Combining micro-CT imaging with traditional histology in a correlative imaging approach to investigate tuberculosis pathology in the human lung

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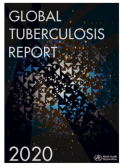
Tuberculosis: the forgotten pandemic

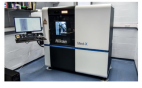
- TB is the leading cause of death by a single infectious agent worldwide.
- In 2019, TB claimed 1.4 million human lives.
- TB is the leading cause of death for people with HIV.

Source: World Health Organization (WHO)



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

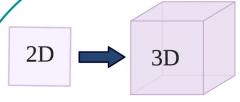
Animal or *in vitro* cell culture models do not recapitulate human disease. (2)



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

X-ray Histology
www.xrayhistology.org

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



2D systems present with limitations regarding tissue connectivity and three-dimensionality of tissue structures.

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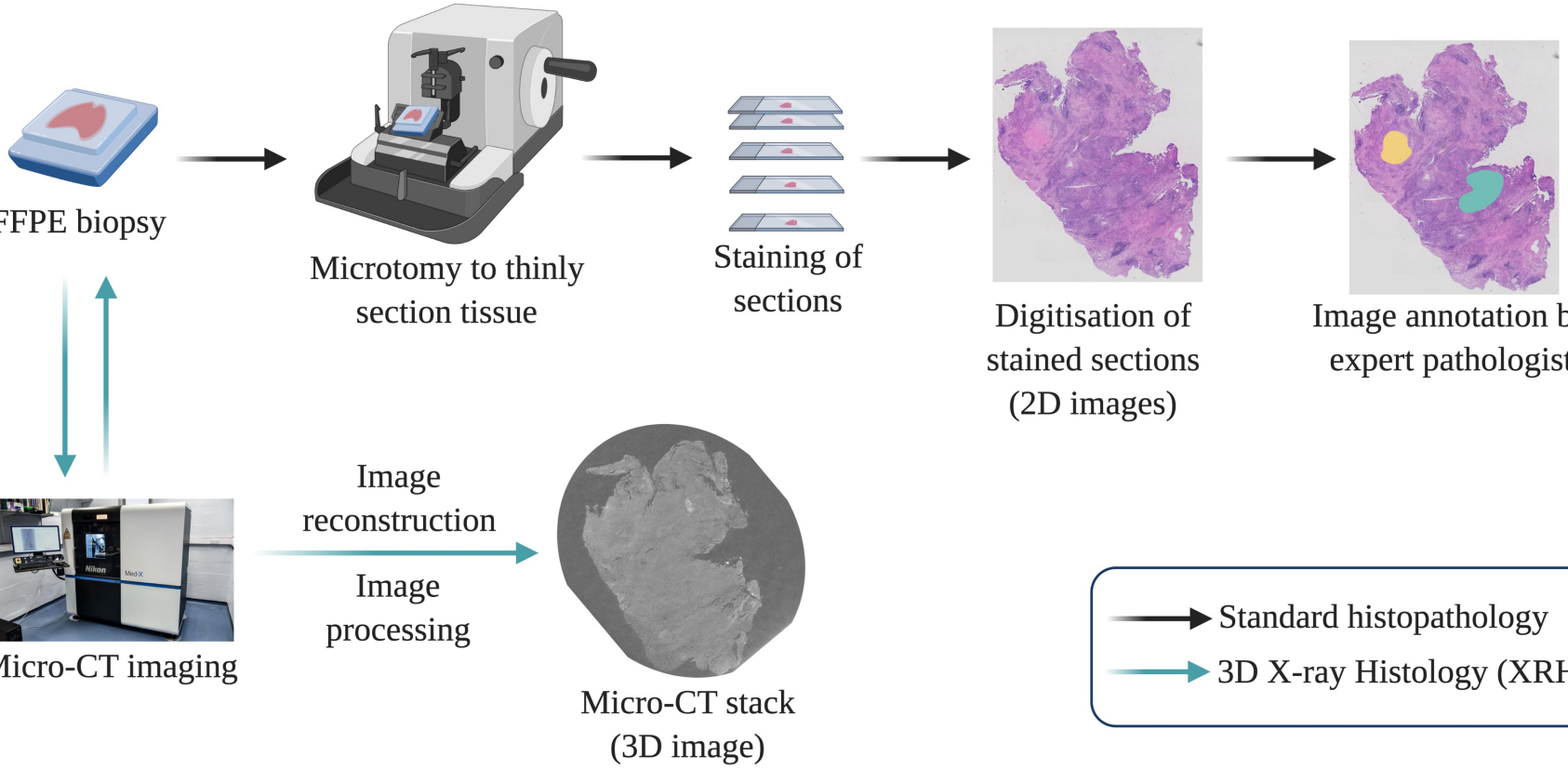
Imaging/Sample processing workflow:



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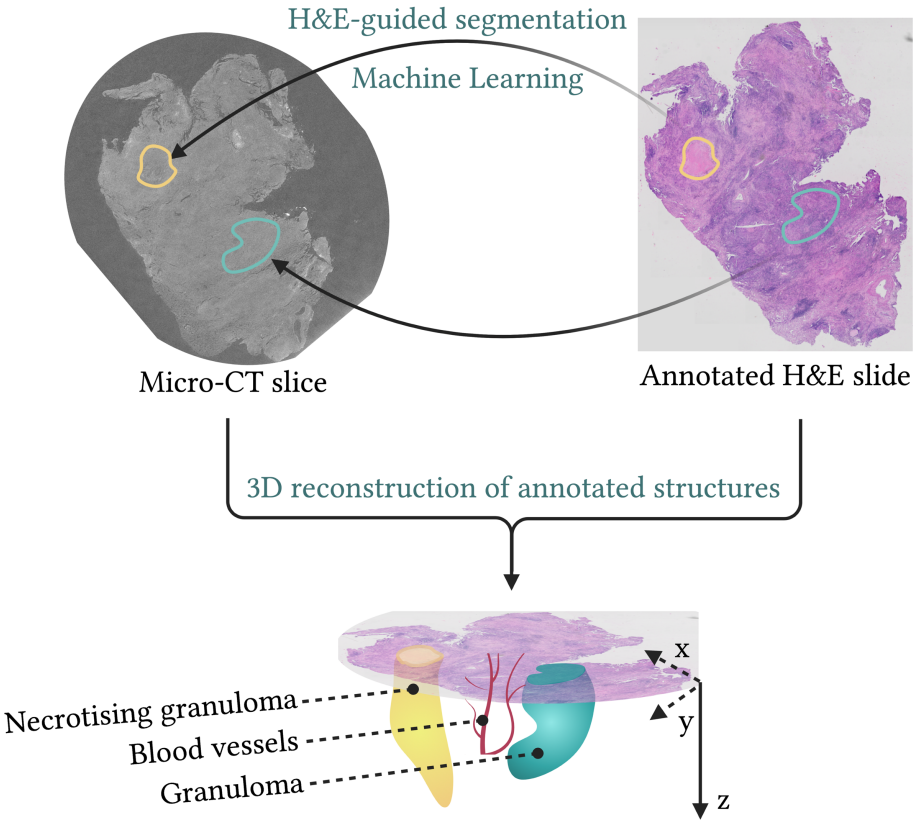

- ✓ Imaged 7x FFPE lung biopsies that have tested positive for tuberculosis with micro-CT.
- ✓ Sectioned and stained with histological stains to extract information about the cellular composition and extracellular matrix.
- ✓ Performed elastic registration: between the annotated histology slide and micro-CT 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.