3D X-RAY HISTOLOGY: MICRO-CT GOES MEDICAL

Philipp Schneider

[1]Bioengineering Science Research Group, Faculty of Engineering and Physical Sciences, University of Southampton, UK; [2]μ-VIS X-ray Imaging Centre, University of Southampton, Southampton, UK

Background

Living structures are an intricate three-dimensional (3D) arrangement of cells and tissue matrix across many length scales. Contemporary capabilities to quantify tissue architecture, connectivity and cell relationships are however fundamentally constrained by a lack of 3D analytical platforms with appropriate resolution, penetration, structural differentiation, consistency, volumetric analysis capability and sample throughput. Structural analysis of tissues, whether for research or diagnostic purposes, remains overwhelmingly bounded and constrained by microscopic examination of relatively sparse 2D tissue sections, providing only a snapshot from which 3D spatial relationships can only be inferred. Therefore, whilst 3D medical imaging is commonplace, microscopic tissue structure analysis (i.e., histology) remains overwhelmingly wedded to ~200-year-old practices of microscopic 2D examination of tissue sections.

Recent advances

We have demonstrated previously that X-ray imaging by micro-computed tomography (μCT) allows non-invasive 3D imaging of the microstructure of standard tissue biopsies [1]. This yields details comparable to two-dimensional (2D) optical microscope sections but for the whole tissue volume, which can for example overturn misconceptions of disease development based on 2D assessment. One exemplar is the pathogenesis of idiopathic pulmonary fibrosis [2], where 3D structural insight into co-localisation of tissue features and dysmorphia within substantive tissue volumes suggested previously unrecognised fibroblast foci plasticity. Based on this encouraging μCT results for soft tissues, in collaboration with an industrial partner, we developed a custom-design and soft-tissue optimised μCT scanner [3]. Currently, we are establishing the foundations for routine 3D X-ray histology [4], including new X-ray equipment and standardised & automated workflows, where sample throughput will be increased and scan times reduced, providing the foundations for day-to-day 3D X-ray histology.

Future directions

Applicable to vast existing sample archives and a wide range of soft tissue types including musculoskeletal tissues, the technology will open new research areas, such as large-scale 3D histological phenotyping (i.e., histomics). Furthermore, 3D X-ray histology can translate directly into next-generation clinical image-based diagnostics and patient stratification using artificial intelligence and deep learning, and time-critical intraoperative 3D examination of tissue biopsies will become a realistic future target in this research programme. Here, we will present first results of our 3D X-ray histology approach and portray a vision, how high-throughput and non-destructive 3D histological assessment can offer new opportunities in basic biomedical and translational research, following our ambition to provide a day-to-day imaging tool that complements and augments standard 2D histology.

Philipp is Associate Professor in Biomedical Imaging at the University of Southampton (UoS), the Academic Lead Biomedical Imaging and Academic Director of the μ-VIS X-ray Imaging Centre at UoS. Philipp and team are developing and applying multi-scale and correlative biomedical imaging approaches, specifically in domains where quantitative 3D imaging techniques are not yet established, such as palaeontology or for soft tissues. In collaboration with partners at the University Hospital Southampton, he undertakes translational efforts to integrate engineering knowledge into biomedical and pre-clinical applications, for instance for early diagnosis of colorectal cancer, informed by high-resolution 3D imaging. Philipp is author of ~70 publications and >100 conference contributions, with the development and application of multi-scale 3D imaging of biological systems being the main common theme.

References

1. Scott AE et al., PLoS One 10:e0126230, 2015.
2. Jones MG et al., JCI Insight 1:e86375, 2016.
3. Sinclair I et al., Wellcome Trust Pathfinder Award "Development of micro-computed tomography (μCT) for enhanced diagnosis and prognosis in interstitial lung diseases (ILD)", 2016-17.
4. Schneider P et al., Wellcome Trust Biomedical Resource and Technology Development "Foundations for routine 3D X-ray histology", 2019-22.

Acknowledgements

Engineering at University of Southampton (UoS): Simon Cox, Orestis Katsamenis, Mark Mavrogordato, Anna Scott, Ian Sinclair. Medicine at UoS: David Chatelet, Mark Jones, Peter Lackie, Anton Page, Luca Richeldi, Giacomo Sgalla, Gareth Thomas, Jane Warner. International histopathologist panel for [3]: Alberto Cavazza (Santa Maria Nuova Hospital, Reggio Emilia, Italy), Aurelie Fabre (St Vincent's University Hospital, Dublin, Ireland), Jeffrey Myers (University of Michigan, Ann Arbor, US), Andrew Nicholson (Imperial College, London, London, UK), William Roche (UoS). Nikon X-Tek Systems Ltd., Tring, UK: Ian Haig, Oliver Larking, Michael Olding, Bennie Smit. DECTRIS Ltd., Baden-Daettwil, Switzerland: Spyridon Gkoumas, David Murer. Wellcome Trust awards WT109682MA [3] and 212940/Z/18/Z [4].