

TRANSLATION OF THIRD AND SECOND HARMONIC GENERATION MICROSCOPY INTO THE CLINIC FOR THE ASSESSMENT OF FRESH LUNG TUMOR TISSUE

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BACKGROUND Third and second harmonic generation (THG/SHG) microscopy is a novel imaging technique that has been suggested as a promising clinical tool, mainly for cancer diagnosis. In lung surgery, immediate feedback on the nature of the excised tissue is important. During the operation a ‘fast’ diagnosis can be made using frozen section analysis, which takes up to 45 minutes. Alternative techniques are therefore required that can assess lung tissue with a speed that enables ‘live’ feedback to surgeons while they operate.

THG/SHG/2PEF MICROSCOPY A technique that meets these requirements is third and second harmonic generation (THG/SHG) and two-photon excited autofluorescence (2PEF) microscopy, which is non-invasive, label-free and provides 3D images with a high, sub-cellular resolution, within seconds. Before, we demonstrated on lung tissue that THG/SHG/2PEF imaging modalities can generate high quality images of freshly excised unprocessed tissue, in less than a minute with information content comparable to that of the gold standard, histopathology [1].

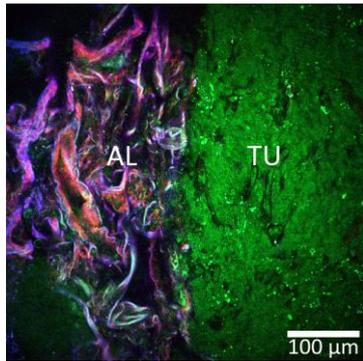


Figure 1: THG(green)/ SHG(red) /2PEF(blue) image of fresh human lung tissue with a sharp transition between alveolar (AL) and tumor tissue (TU).

RESULTS We demonstrated that we could successfully reveal alveolar structures and histopathology hallmarks, including cell morphology and general tissue architecture (collagen and elastin organization). Here, we will present the first results of an ongoing study where we elaborate on the previous study by imaging a large number of biopsies of patients that are suspected of lung cancer, comparing the THG/SHG/2PEF images with the histopathology, assessing the quality of diagnoses by independent pathologists, and examining the clinical impact of the portable THG/SHG/2PEF microscope. In addition, we show whether THG/SHG/2PEF microscopy is able to distinguish different immune cells, which is important for the pathological assessment of lung tumor tissue.

REFERENCES

[1] L. M. G. van Huizen, T. Radonic, F. van Mourik, D. Seinstra, C. Dickhoff, J. M. A. Daniels, I. Bahce, J. T. Annema, and M. L. Groot, “Compact portable multi-photon microscopy reveals histopathological hallmarks of unprocessed lung tumor tissue in real time,” *Translational Biophotonics*, **2**(4), (2020).