# Towards deep learning segmentation of lung nodules using micro-CT data

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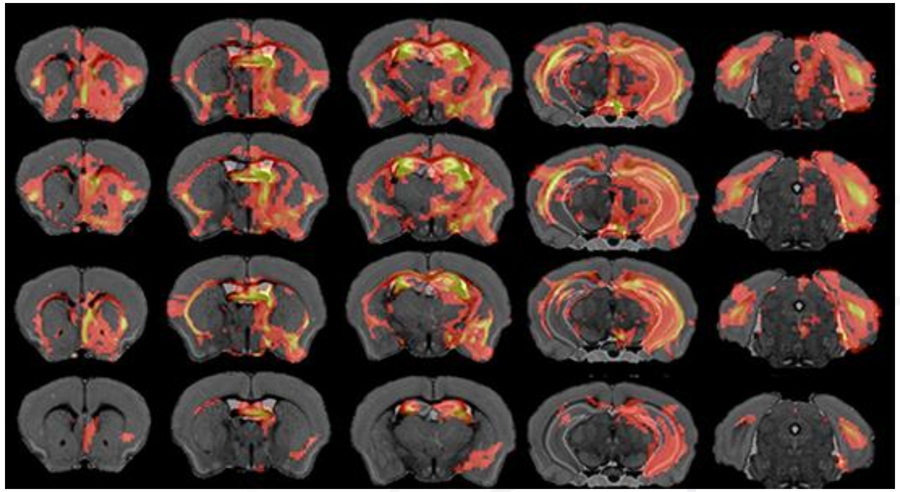
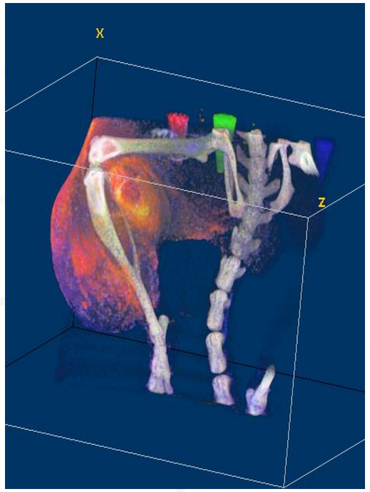
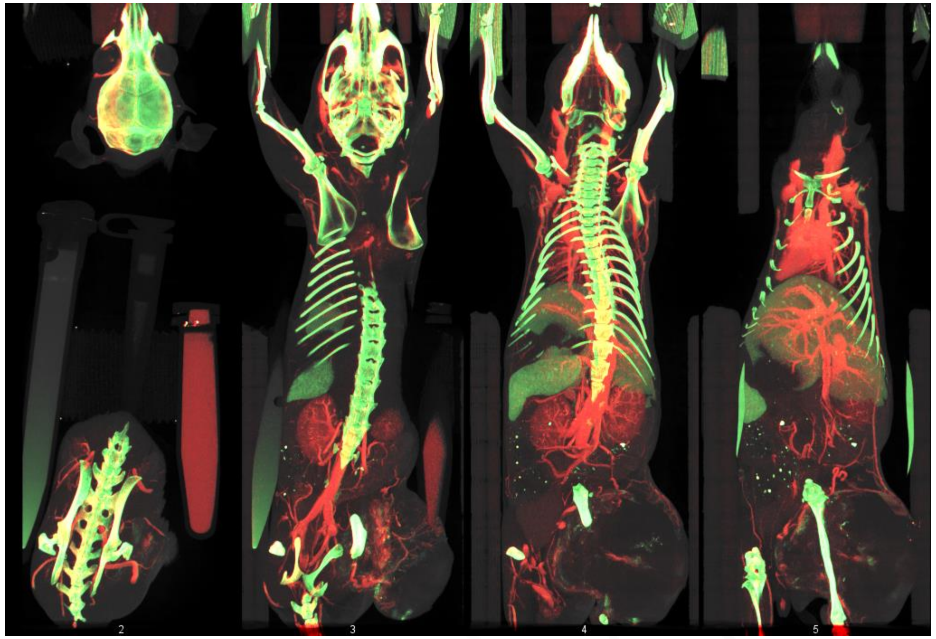
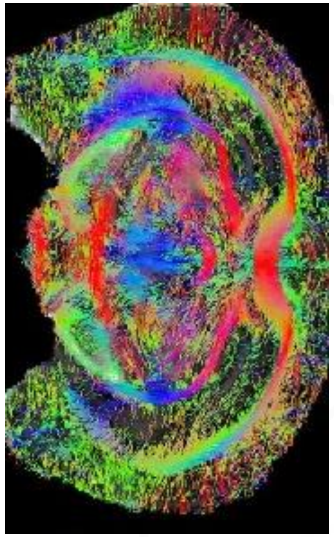
# QIAL Quantitative Imaging and Analysis Lab

https://sites.duke.edu/qial/



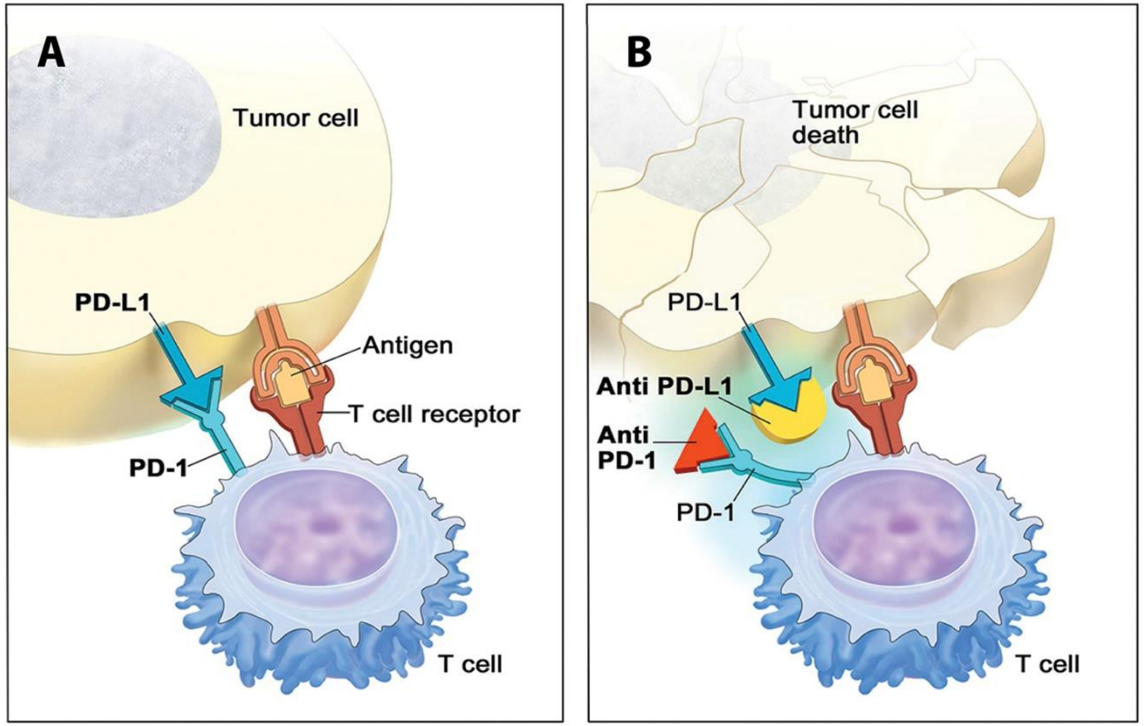






# Background

- We are involved in a co-clinical trial studying synergy between immune checkpoint block and radiotherapy
- Small animal imaging enhances the simulation of clinical practice
- High resolution images can describe changes in tumors over time and treatment




https://www.genengnews.com/magazine/312/supplement-cancer-immunotherapies-development-barriers/


[1] S. J. Blocker *et al.*, "Bridging the translational gap: Implementation of multimodal small animal imaging strategies for tumor burden assessment in a co-clinical trial," *PloS one*, 2019.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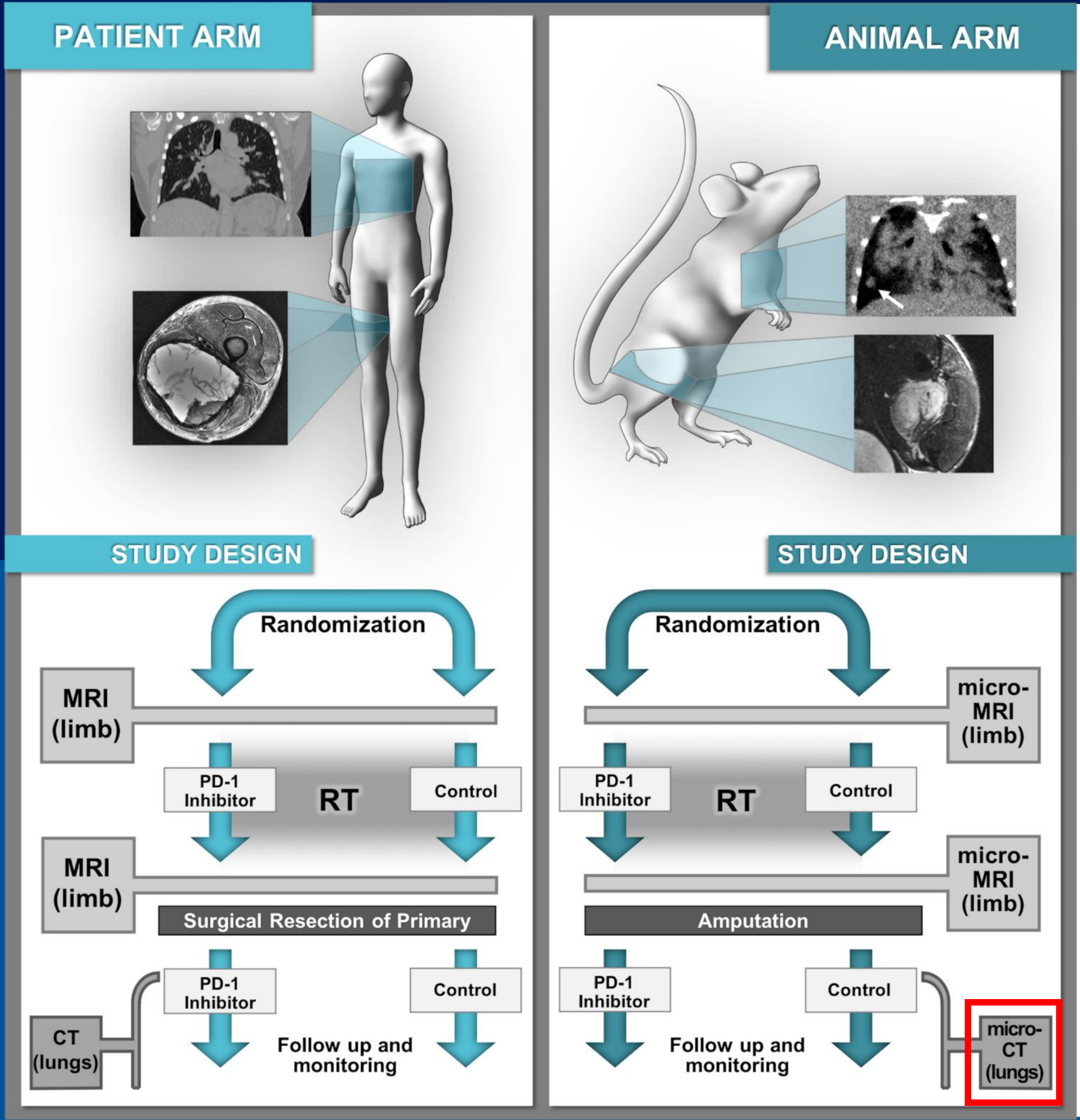


# Preclinical trial

Mouse model:

- *p53*$^{fl/fl}$ mouse model [1]
- Hind limb sarcoma generated by delivery of Adeno-Cre followed by carcinogen 3-methylcholanthrene
- High probability of lung metastases

Trial Protocol:

- MR imaging
- RT (20 Gy) on a small animal irradiator
- One week later, the mice were re-imaged
- Tumor was surgically removed by amputating the tumor-bearing hind limb
- Mice are periodically screened for lung tumors using micro-CT for up to 6 months

**Study is ongoing**

[1] S. J. Blocker *et al.*, *PloS one*, 2019.

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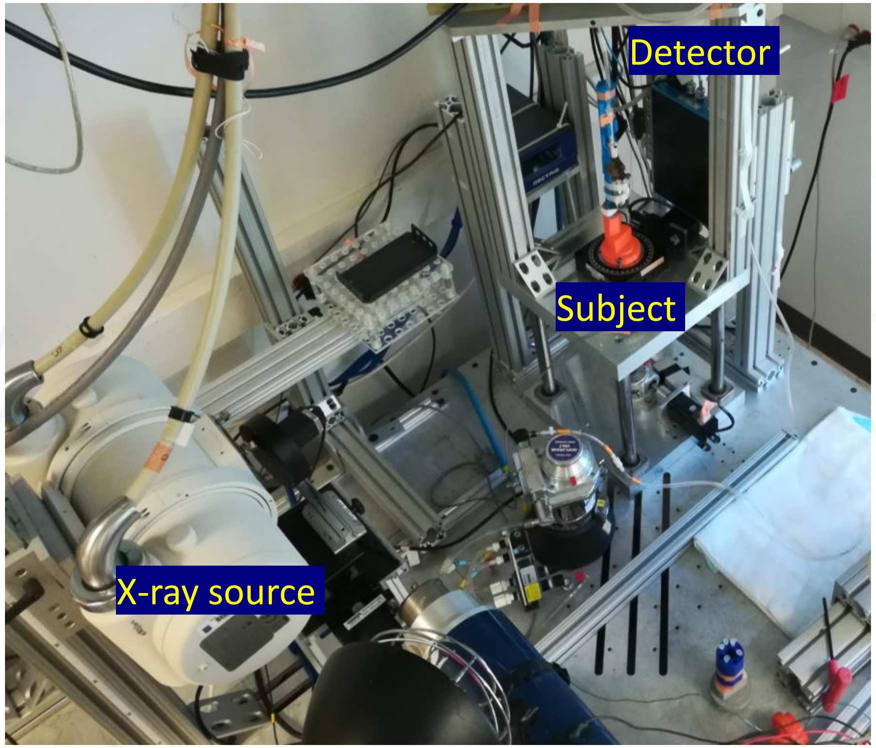
# Micro-CT Imaging Protocol

- Scanning was performed using a micro-CT developed in-house
- A pneumatic pillow allows for respiratory gating
- Acquisition settings:
  - 80 kVp, 40 mA, 10 ms exposures
  - 360 views over 360° rotation
  - Radiation dose: 17 mGy (~300 less than LD50/30)
- Reconstruction settings:
  - Filtered backprojection via Feldkamp algorithm [1]
  - Bilateral filtration to reduce noise
  - 63 µm isotropic voxels




[1] Feldkamp *et al.*, J Opt Soc Am, 1984.

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# Project goal

Build and evaluate a deep learning solution for detection of lung tumors in preclinical micro-CT scans.

# Overcoming data scarcity

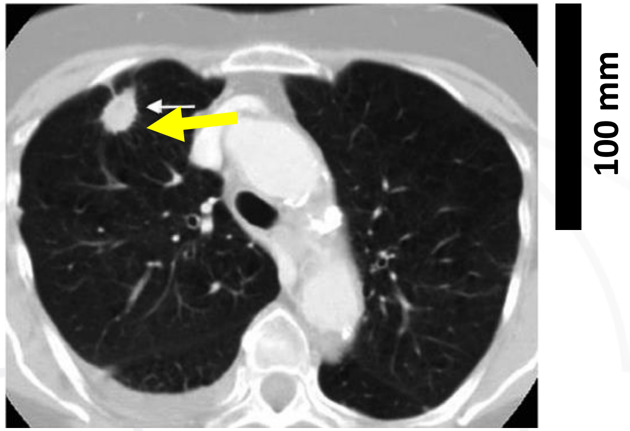
## Data scarcity

- Repositories of micro-CT lung scans for mice are not readily available
- Building a micro-CT dataset is intensive
  - Our preclinical trial is in progress
  - We would like to use an automated tool during the trial

## Solution

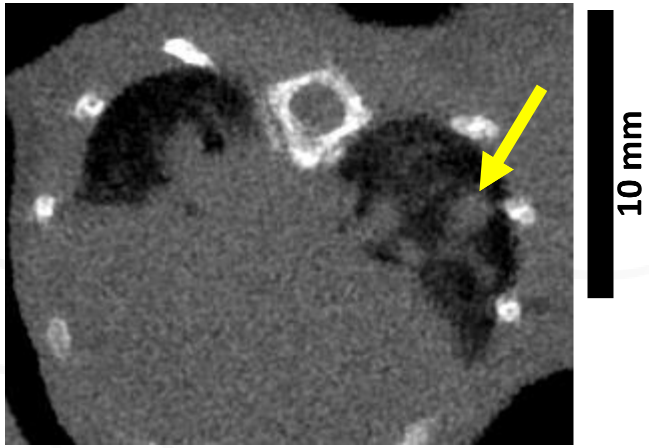
- Create synthetic training sets with similar attributes as micro-CT data

Human CT




Source: LIDC/IDRI Database

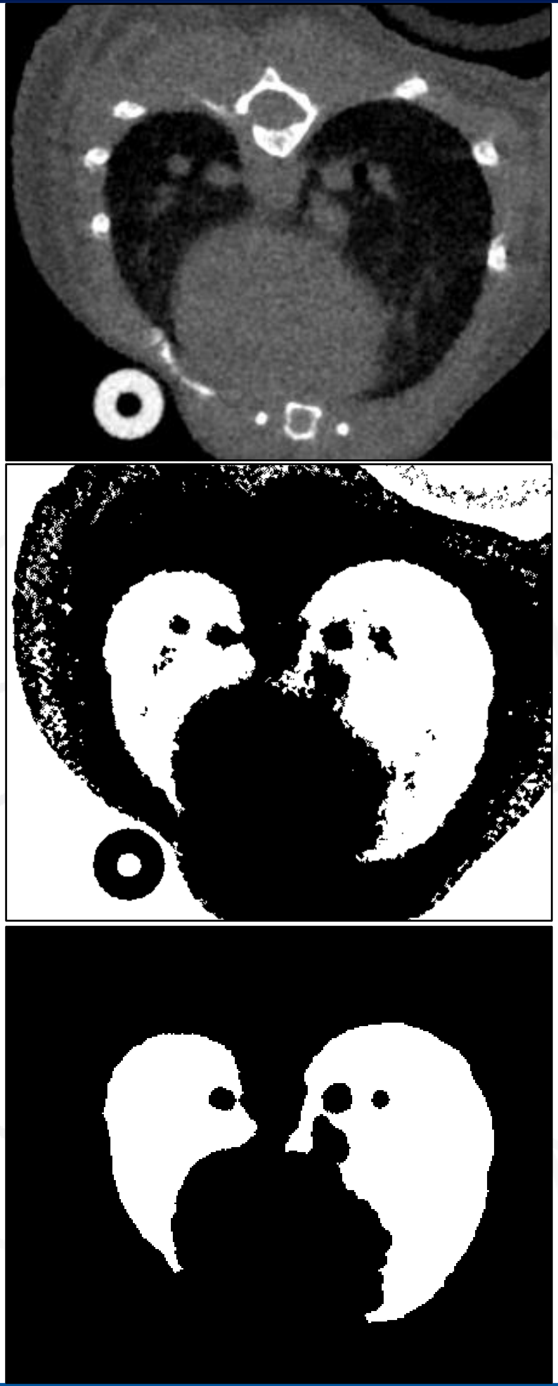
Mouse micro-CT



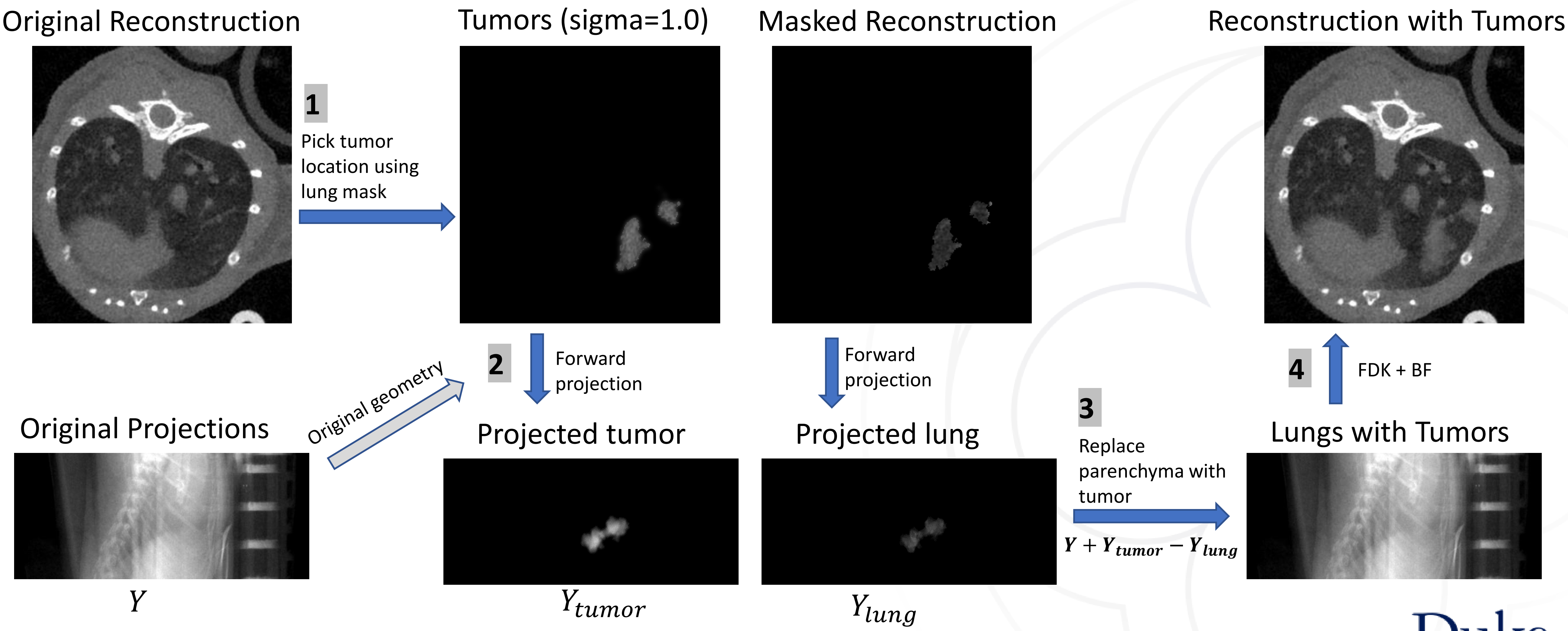
# Lung segmentation

First step for creating datasets and processing detection output

- Lung masks are created via thresholding
- Regions are smoothed
- Filtered based on:
  - HU values
  - Location
  - Region size and shape



# Overcoming data scarcity with synthetic data

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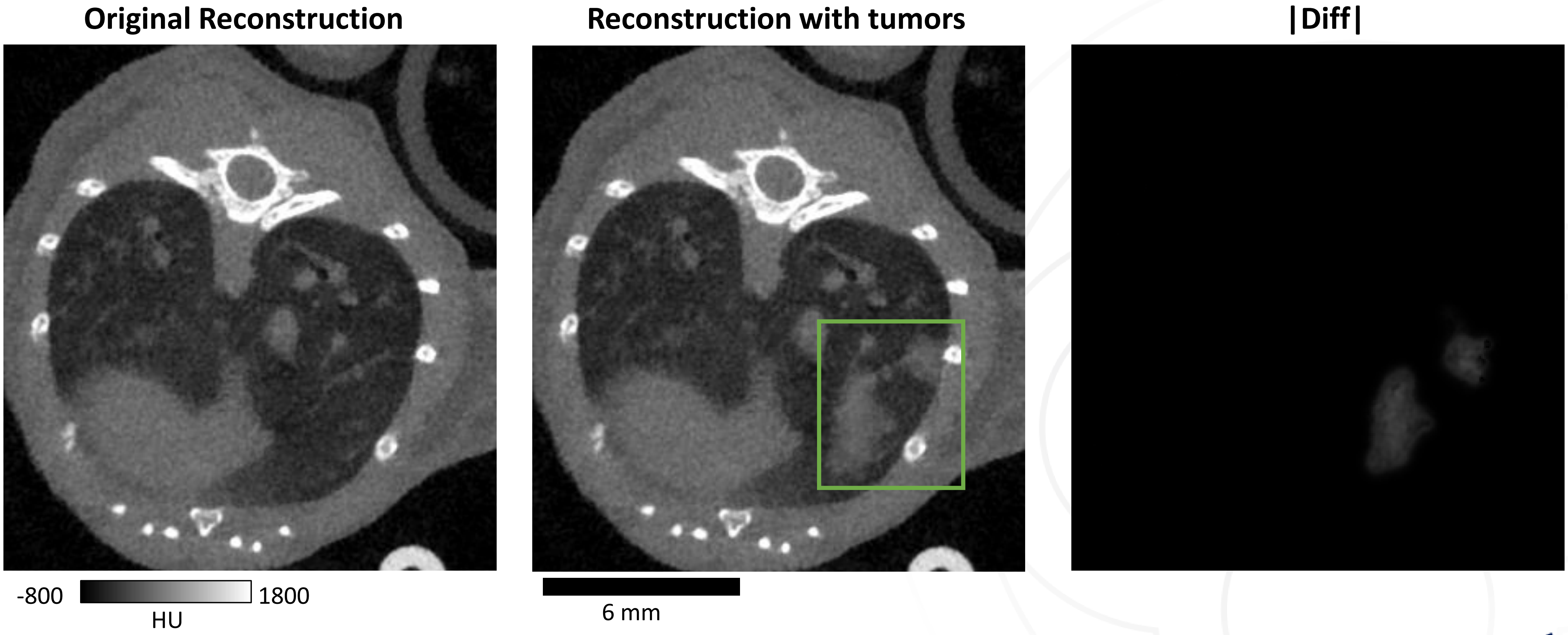
# Synthetic tumor analysis

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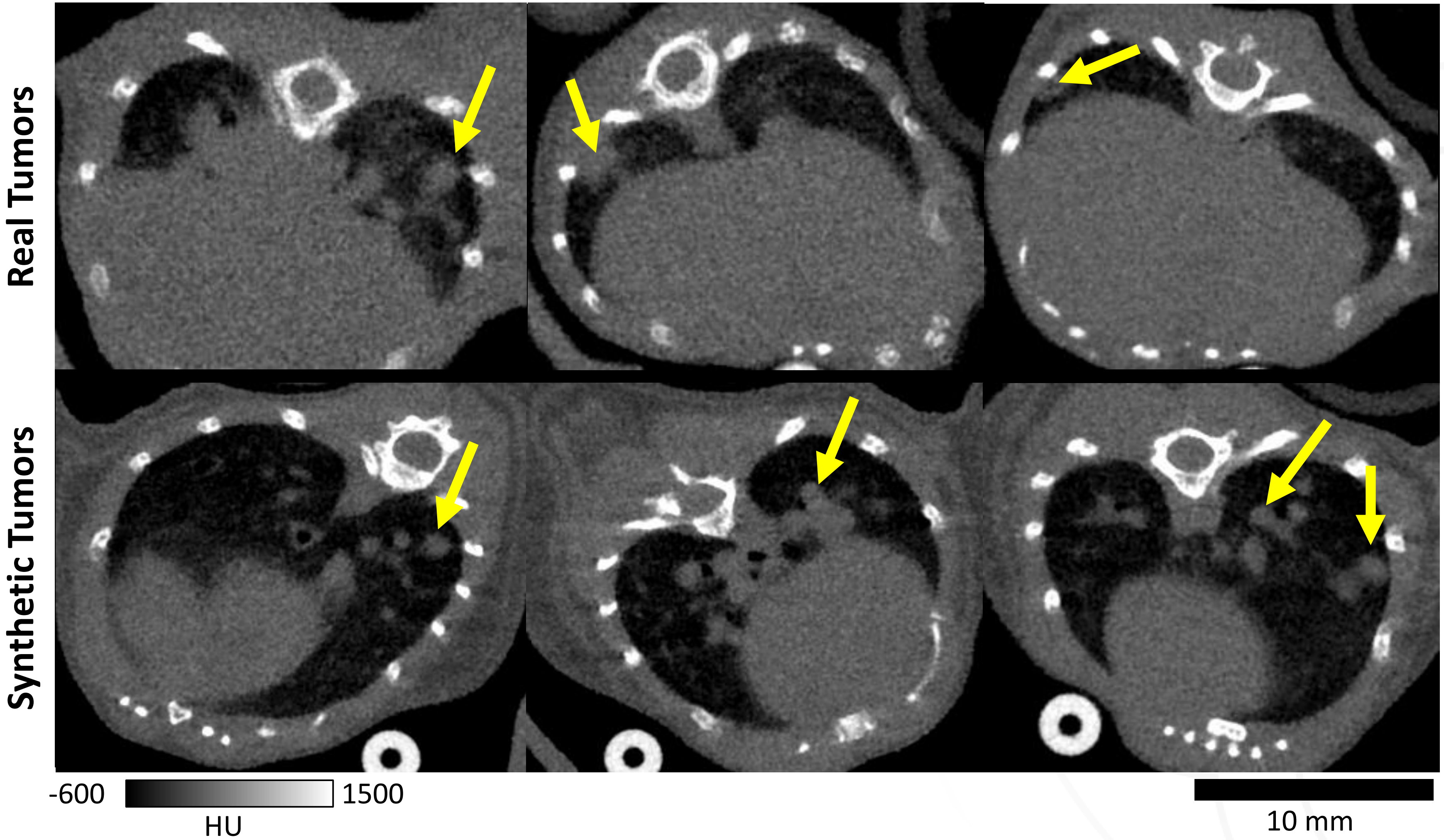
# Comparison of Real and Synthetic data



# Training and testing datasets

**Simulated datasets**

- Random combinations of
  - 7 segmented lung tumors
  - 6 healthy lung scans
- 0 to 2 tumors were warped and placed in each scan
  - Location favored lung boundaries
- **60 training sets**
- **13 validation sets**

**Real datasets**

- 5 scans of mice with tumors
  - Heavy tumor burden
- 3 training sets
- 2 test sets

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# Network Structure

V-Net [1] structure

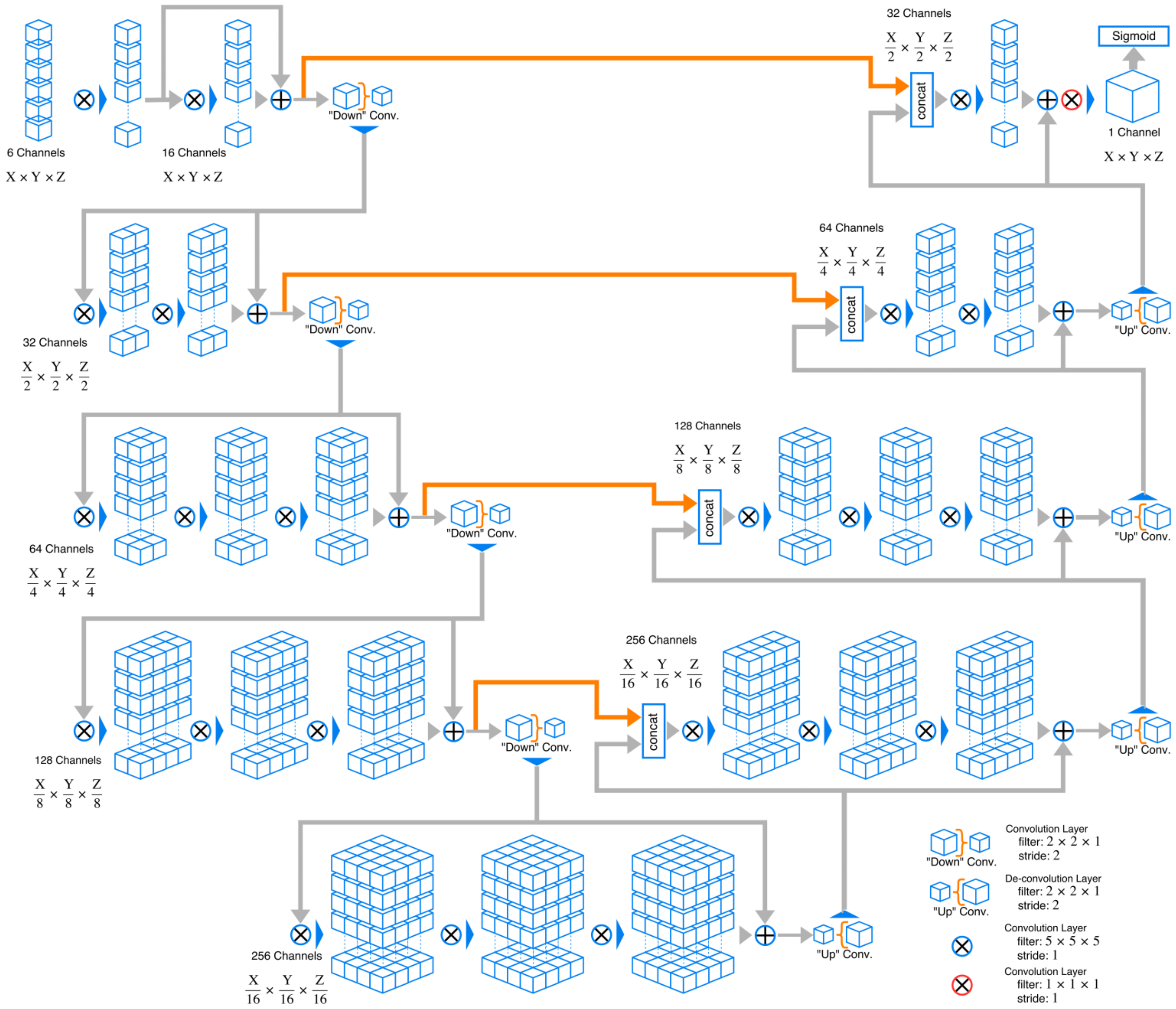
- Designed for volumetric images
- Inputs: 3D image patches
  - 96 x 96 x 96 voxels
- Outputs: 3D binary label

Dice loss function

$$Dice = 2 * \frac{|Prediction\ - Truth|}{|Prediction| + |Truth|}$$

Training

1. Wholly synthetic training
2. Transfer learning on small real dataset




https://github.com/MiguelMonteiro/VNet-Tensorflow

[1] Milletari et al., 2016.

# Post processing

- Results outside of lung mask are rejected
- Overlap between labeled tumors and detection maps constitute detection
    - Predicted regions with too few voxels (> 15) were ignored.
- Network output is a volume with continuous range of values [0, 1]
- Ideal detection thresholds are found by computing precision and recall curves

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# Initial training results: Precision and Recall

Precision

- Accuracy of positive prediction

$$precision = \frac{TP}{FP + TP}$$

Recall

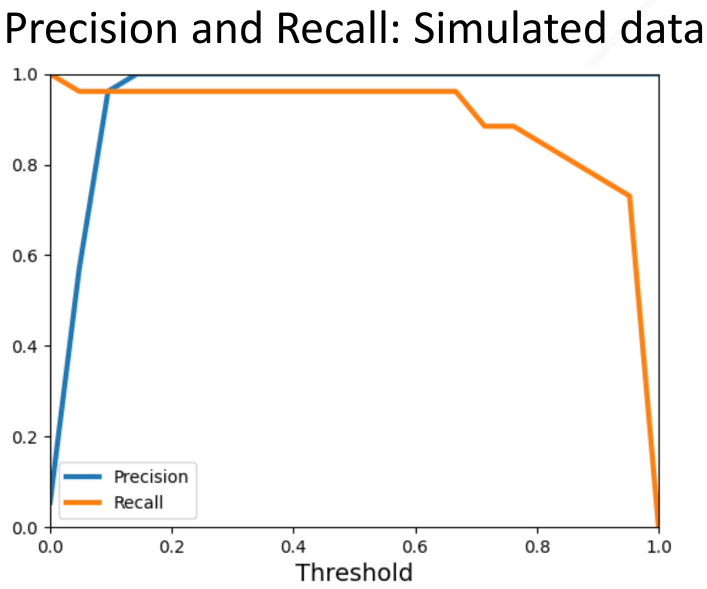
- Ratio of correct positives

$$recall = \frac{TP}{FP + FN}$$

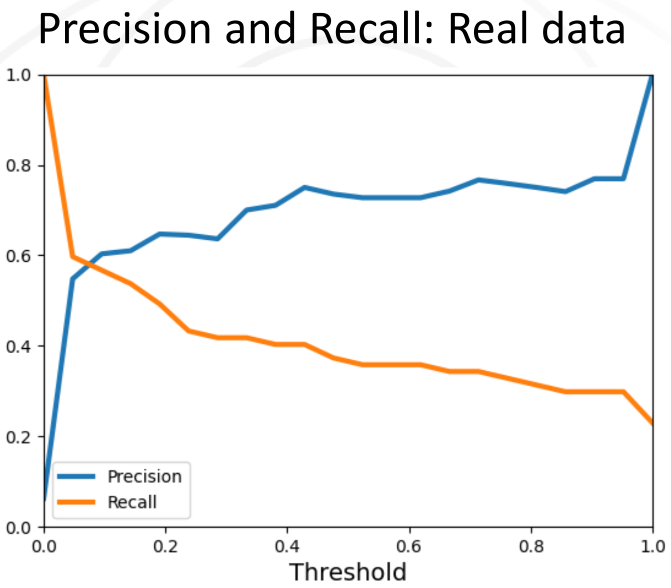
Useful to find a decision threshold for probabilistic (float) outputs

- Dependent on task
- Often the intersection of precision and recall is chosen

<u>Initial Training</u>




<u>Final Training</u>

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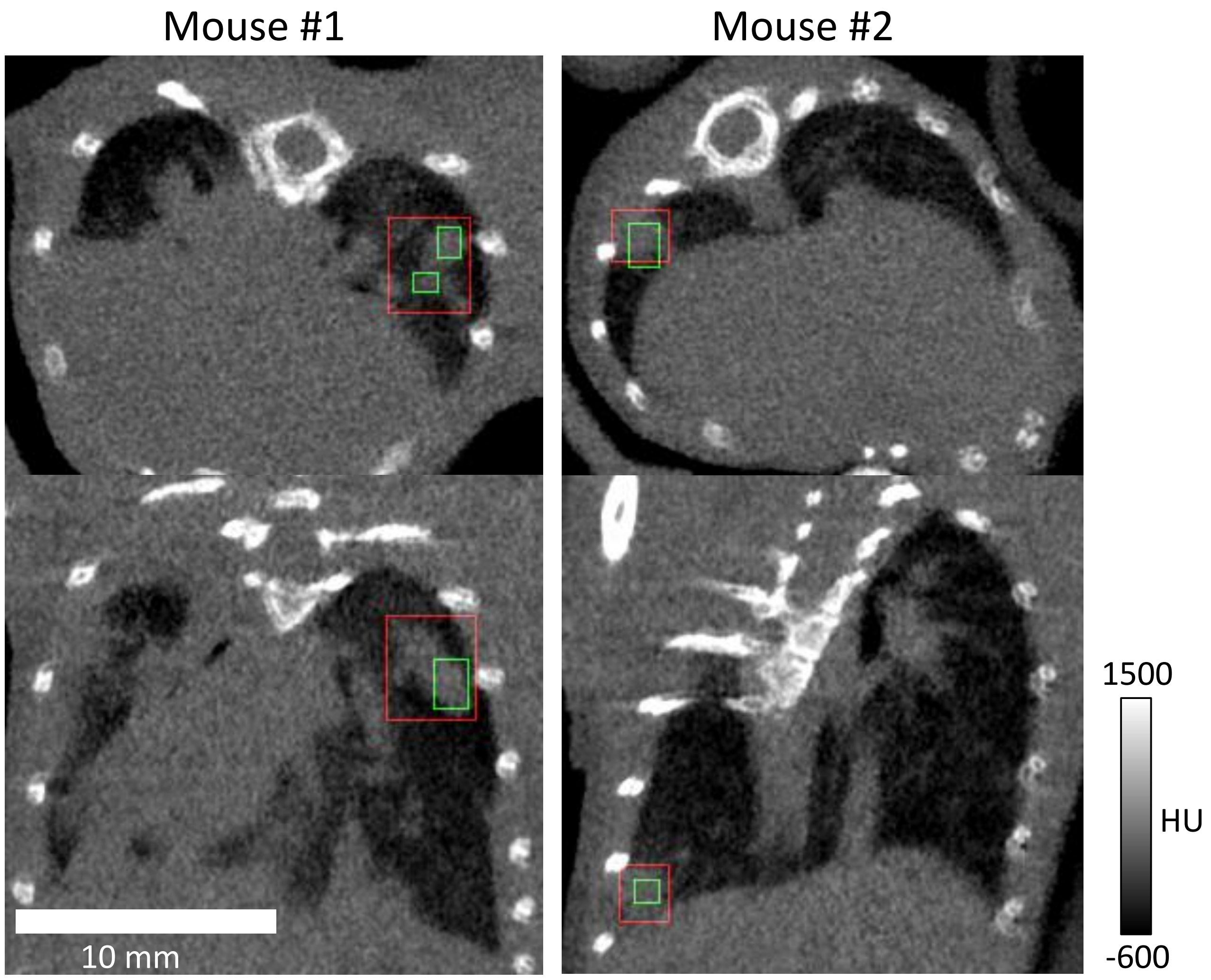
# Detection results after transfer learning




Lung tumor detection from 2 test mice

- Labels marked by observer
- Network predictions

All tumors were found in these two mice.

- Due to thresholding in continuous images predicted tumors often appear smaller than the label

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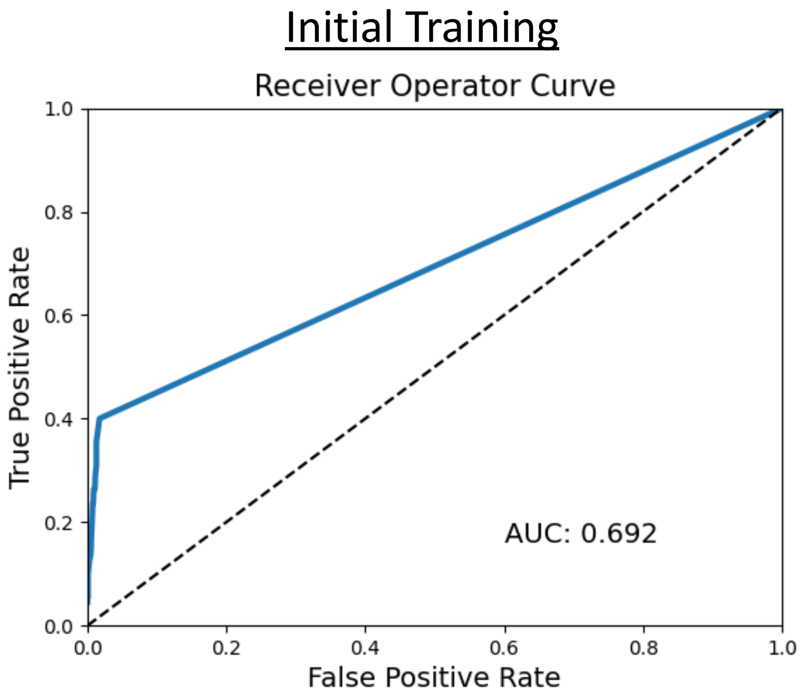
# Effect of transfer learning: ROC

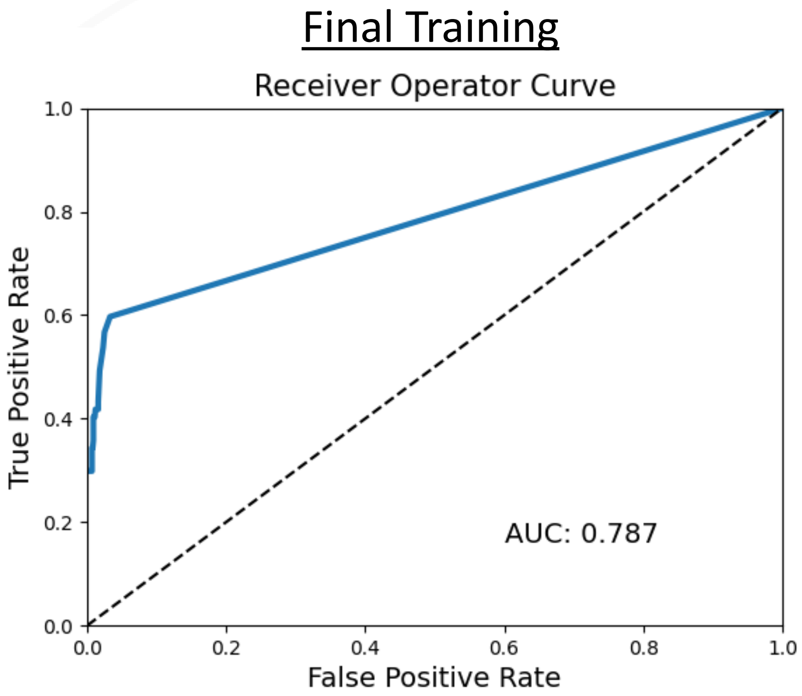
Receiver operating curves show performance at all classification thresholds.

Area under the curve is an aggregate measure of performance.

On real data the AUC increases after transfer learning.

The final network performs less well on simulated data after transfer learning (AUC: 0.98 vs 0.95)

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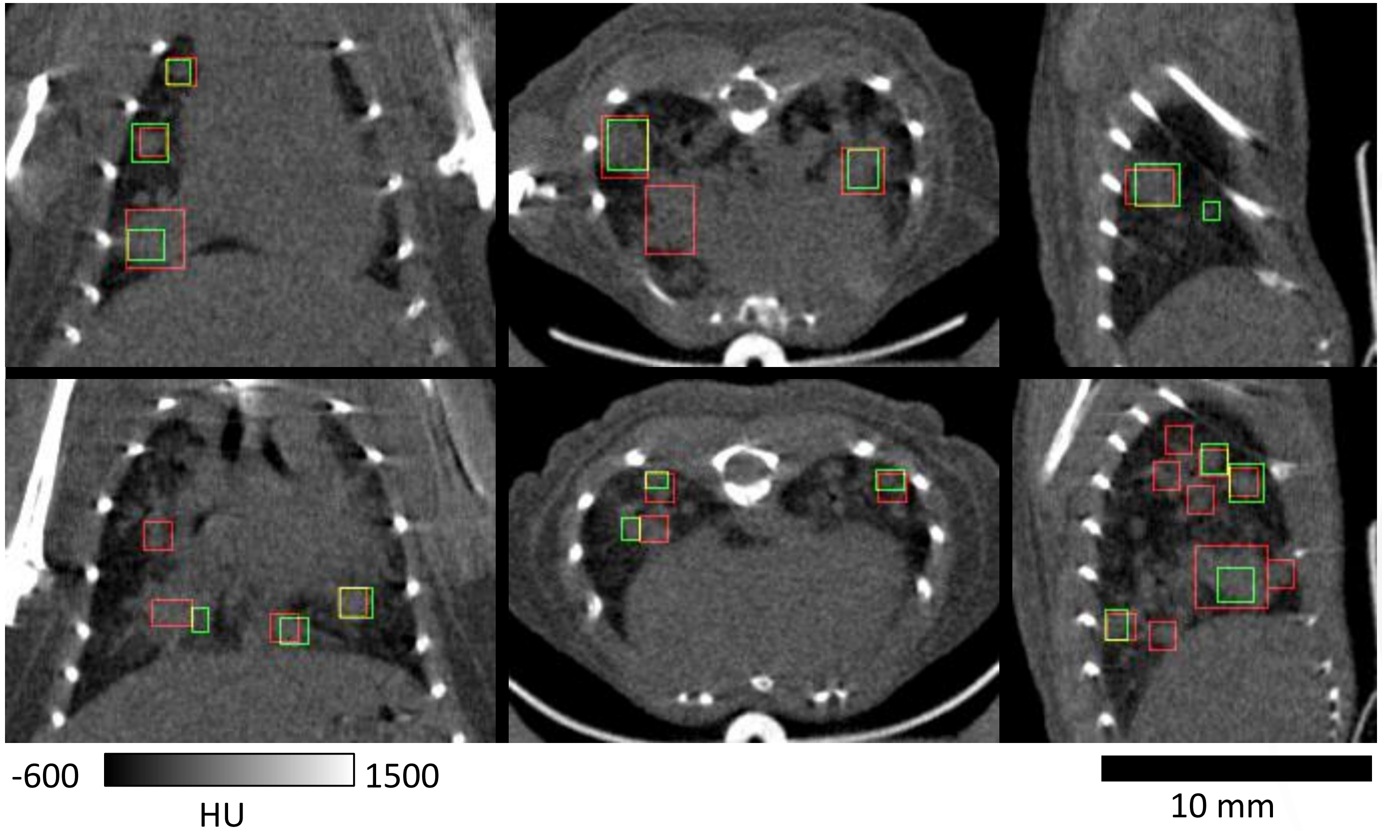
# Detection difficulties




- Labels marked by observer
- Network predictions

In extreme cases predictions suffer

This mouse contains 25 tumors marked by an observer.

Tumors very close together or nestled into other structures are prone to being missed.

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# Conclusions and future work

- We have built and analyzed an image processing network for lung tumor detection our preclinical trial
- The network was trained largely on synthetic data
- Significantly reduce processing time for large datasets
- Can identify lung tumors in this small dataset (AUC: 0.78)
- Tools like these will leverage preclinical results to influence clinical practice and patient outcomes

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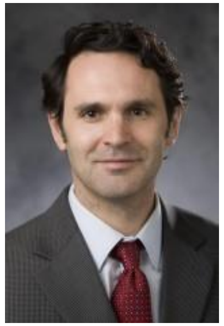
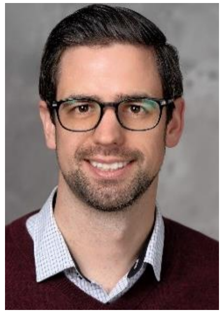
# OUR TEAM


Dr. C.T Badea


Dr. D Clark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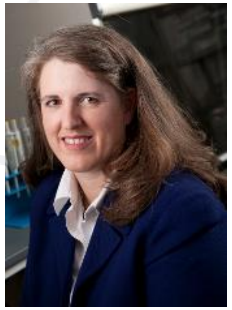
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**Funding**

NIH NATIONAL CANCER INSTITUTE

**R01 CA196667, U24 CA220245**


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