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High-Resolution 3-D Imaging of Sentinel Lymph Nodes for Detecting Metastatic Tumor Cells in Malignant Melanoma †

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Abstract: Light Sheet Microscopy and optical tissue clearing allow the imaging of much larger biomedical than classical microscopic methods such as confocal or multiphoton microscopy. Several cubic centimeter volume samples can be optically imaged with cellular and subcellular resolution. Specific cells can be detected at the single-cell level or as small ensembles. After introducing Light Sheet Microscopy and the principles of optical clearing, we will show the use of 3D imaging of sentinel lymph nodes for detecting metastatic tumor cells in malignant melanoma. High-resolution imaging of sentinel lymph nodes (SLN) from melanoma patients is a crucial approach to specify staging and determining individuals requiring adjuvant treatment. Current histologic SLN analysis has a substantial drawback: only a small portion of the node is sampled. At the same time, most of the tissue is discarded, which might explain the high false-negative rate of SLN diagnosis. Therefore, we developed algorithm-enhanced light-sheet fluorescence microscopy (LSFM) approach to three-dimensionally reconstruct the entire SLN with the power to identify single tumor cells. We comprehensively quantified total tumor volume while simultaneously visualizing cellular and anatomical hallmarks of the associated SLN architecture. In a first-in-human prospective study (21 SLN from 11 melanoma patients), LSFM not only identified all metastases seen histologically but additionally detected metastases not recognized by routine histology. Thus, our 3-D digital pathology approach can increase the sensitivity and accuracy of SLN-metastasis detection and potentially alleviate the need for conventional histopathological assessment in the future. The original paper is available at https://www.medrxiv.org/content/10.1101/2020.07.22.20159103v1.

Keywords: light-sheet microscopy; tissue clearing; sentinel lymph nodes, metastatic tumor cells;

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Conflicts of Interest

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