Automated PET/CT Analysis of Pulmonary TB Biomarkers in Non-Human Primates

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FACTS & FIGURES

Start date:	January 2020
End date:	December 2026
IMI funding:	€89.8 M
EFPIA in kind:	€118 M
Total Cost:	€208 M
Project website:	era4tb.org
Social media:	@IMI_ERA4TB

CHALLENGE

Tuberculosis (TB) remains one of the world's leading infectious killers. Non-human primate (NHP) models are central to developing new regimens, and PET/CT imaging offers a non-invasive way to track TB burden. However, quantitative analysis is heavily dependent on manual analysis and segmentation. Macaque size, distinct anatomy, and PET signal spill-in from nearby avid extrapulmonary tissue complicates the development of automatic image tools, such as segmentation and biomarker extraction.

APPROACH & METHODOLOGY

We built and validated a three-module, open-source pipeline, implemented in 3D Slicer, that automates the full analysis chain from raw macaque PET/CT to standardized biomarkers. Each module can run stand-alone or as part of the full pipeline (see steps below).

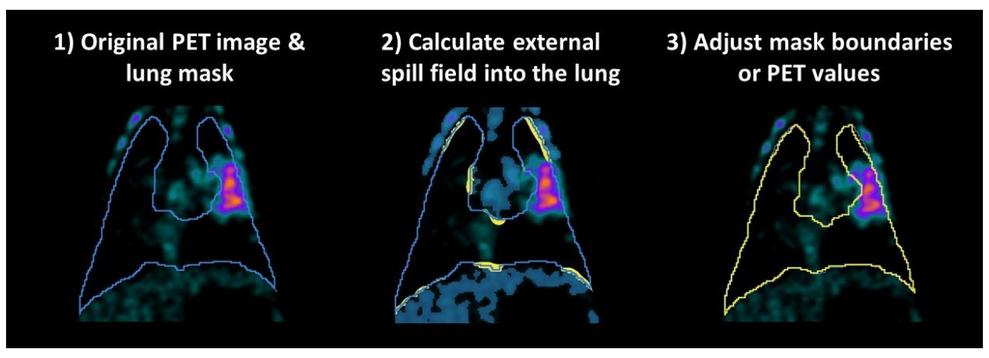
1 CT Lung Segmentation



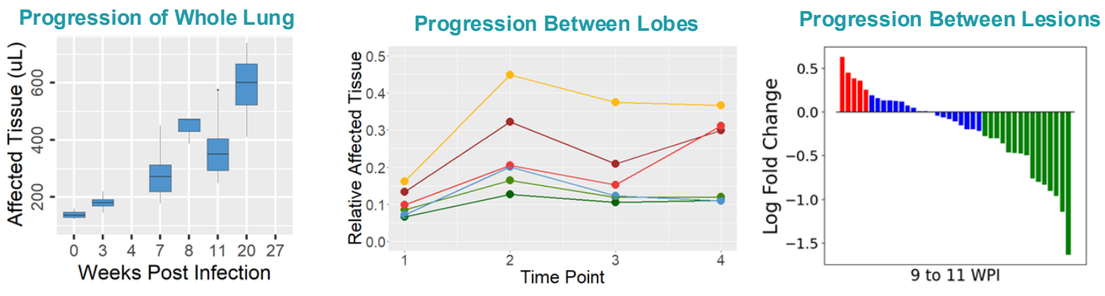
Inputs: 3D CT Volume
Outputs: Lung Prediction

Inputs: 3D CT Volume & Lung Prediction
Outputs: 6 Lobe Prediction

2 PET Spill-in Correction



3 Standardized Quantification



RESULTS

Across cross-validation and independent hold-out testing, the automated pipeline approached expert manual analysis, offering a faster, more consistent route to TB burden quantification that can scale to support preclinical evaluation of new treatment regimens.

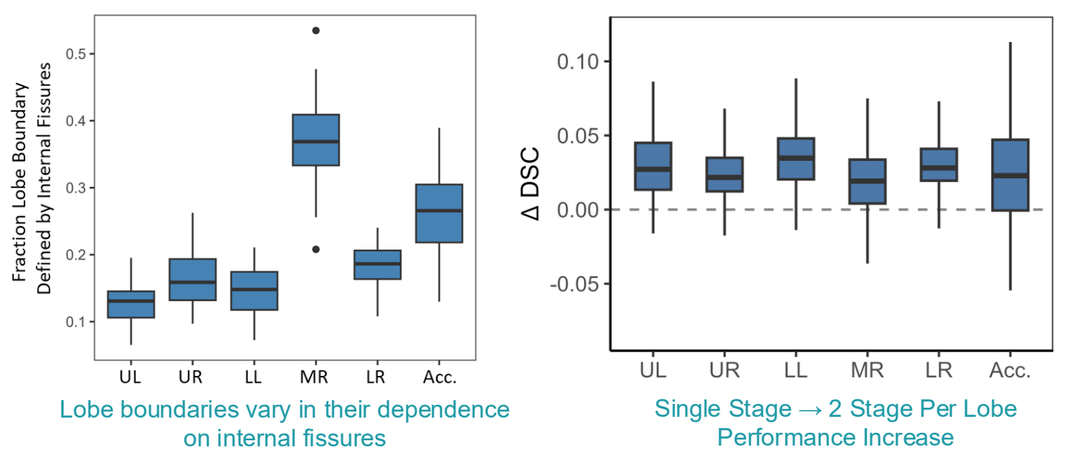
0.910
Average Lobe DSC
Two Stage 3D Attention U-Net
Compared to 0.879 in Single Stage
(5-fold CV)

0.888
Average Lobe DSC
Two Stage 3D Attention U-Net
(External Holdout Set)

0.976
ICC of LocalBG background PET correction relative to manual correction

TB-Infected Macaque Pulmonary Lobe Segmentation:

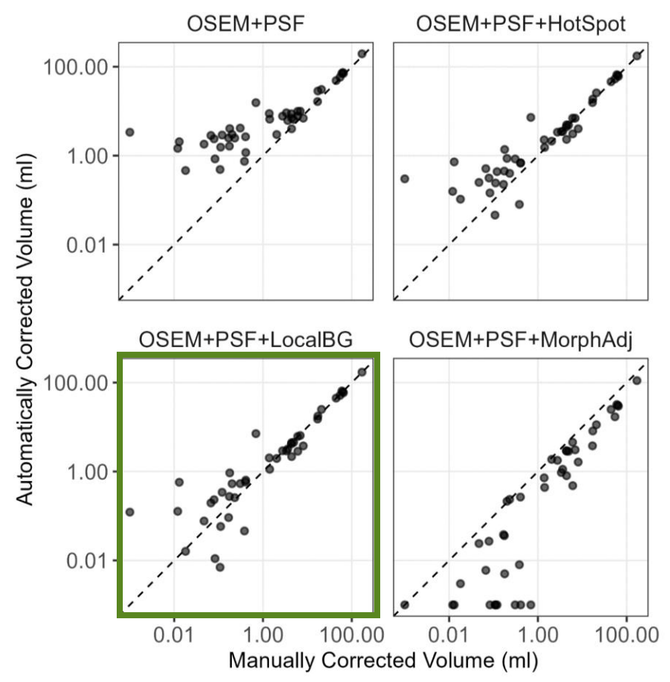
Despite variation in the proportion of boundaries defined by internal fissures, whole-lung context from the 2 stage U-Net improves segmentation across all lobes compared to a single stage U-Net.



Lobe boundaries vary in their dependence on internal fissures

Single Stage → 2 Stage Per Lobe Performance Increase

Biomarker Extraction Following Automatic PET Spill-in Correction



Log-log correlation of the **avid tissue volume extracted from TB-infected Macaque**

Each automatic PET spill-in correction method evaluated (HotSpot, LocalBG, MorphAdj) improves agreement with the manually refined biomarker over the default images (OSEM+PSF)

VALUE OF IMI COLLABORATION

Longitudinal BSL3 PET/CT imaging of TB-infected NHPs is technically demanding and available at only a few sites globally.

The IMI framework made it possible to pool PET/CT data across BSL3-capable partner sites (UKHSA, CEA/IDMIT), producing a more robust, generalizable pipeline whose open-source Slicer modules are now available through ERA4TB and the wider IMI AMR Accelerator.

ERA4TB consortium & funders

CAREER IMPACT

ERA4TB was my first experience of public-private drug development, working across academic, public and industry partners including GSK, NIH, UKHSA and CEA/IDMIT. I began my PhD in this environment, expanding my experience from academic research into translational and collaborative drug development.

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