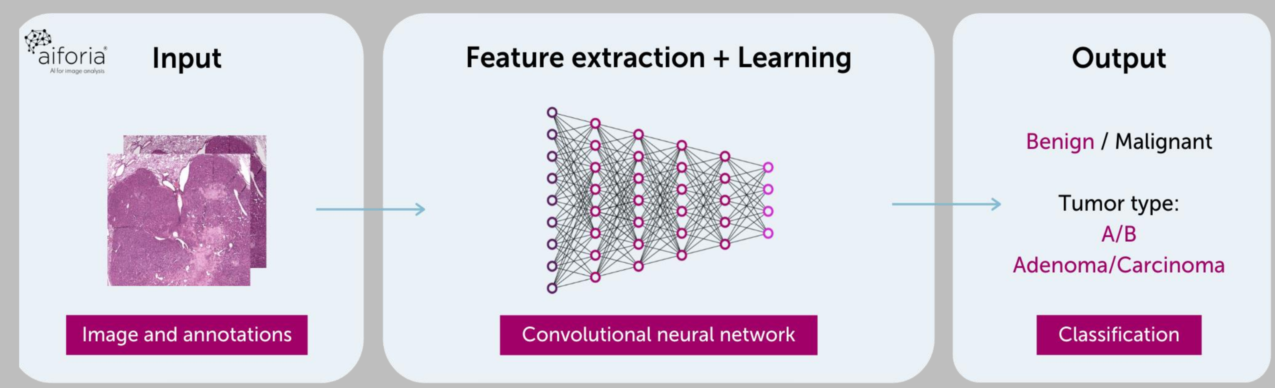
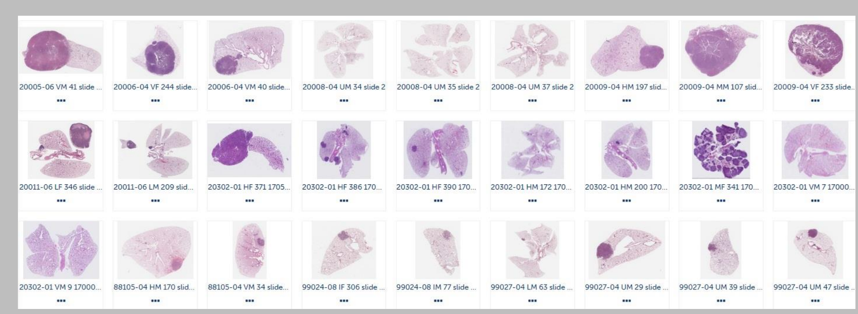



**Fig 1. Training workflow overview**



**Training Data Set:**
11 Adenoma
11 Carcinoma
5 Normal

**Fig 2. Variability in WSI used in the AI model training image set**

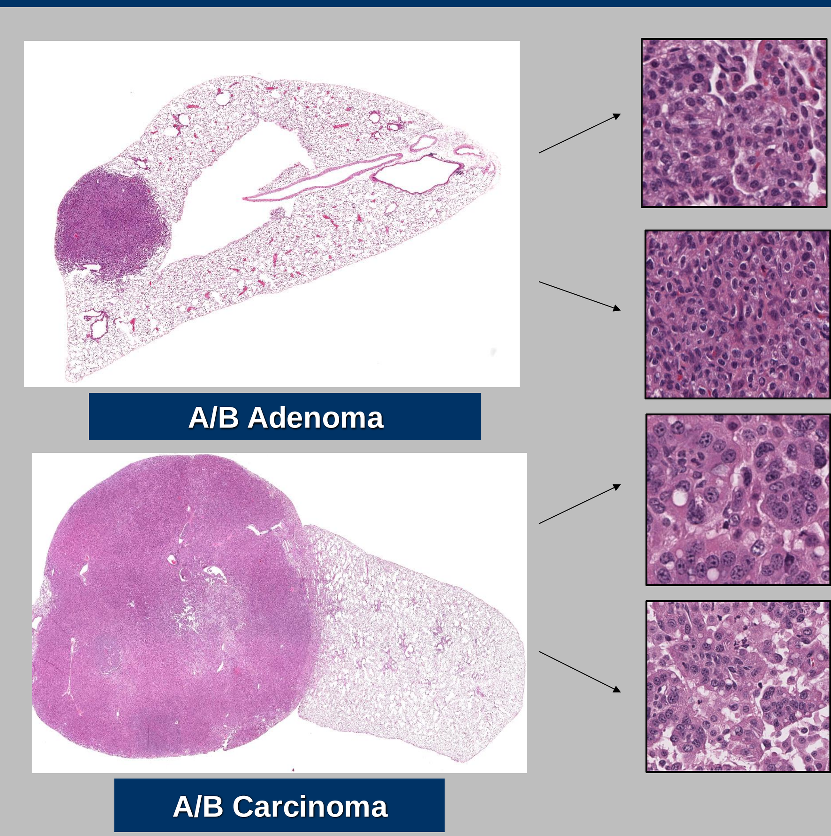



**Fig 3. Examples of adenoma and carcinoma patterns**

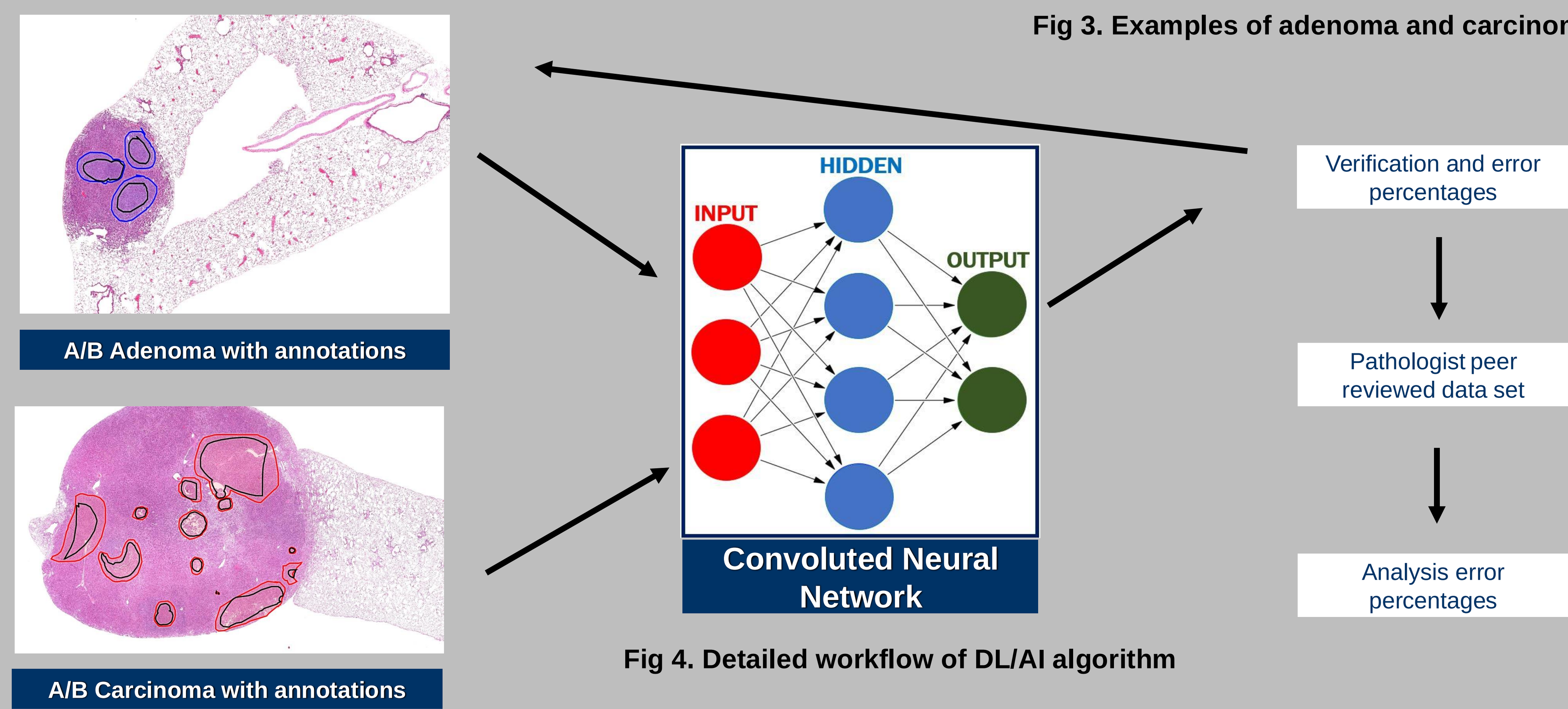
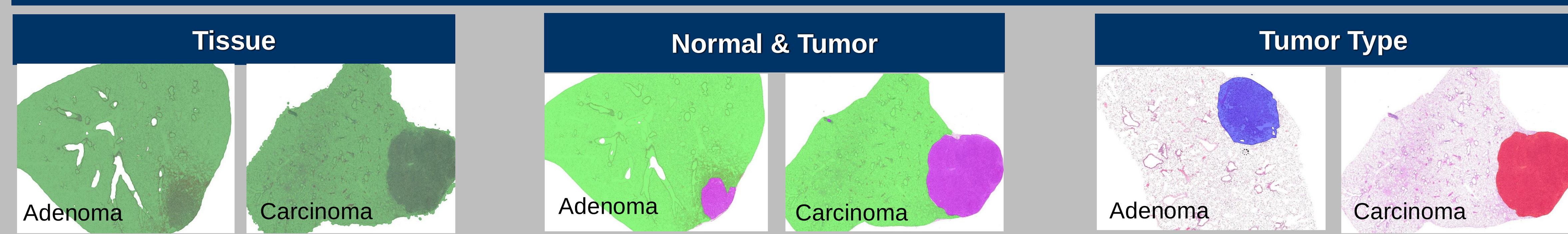



**Fig 4. Detailed workflow of DL/AI algorithm**

## Results

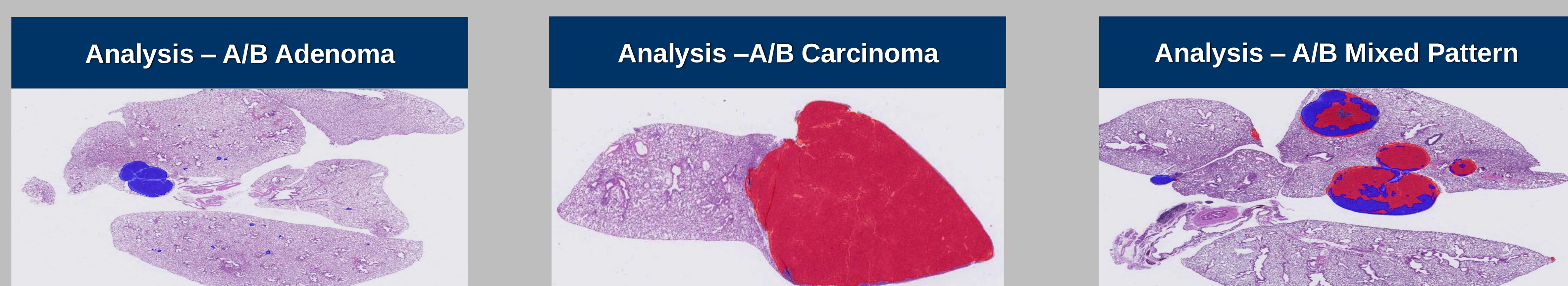



Tissue segmentation (mm²) identified by the trained AI model in dark green.

Normal segmentation (mm²) identified by the trained AI model in light green and tumor in purple.

Segmentation (mm²) identified by the trained AI model with adenoma in blue and carcinoma in red.

**Fig 5. WSI AI analysis results**




Adenoma identified by the trained AI model in blue.

Carcinoma identified by the trained AI model in red.

Carcinoma identified by AI model in red due to higher percentages.

**Fig 6. Analysis of NTP study set**

## Results

**(7a.) Verification Sensitivity Rates:**
Tissue layer 99.9%
Tumor/Normal layer: 98.4%
Adenoma/Carcinoma layer: 77.1%

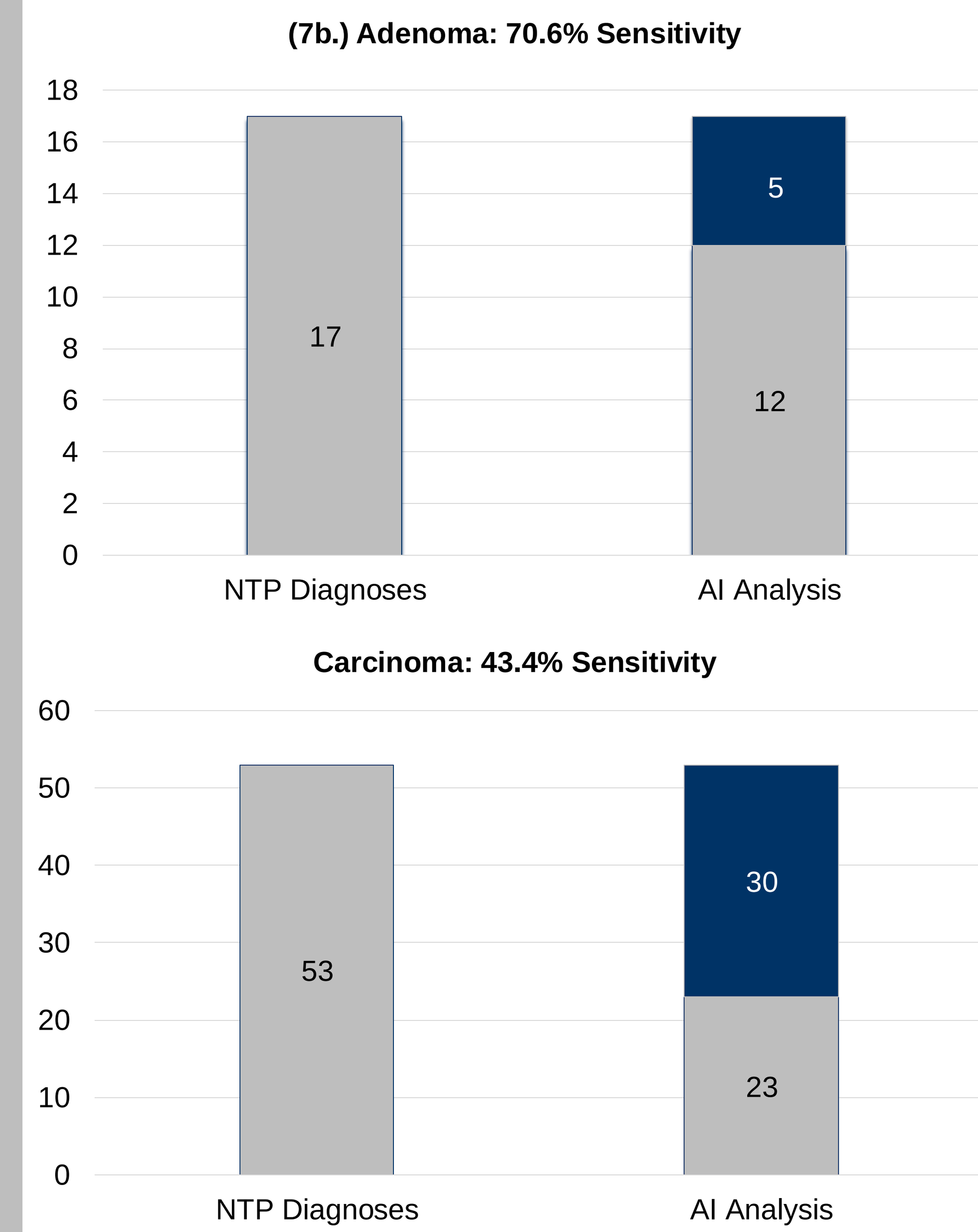



**Fig 7b. Comparison of results from NTP diagnoses and AI analysis.**

## Conclusion

- Results suggest that the CNN algorithm could increase sensitivity for classifying carcinomas, and an automated model to screen, detect, and diagnose proliferative lesions in lung tissue sections from B6C3F1 mice.
- Increasing annotations and images to the data set are likely to improve the CNN to decrease error percentages.

## References


Tokarz DA, *et al* (2021). Using Artificial Intelligence to Detect, Classify, and Objectively Score Severity of Rodent Cardiomyopathy. *Toxicol Pathol*. Vol. 49(4):888-896.

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## Acknowledgements


We thank Ms. Eli Ney of the NIEHS Imaging Core Laboratory for her expert assistance editing the layout of the poster.