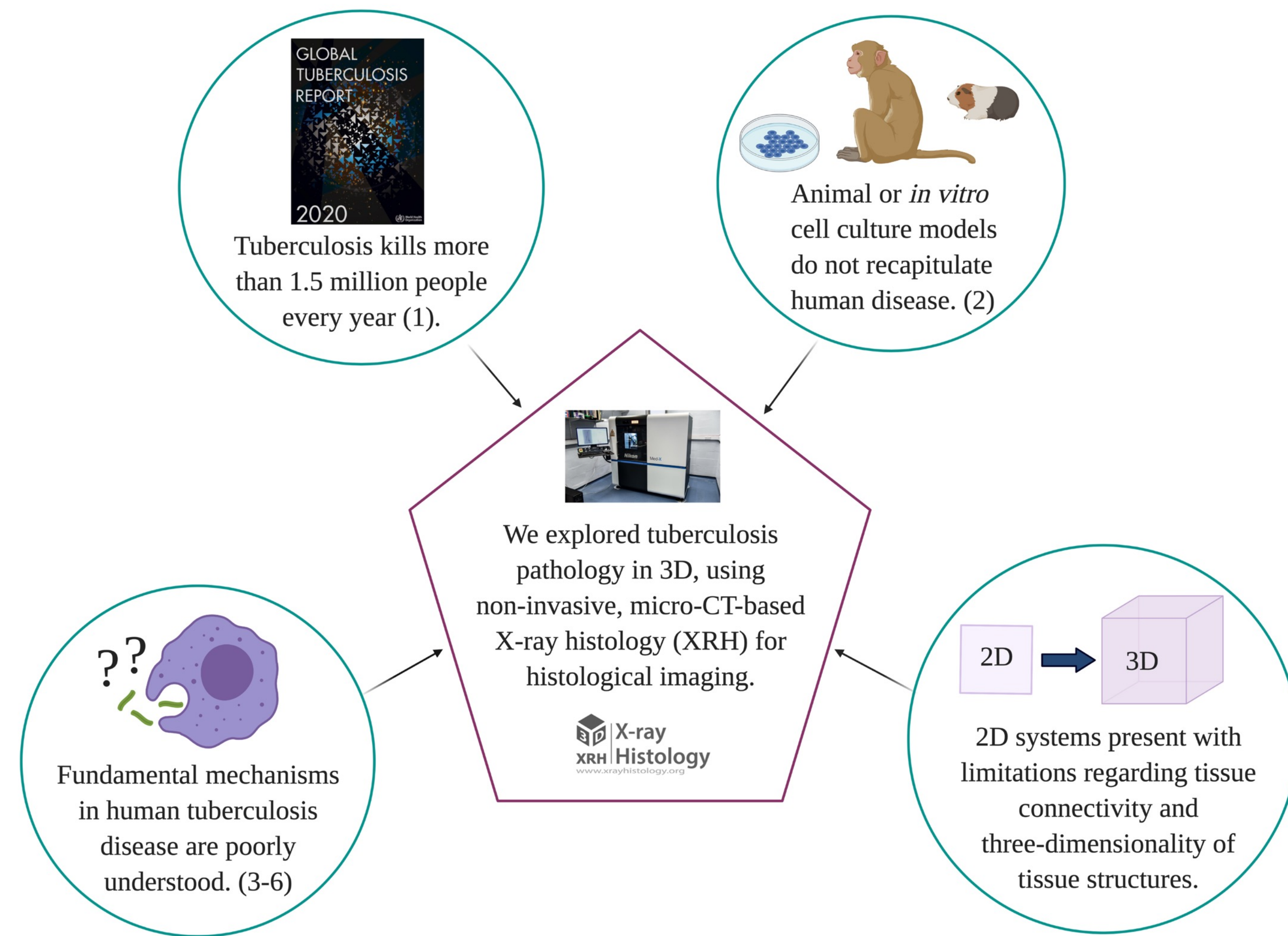# Investigating tuberculosis pathology in the human lung with 3D X-ray Histology; a correlative imaging approach

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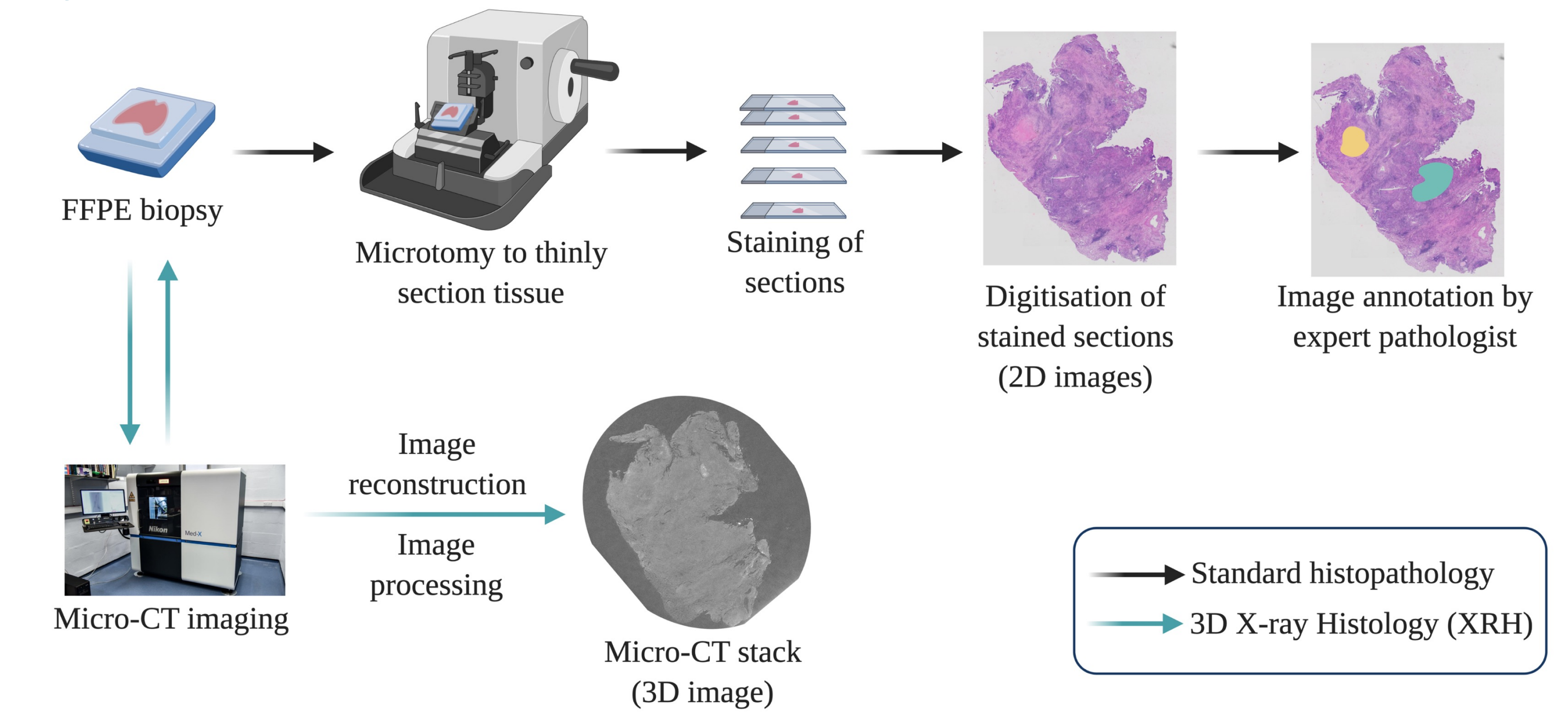
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1. Tuberculosis: the forgotten pandemic

GLOBAL TUBERCULOSIS REPORT 2020

Tuberculosis kills more than 1.5 million people every year (1).

Animal or *in vitro* cell culture models do not recapitulate human disease. (2)

We explored tuberculosis pathology in 3D, using non-invasive, micro-CT-based X-ray histology (XRH) for histological imaging.

Fundamental mechanisms in human tuberculosis disease are poorly understood. (3-6)

2D → 3D

2D systems present with limitations regarding tissue connectivity and three-dimensionality of tissue structures.
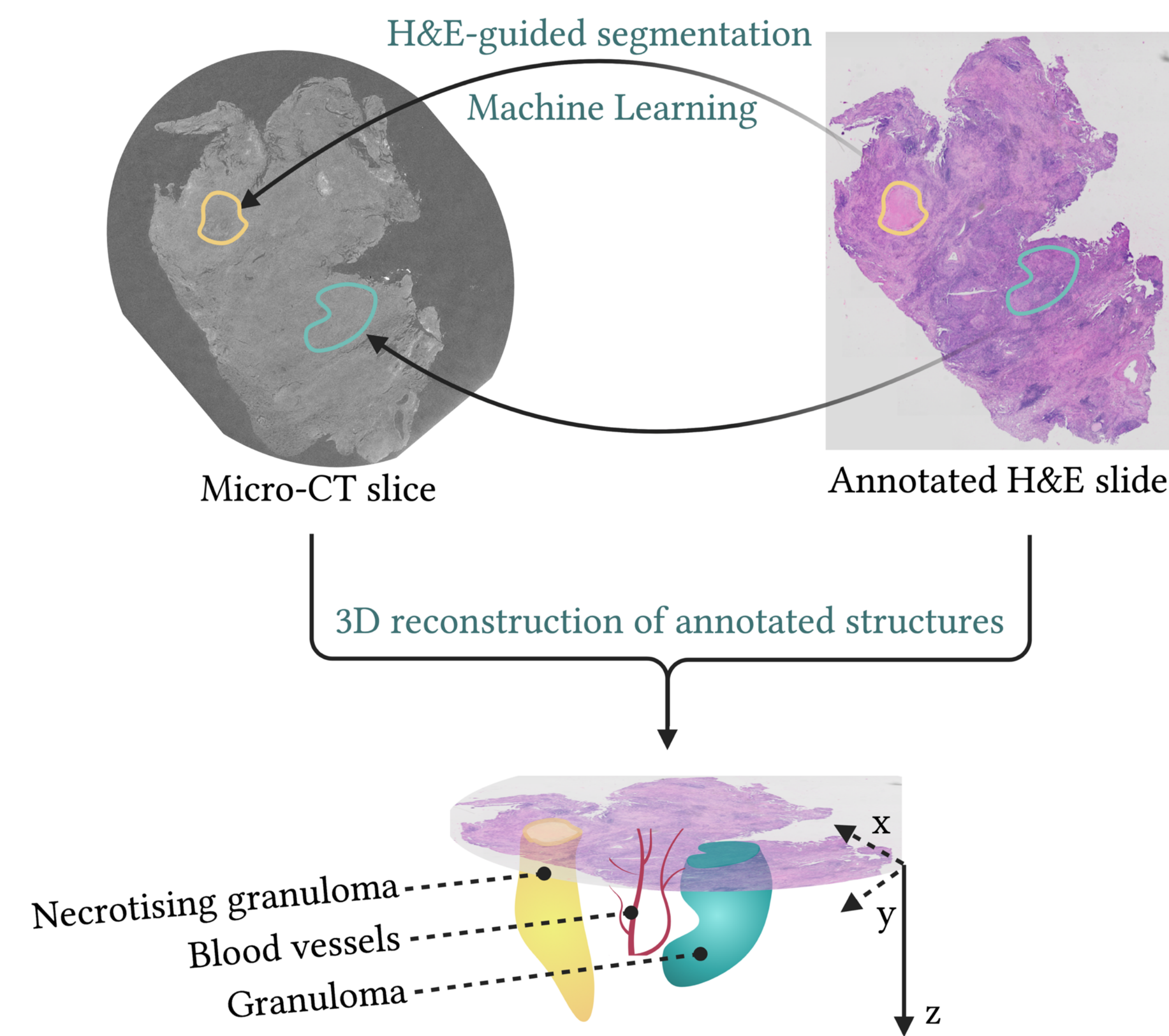
2. How XRH fits into the standard histopathology sample workflow

❖ The formalin-fixed paraffin-embedded (FFPE) biopsy is first imaged with micro-CT non-invasively and then re-enters the standard histopathology workflow. (7-9)

❖ Sections from the FFPE block are stained and then digitized using slide scanning.

❖ Digitised slides are annotated by an expert pathologist to highlight important features of tuberculosis pathology, such as areas of caseous necrosis, granulomas etc.

FFPE biopsy → Microtomy to thinly section tissue → Staining of sections → Digitisation of stained sections (2D images) → Image annotation by expert pathologist

Micro-CT imaging → Image reconstruction / Image processing → Micro-CT stack (3D image)

→ Standard histopathology
→ 3D X-ray Histology (XRH)

3. Correlative imaging workflow

H&E-guided segmentation
Machine Learning

Micro-CT slice — Annotated H&E slide

3D reconstruction of annotated structures

Necrotising granuloma
Blood vessels
Granuloma

In this project, we:

❖ Have collected and imaged with micro-CT a total of 7 FFPE lung biopsies that have tested positive for tuberculosis and have sectioned and stained them with standard histological stains to extract information about the cellular composition and extracellular matrix.

❖ Have performed elastic registration between the annotated histology slide and micro-CT image to correct for distortions introduced by FFPE processing and the knife of the microtome.

❖ Are in the process of transferring annotations from the histology sections to the micro-CT image to determine how these features develop in 3D.

❖ Will test machine learning approaches to aid with segmentation of the most prominent features in the tissue.

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Get involved, get in touch with the XRH team!

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Setting the foundations for X-ray micro-computed tomography workflow for non-destructive 3D X-ray histology (XRH)
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We are always **looking for collaborations** to explore the full potential of the technology, and **can provide open access to the technique** for *proof-of-concept* studies with qualitative inspection and quantitative image-based characterisation of the tissue.

We are particularly interested in stimulating and supporting novel and exploratory projects, introducing 3D X-ray Histology to the wider biomedical research and clinical pathology community and identifying application-specific imaging needs.

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