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3D virtual histology of lung and heart tissue affected by severe causes of Covid-19

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Severe progression of Covid-19 is frequently accompanied by lethal respiratory failure. The underlying lung injury can already be detected by radiographic chest imaging and clinical
computed tomography (CT). However, in order to study disease mechanisms at the cellular level, a much higher resolution is required. For this purpose, the tissue obtained by surgical intervention or from a post mortem autopsy is cut into thin sections, stained and observed in an optical microscope. However, conventional histology suffers from some important
limitations. Images are obtained only of two-dimensional sections but not of the entire three-dimensional (3D) volume. In order to accurately track the tree of blood vessels, to
visualise alveolar morphology and to perform precise measurements of alveolar wall thickness which is important for gas exchange in the lung, the cyto-architecture of the lung
has to be visualised in 3D and at high resolution, after locating regions of interest such as inflammation sites. For this purpose, we have adapted phase-contrast (PC) X-ray
computerised tomography (CT) such that three-dimensional imaging tasks can be performed non-destructively on lung autopsies or biopsies. We have used this new technique to
investigate tissue samples from Covid-19 patients, as well healthy control samples [1].
Using multi-scale phase contrast X-ray tomography we can augment the pathological assessment and understanding of Covid-10 pathophysiology based on detailed 3D visualizations of diffuse alveolar damage (DAD) with its prominent hyaline membrane formation, mapping out the distribution of immune cells infiltrating the tissue, and by providing histograms of characteristic distances from tissue interior to the closest air compartment. Most recently, we have extended this to investigations of heart tissue, which can also show severe damage of vasculature.

In this talk, I present the current status of the project, the pathological relevance, and the technical challenges concerning data acquisition, reconstruction and analysis. I will finish with an outlook on how 3D virtual histology and patho-histology can be further developed and be applied to biomedical research.

[1] Marina Eckermann, Jasper Frohn, Marius Reichardt, Markus Osterhoff, Michael Sprung, Fabian Westermeier, Alexandar Tzankov, Christopher Werlein, Mark Kühnel, Danny Jonigk, Tim Salditt, 3D virtual pathohistology of lung tissue from Covid-19 patients based on phase contrast X-ray tomography. eLife 2020;9:e60408 doi: 10.7554/eLife.60408

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