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Title: Linking MRI and CT imaging with lung function measurements in cryptococcal mouse lung infection

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**Body:** Cryptococcus neoformans and C.gattii are pathogenic yeasts causing lung disease, which may spread to the brain causing life-threatening meningitis. Currently, histology remains essential to unravel cellular and molecular interactions, but imaging techniques are indispensable to define the relevant time frames for each animal individually to investigate crucial events in pathogenesis. We aimed at dynamically monitoring cryptococcosis non-invasively in individual animals in a mouse model for cryptococcal pneumonia, establishing the kinetics of cryptococcal lung infection. Balb/C mice were infected by inhalation of GFP-expressing C. gattii R265, scanned at baseline and weekly up to 5 weeks post infection (p.i.) with retrospectively gated MRI at 9.4T and CT. End stage lung function was tested (Flexivent) and lungs were collected for histological analysis. While the mice showed no clinical signs of cryptococcosis, progression of the lung pathology and compensatory mechanisms could be visualized and quantified non-invasively using MRI and CT. The imaging results were in agreement with functional lung measurements and validated by histochemistry and fungal load quantification. This is the first study showing that non-invasive monitoring of pneumonial cryptococcosis is feasible with lung MRI and CT resulting in high resolution and contrast images. This allows mouse individual longitudinal screening, visualizing infection onset and progression far before the appearance of any phenotypical signs of disease. Histological analysis and functional lung tests were found to be suitable to evaluate the disease, but are best considered as end-point measurements due to the invasiveness of the techniques.