AstraZeneca

In Vivo Imaging in Drug Development

Decision making in drug discovery/development using in vivo animal imaging

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Cambridge

Gaithersburg

Gothenburg

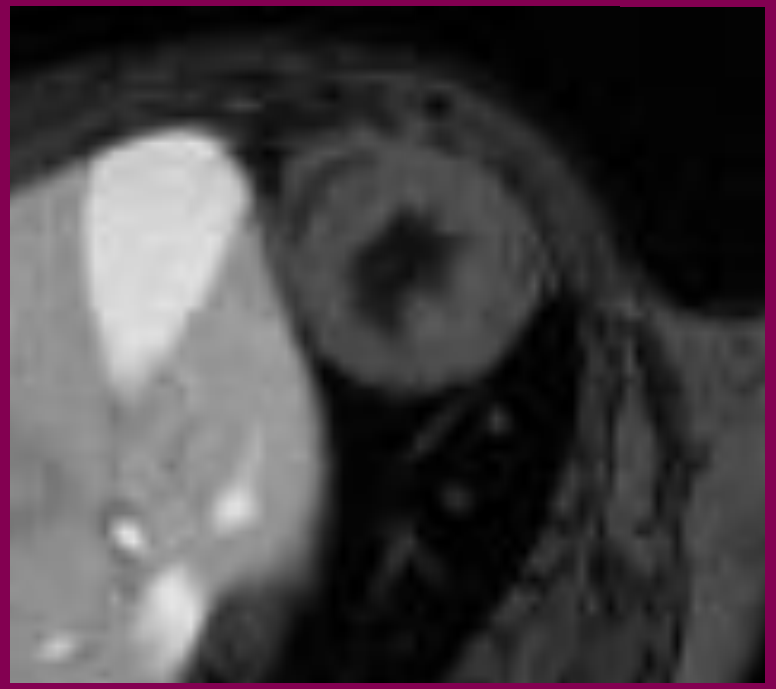
Boston

Allexion

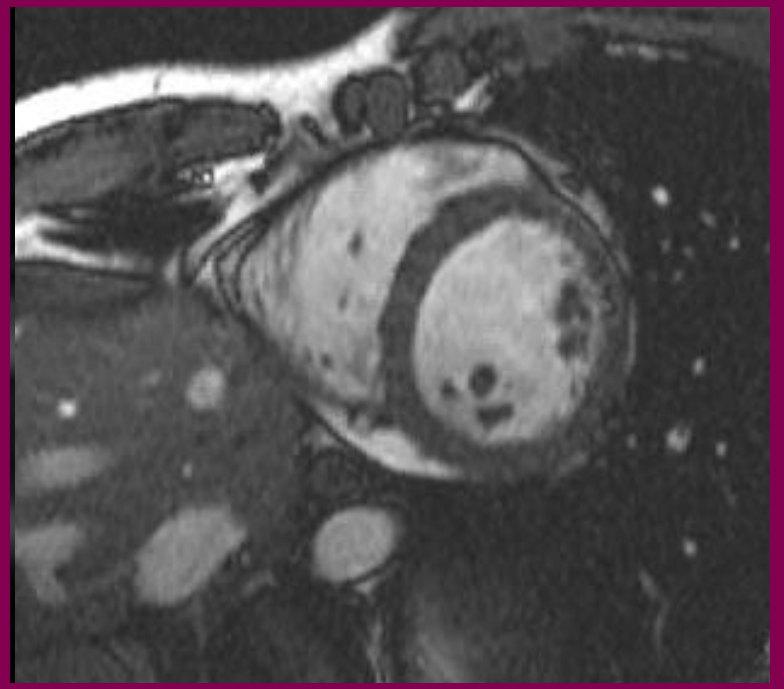
Clinical Imaging

- Diagnostic imaging for detecting and following disease progression and to establish cure of disease.
- Imaging is used in early clinical trials to derisk late stage investment decisions, or to differentiate drugs from competitors.
- Imaging biomarkers are used as inclusion criteria for clinical trials or can act as companion diagnostics.

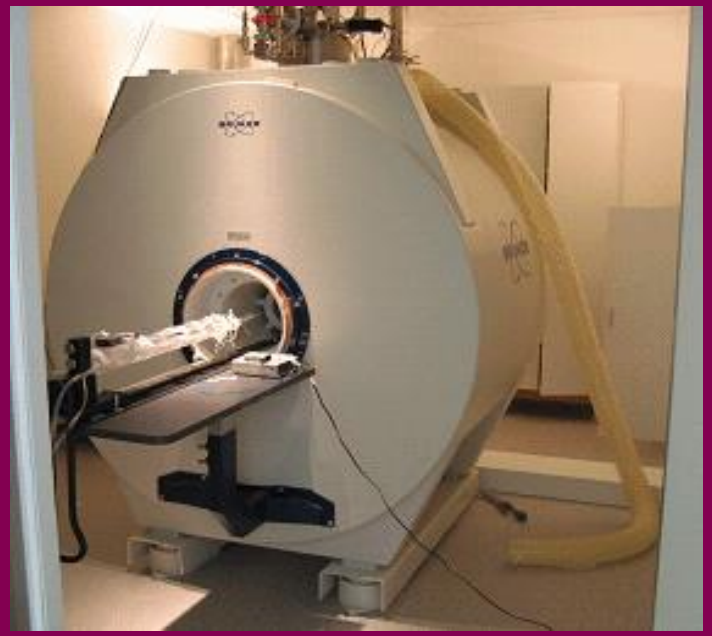
In vivo Imaging



Mouse



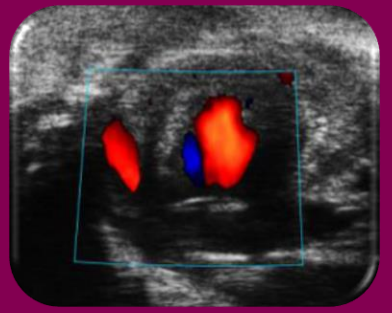
Man



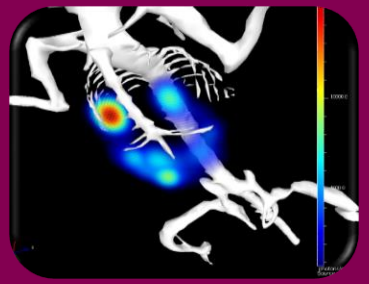
Preclinical in vivo Imaging:
From molecule to patient

1. Unique non-invasive quantitative functional information.
2. Longitudinal studies of disease progression and therapeutical effects in individual animals.
3. Drug distribution, time course and target engagement.
4. High resolution ex vivo 3D tissue imaging.

Biodistribution by SPECT



Cardiac function by Ultrasound

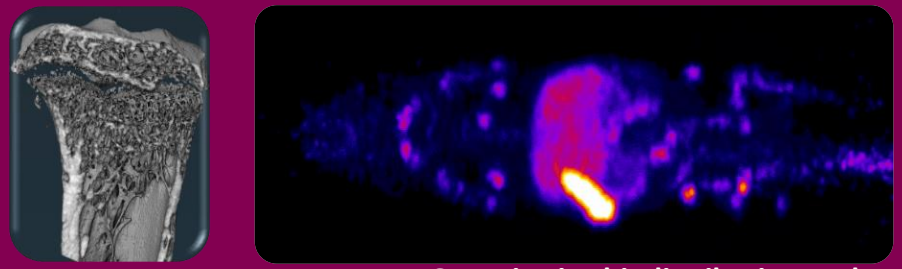


Gene editing by Bioluminescence

Internal visualization in live animals

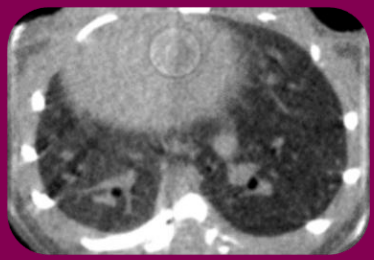
Beating heart in a mouse by MRI

Target delivery by BioFluorescence



Quantitative biodistribution and cell tracking using PET

High resolution *ex vivo* 3D anatomy by µCT



High resolution anatomy by CT

Imaging from molecule to man

Biodistribution and kinetics:
small molecules, antibodies, LNP, gene- or cell therapy.

Target engagement and dose to man prediction

Disease Biology MOA

Validation of disease mechanistic models

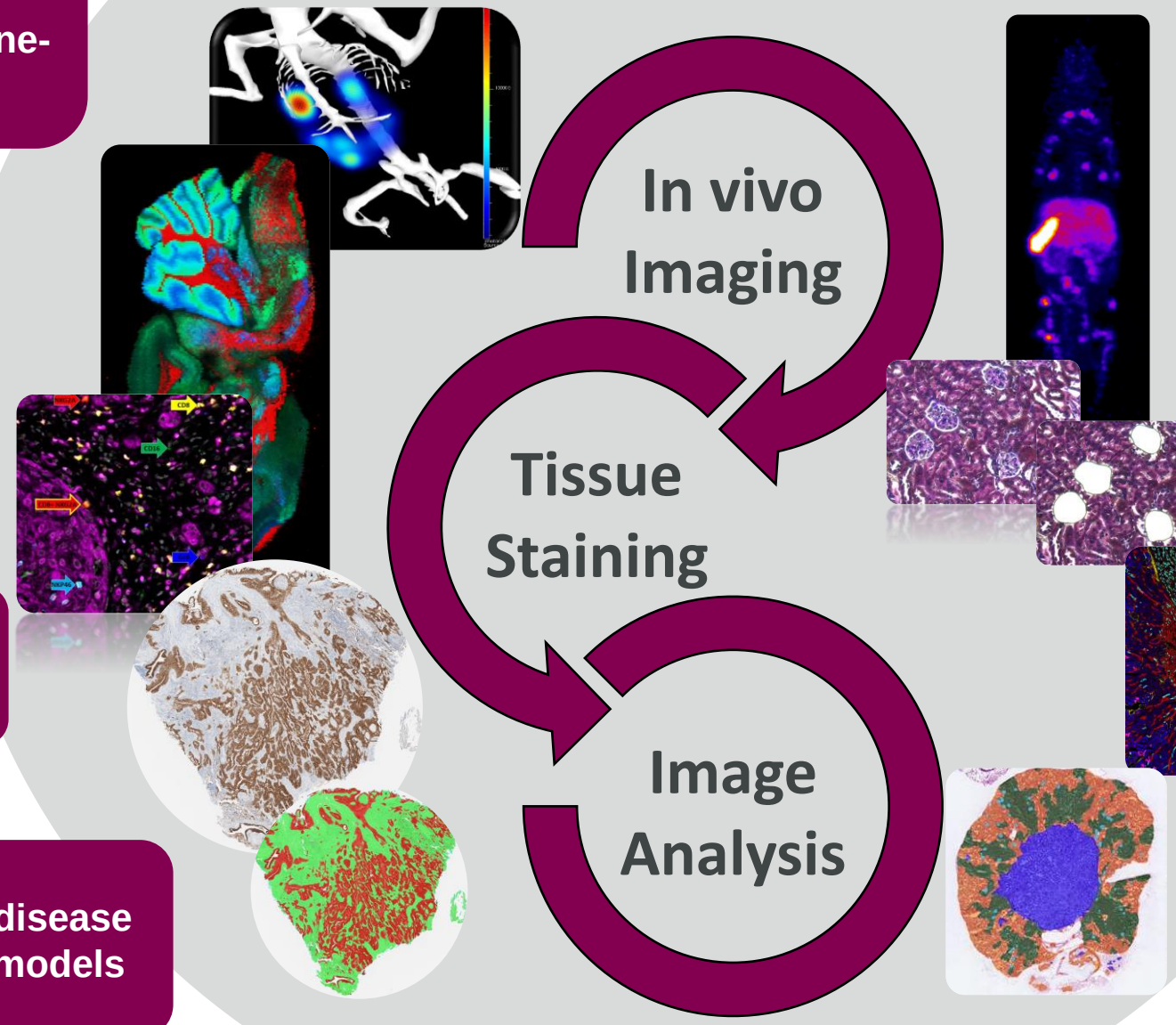
Target Evaluation

Efficacy testing in mechanistic models

Investigative Safety studies

Biomarker Development

Translational Efficacy assessment



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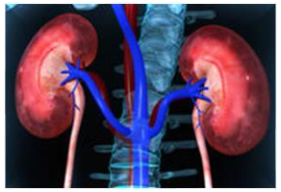
Some Recent Examples:



Heart Failure

- MRI and ultrasound are used as the primary endpoint in all HF projects.
- 31-P MRS PCr/ATP ratio in mice for cardiac energetics and MRI contrasts for fibrosis.

Chronic Kidney Disease

- Localised renal perfusion in CKD models.
- 3D ex vivo µCT quantification of vasculature

Respiratory and autoimmune diseases

- Longitudinal MRI of lung remodelling in bleomycin treated rodents.

NASH and metabolic diseases

- MRI rodent liver fat NASH studies.
- MRI and fluorescence contrasts for fibrosis.

Oncology and transgenic animals

- MRI studies in GEMM lung cancer mice models.

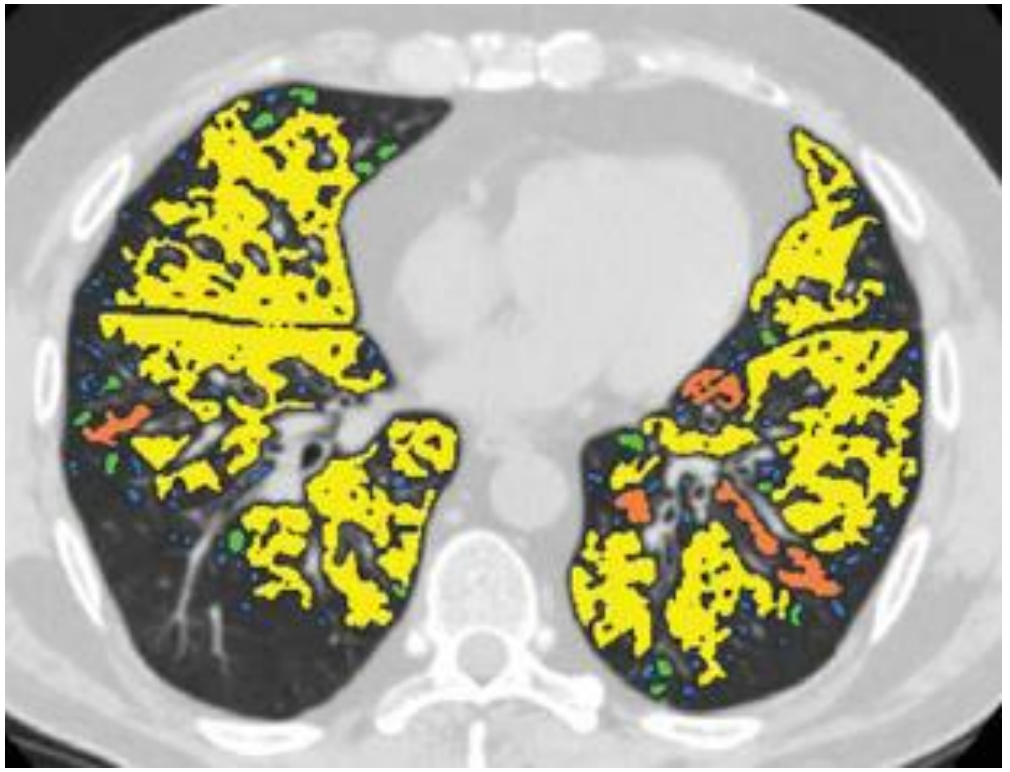
Cell and gene therapy.

- The fate and distribution of cardiac stem cells. Luciferase cells with IVIS and NIS cells with SPECT.

Safety.

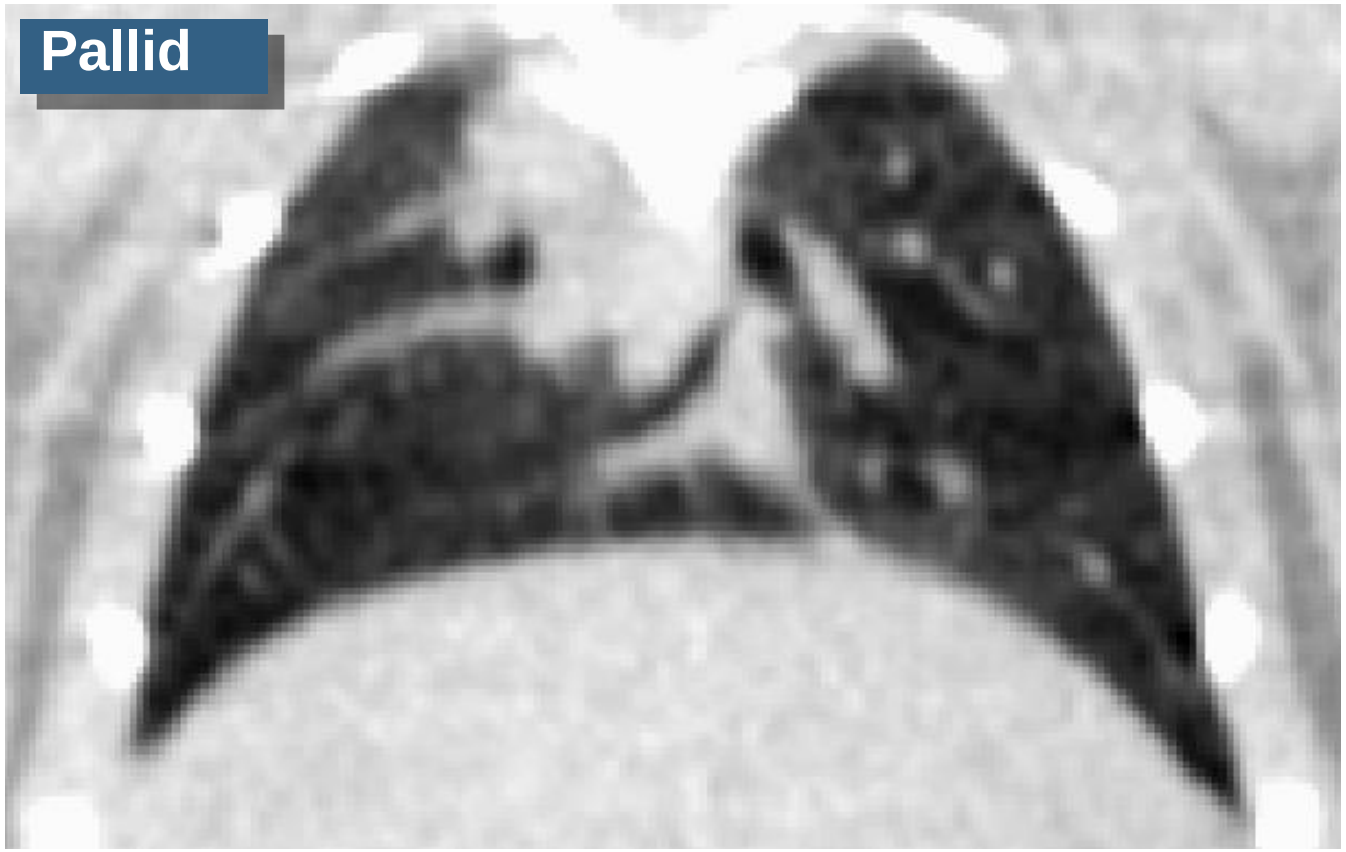
- Ex vivo µCT of trabecular and cortical bone.

Clinical respiratory imaging



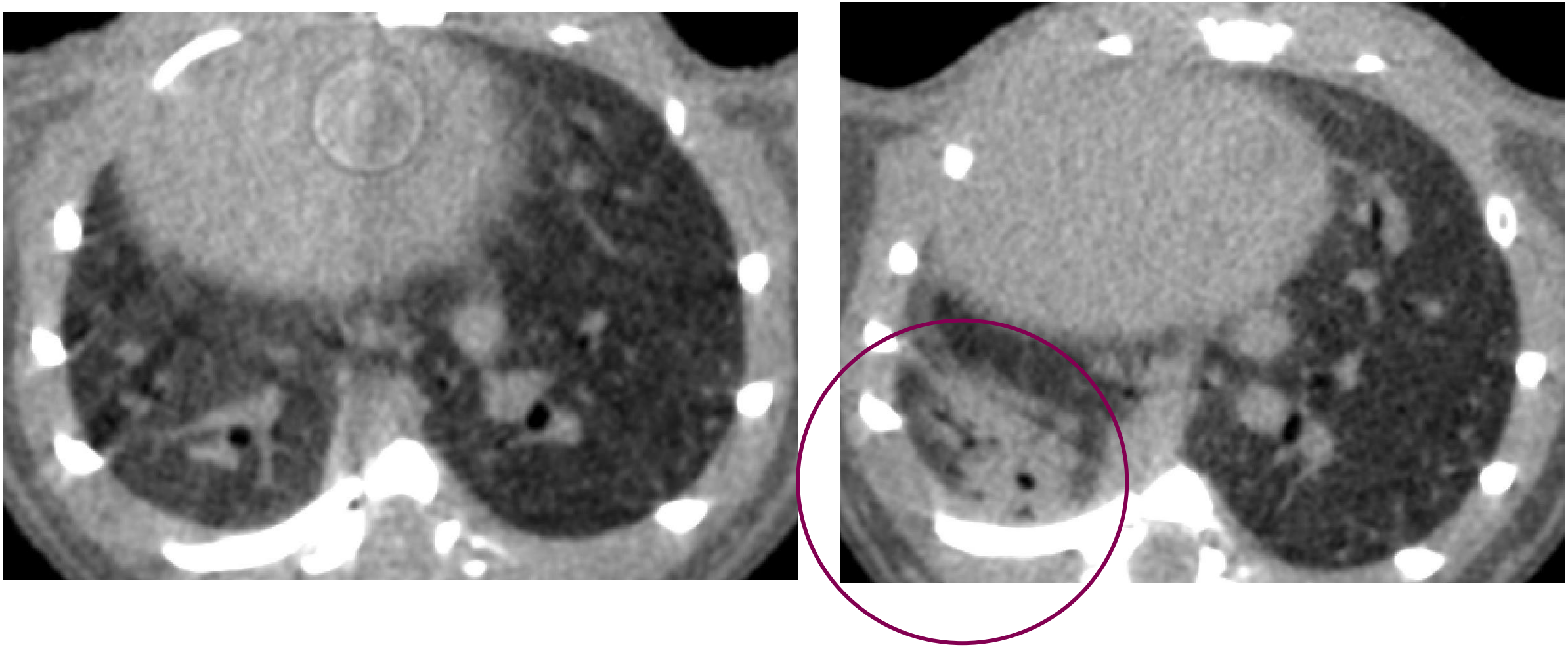
Density mapping

µCT of Emphysema in Pallid mice

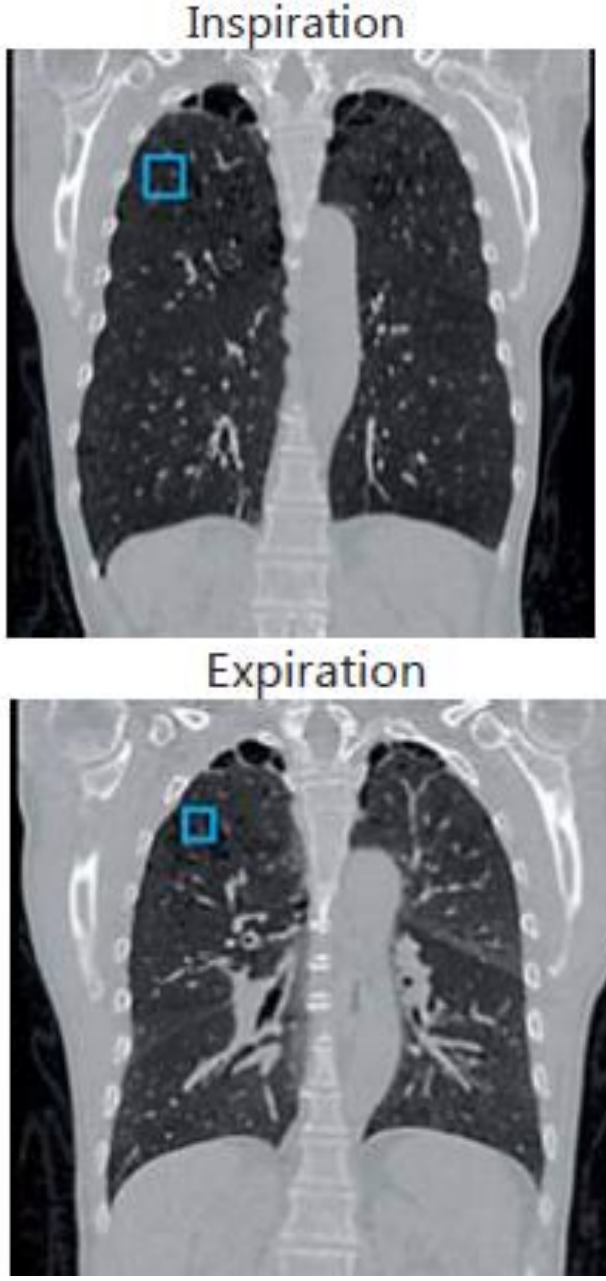


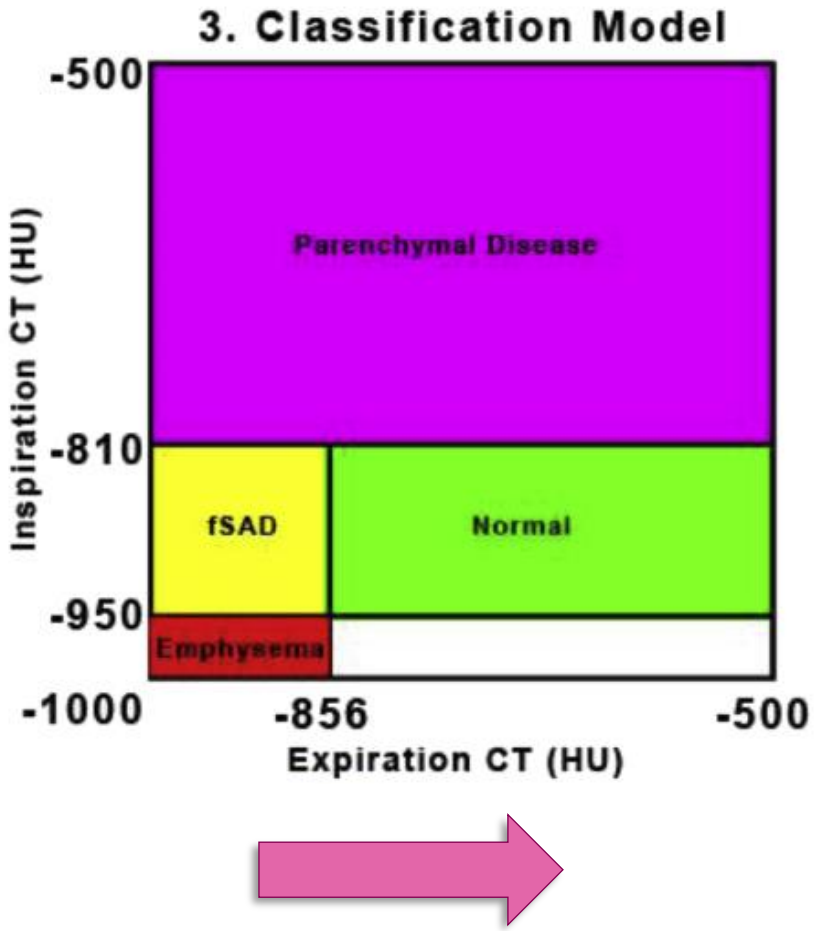
Hultin

µCT of Unilateral Bleomycin Mice Model



Parametric Response Mapping





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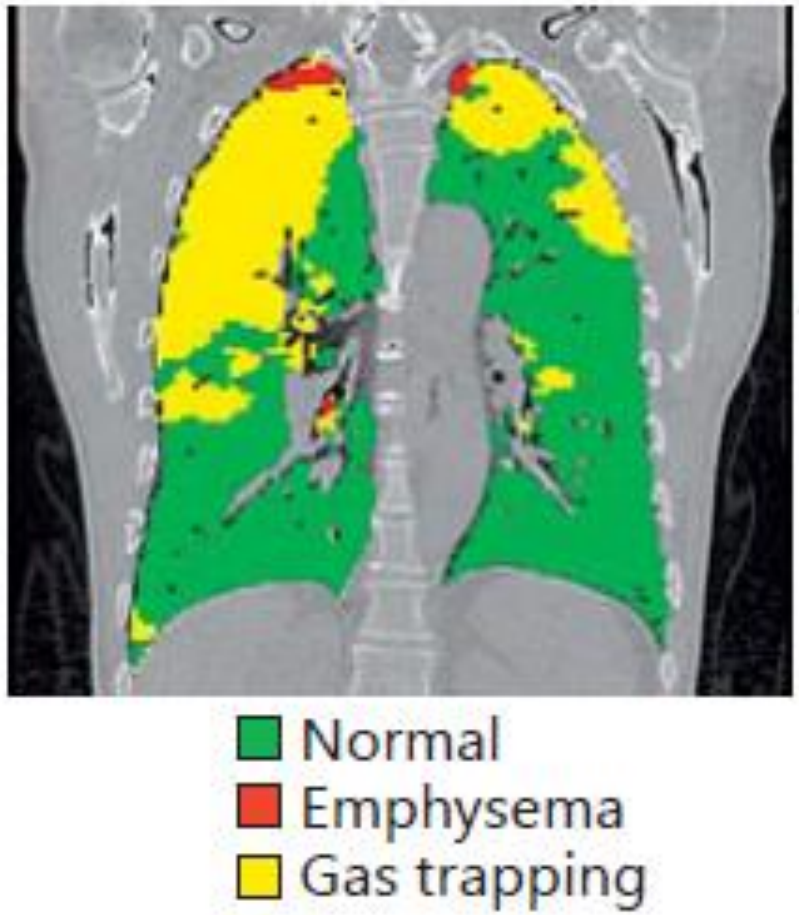
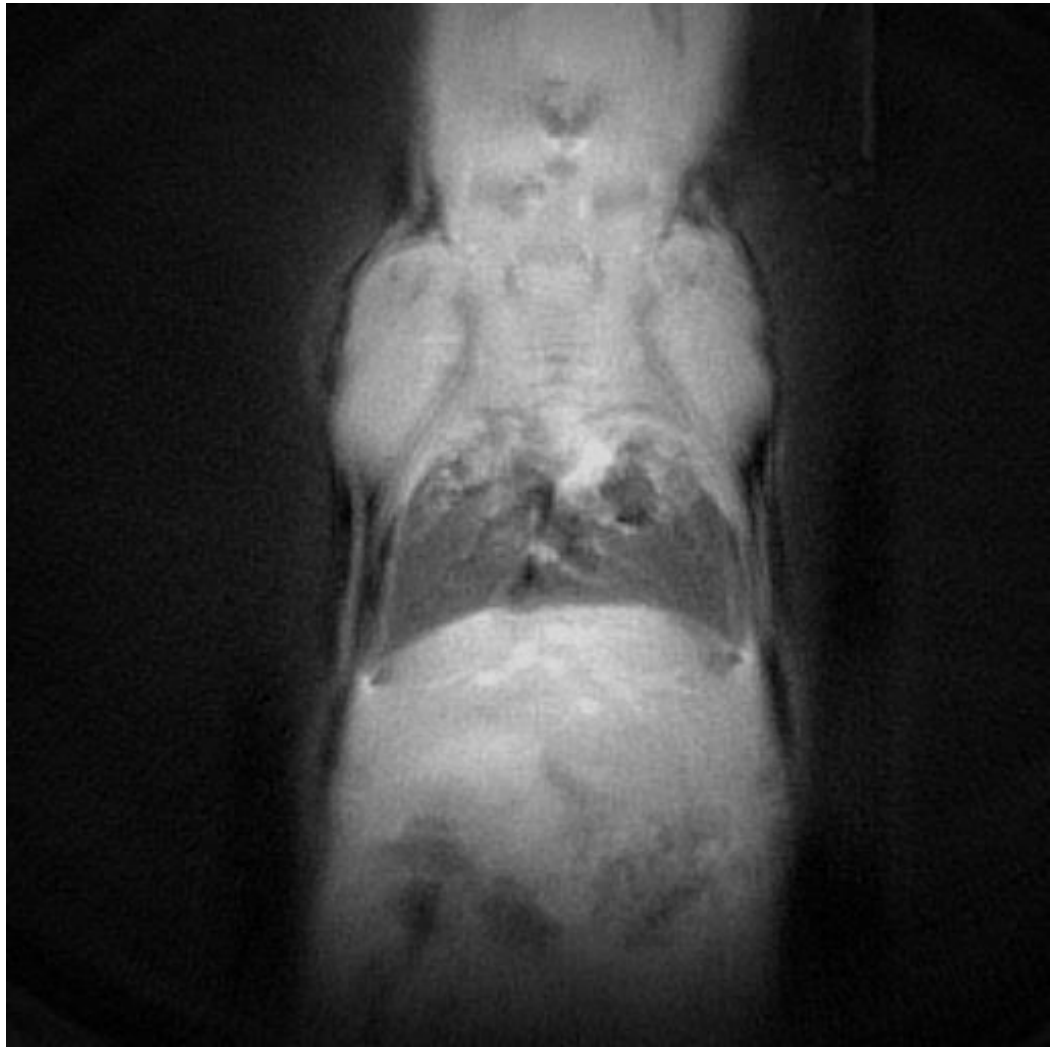
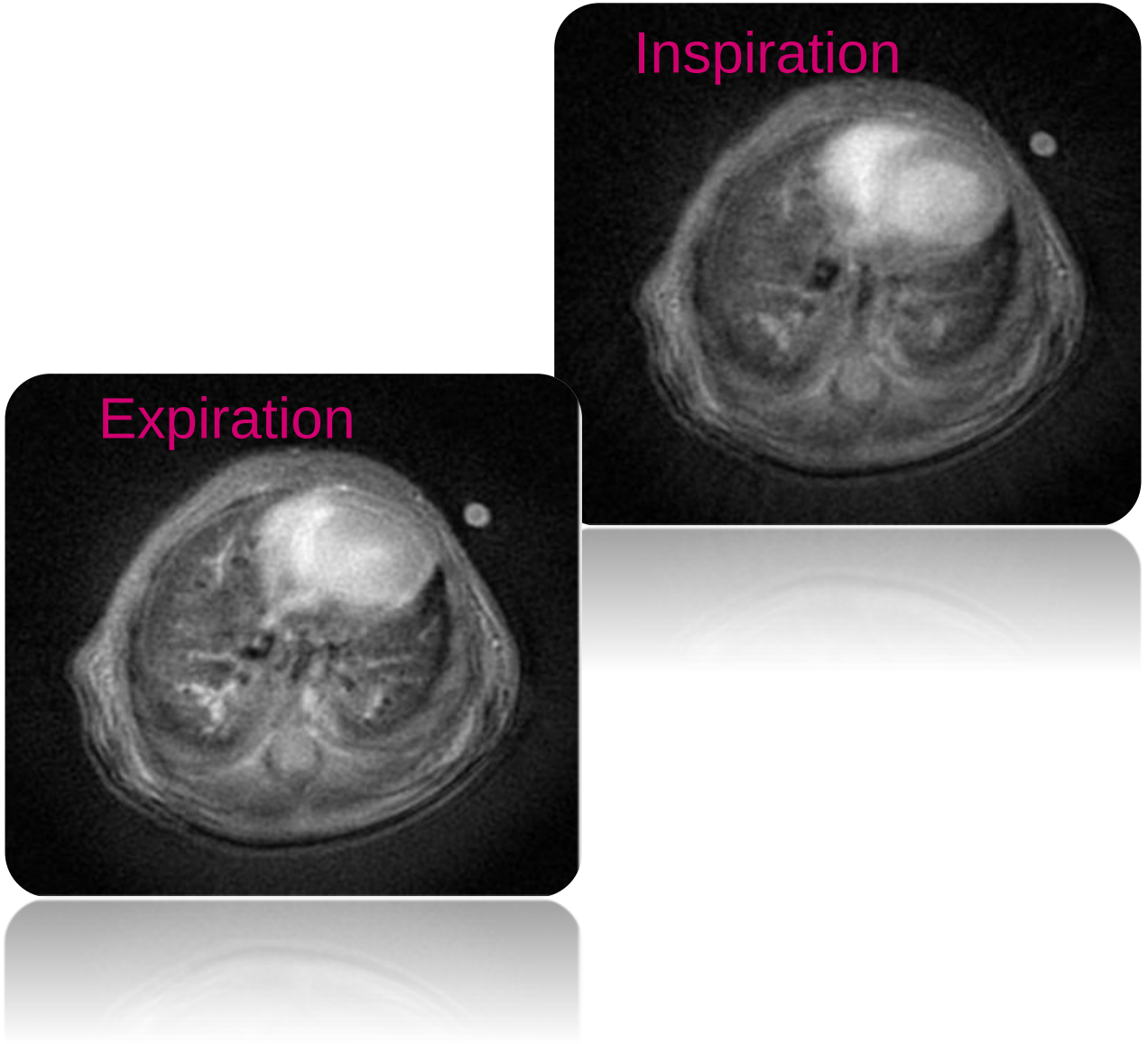


Francoise

Dynamic Lung compliance





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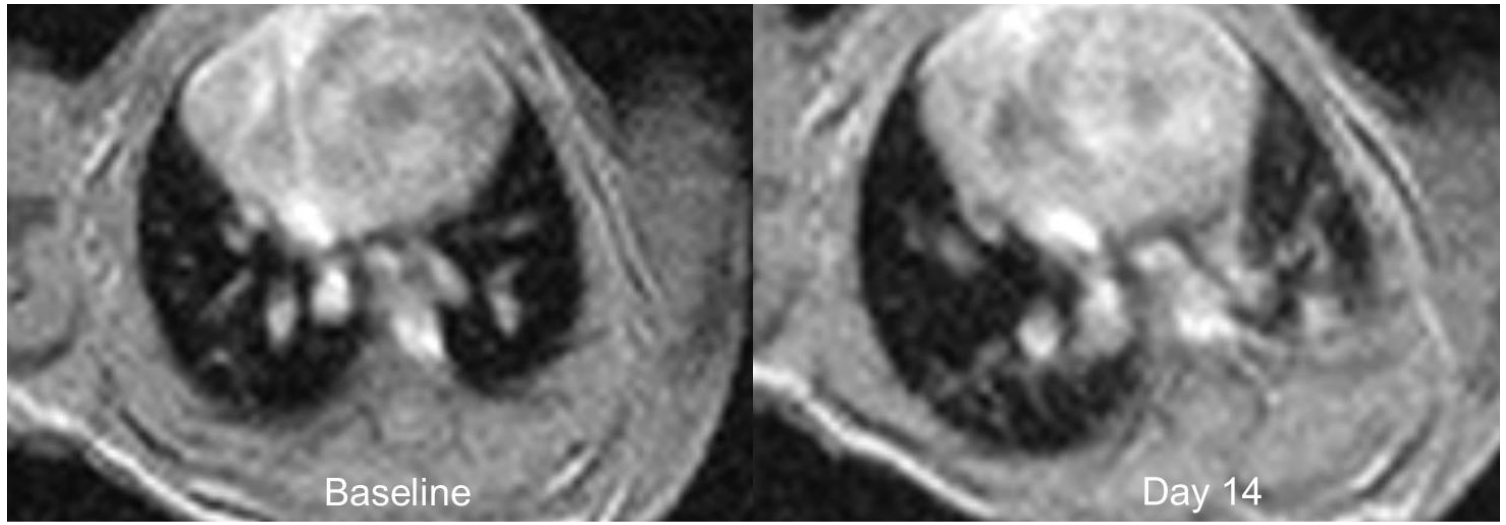
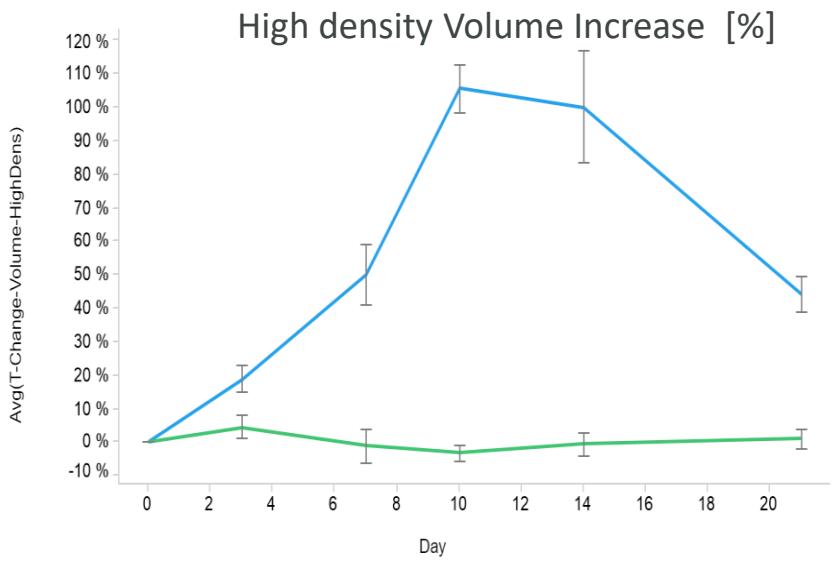
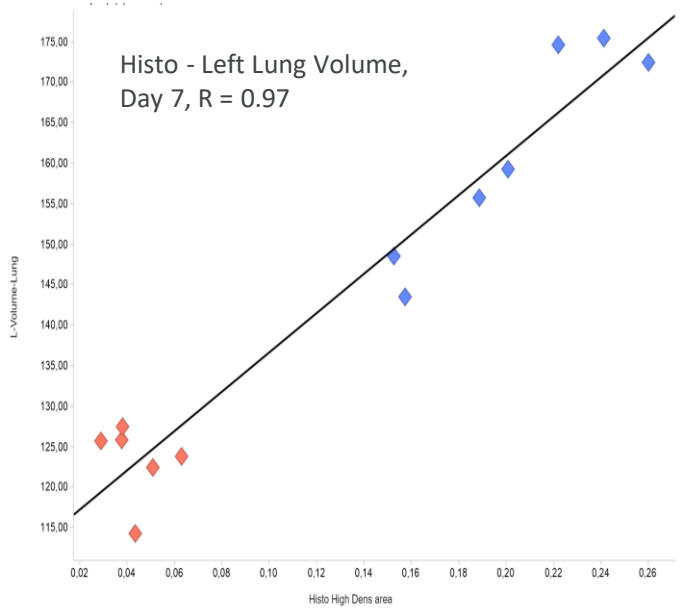
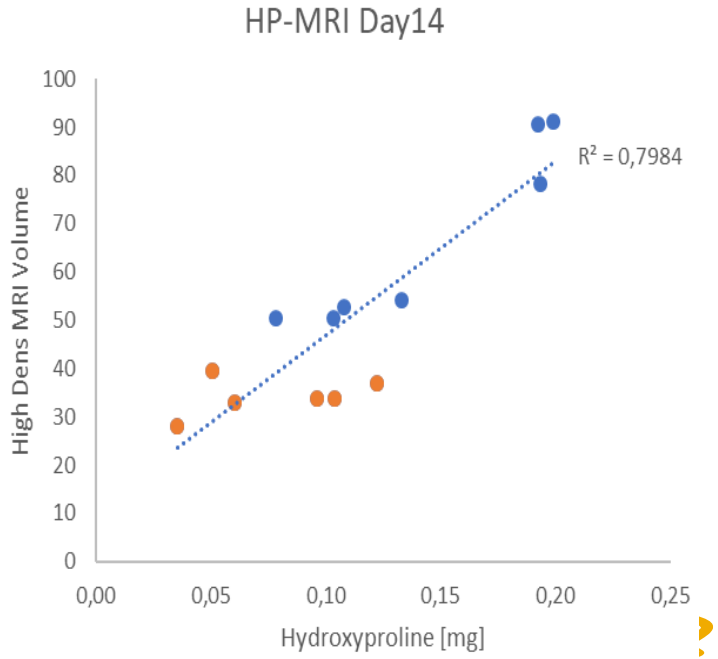
Longitudinal MRI in Bleomycin Mice Model

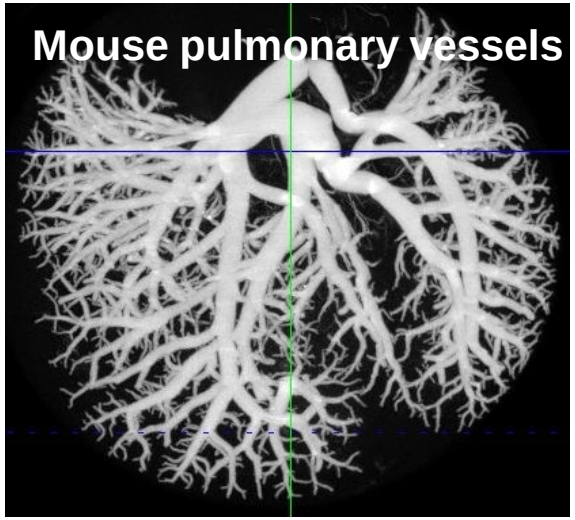


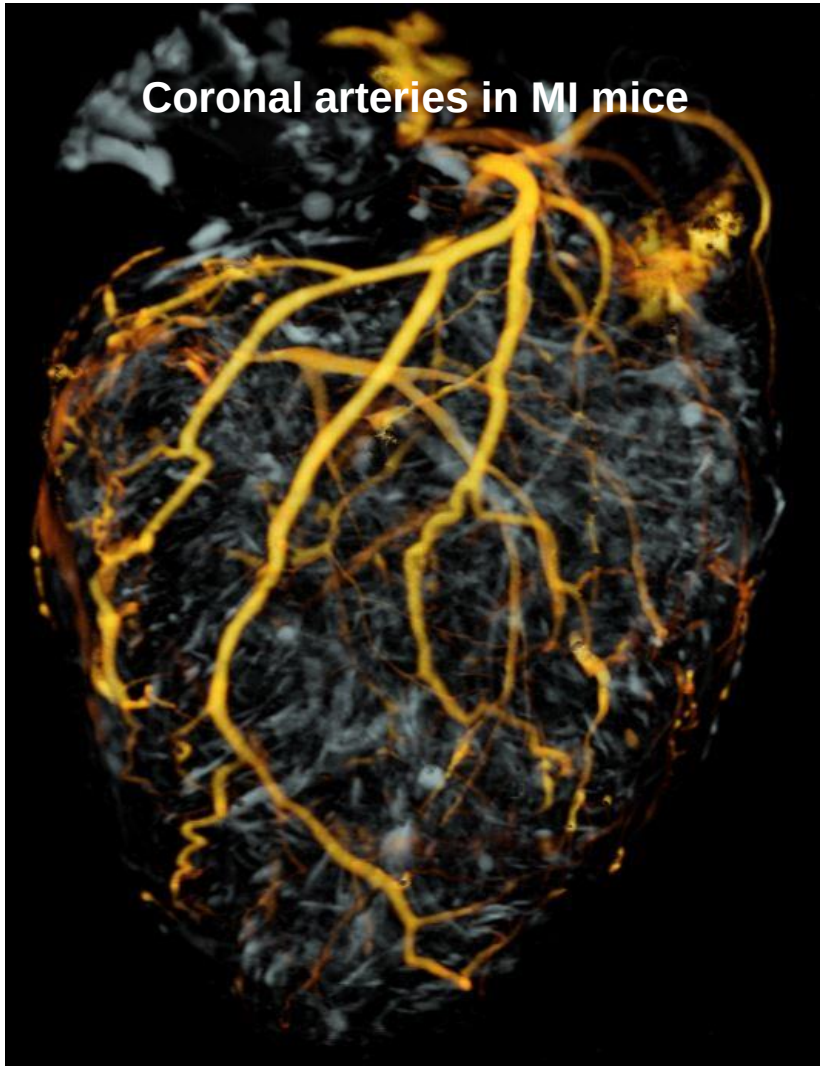


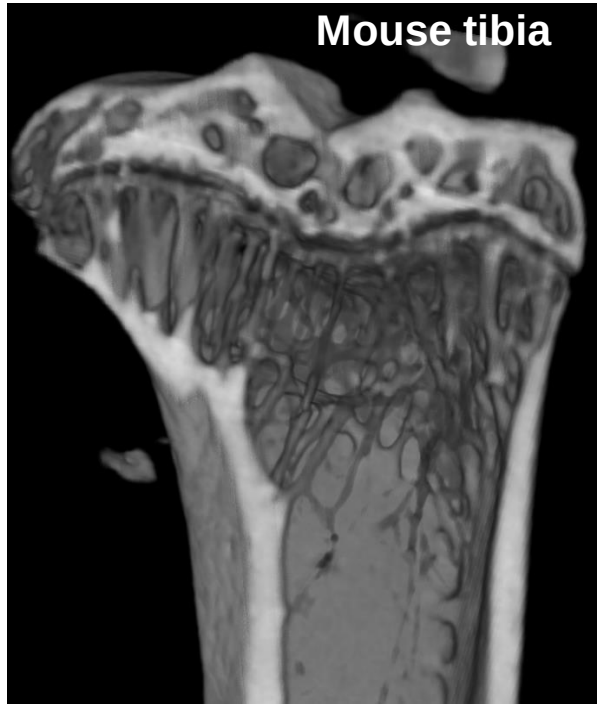




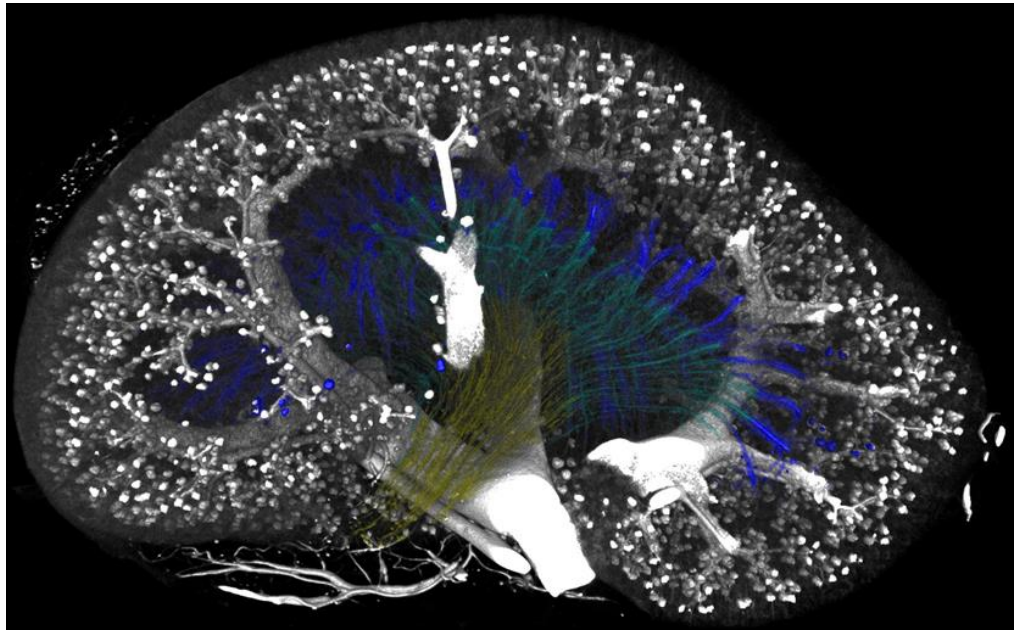
Ex vivo µCT 3D assessment

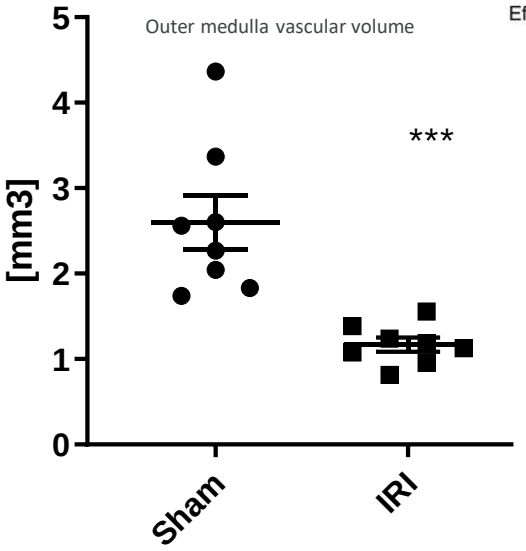


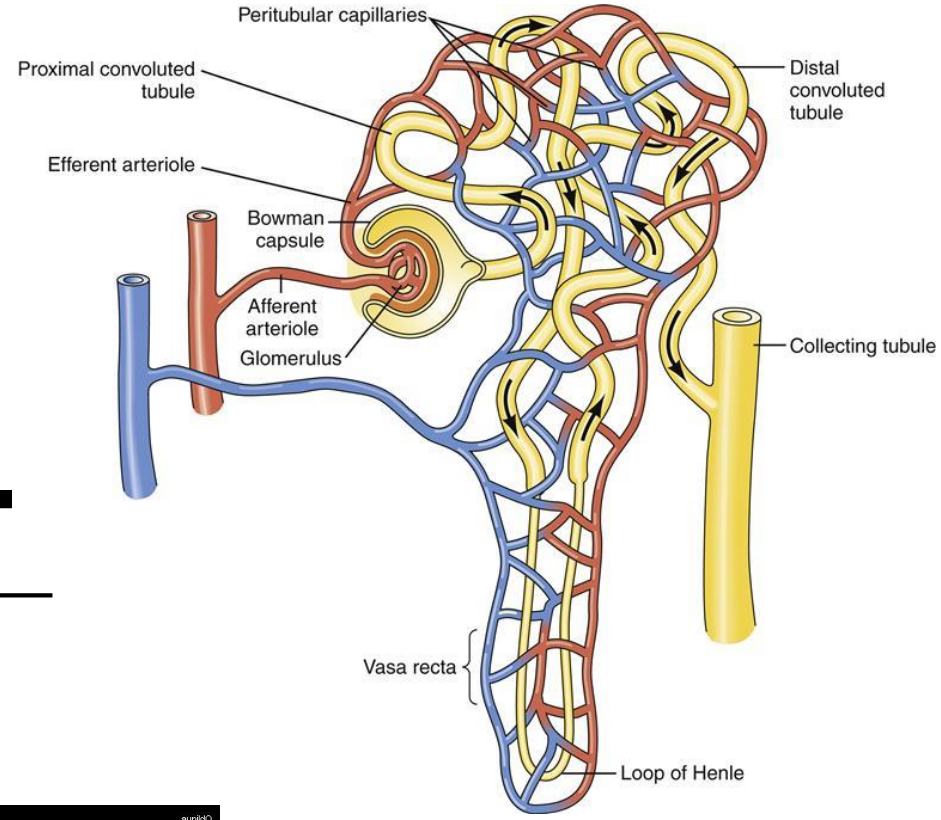


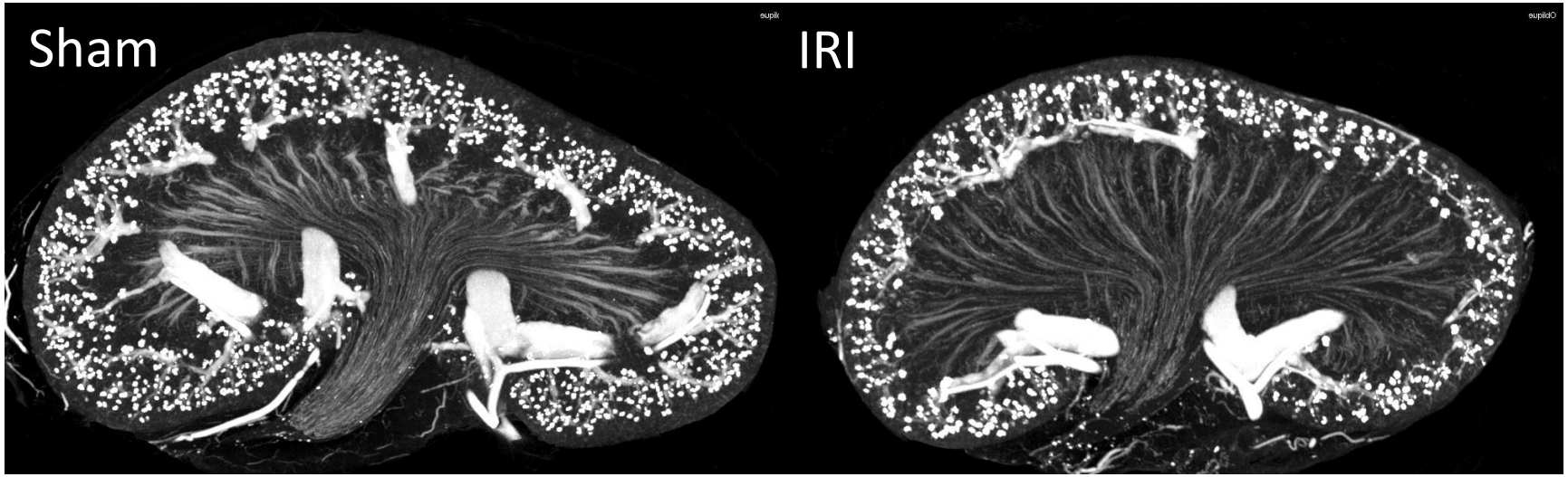


Renal vascularization









Hultin

Decision making in drug discovery/development using in vivo animal imaging

- When it provide unique non-invasive quantitative functional information.

  And/Or

- In longitudinal therapeutic studies.

  And/Or

- IF it provides critical information on drug distribution, time course or target engagement.

  And/Or

- High resolution ex vivo 3D structures are chritical.