

LIGHT SHEET MICROSCOPY FOR 3D-HISTOPATHOLOGY AND CLINICAL APPLICATION

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Histopathology is currently limited to the investigation of thin tissue sections. The lack of volumetric information on pathological material limits the pathologist's view and complicates statistical conclusions. Diagnostic radiology has transitioned from 2D X-ray imaging to 3D visualization tools like CT and MRT. These, however, fail to achieve cellular resolution. Light sheet microscopy offers large field-of-view tomographic imaging possibilities at the mesoscopic resolution scale. We will show how light sheet fluorescence microscopy can be used for 3D imaging of pathological tissue blocks at cellular resolution. For this purpose, we have developed a simple and robust microscope system that allows imaging at the relevant resolution scales. Additionally, we devised a rapid and efficient clearing protocol for blood-containing formalin-stored tissue that is compatible with archival paraffin-embedded material. Our clearing technique can be used with both aqueous and organic solvent-based refractive index matching for deep (up to 5 mm) optical penetration. Our workflow overcomes the constraints posed by the material and routine of histopathology, paving the way toward its integration in daily pathological practice. Our aim is to provide valuable consiliary diagnostic information and to bridge the resolution gap between, and correlate information across, histopathological microscopy and radiological tomography to enable multi-scale clinical imaging.