Plataus lauko antros harmonikos generacijos mikroskopija su mašininiu mokymusi skydliaukės vėžio detekcijai

Wide-field second harmonic generation microscopy with mashine learning for thyroid cancer detection

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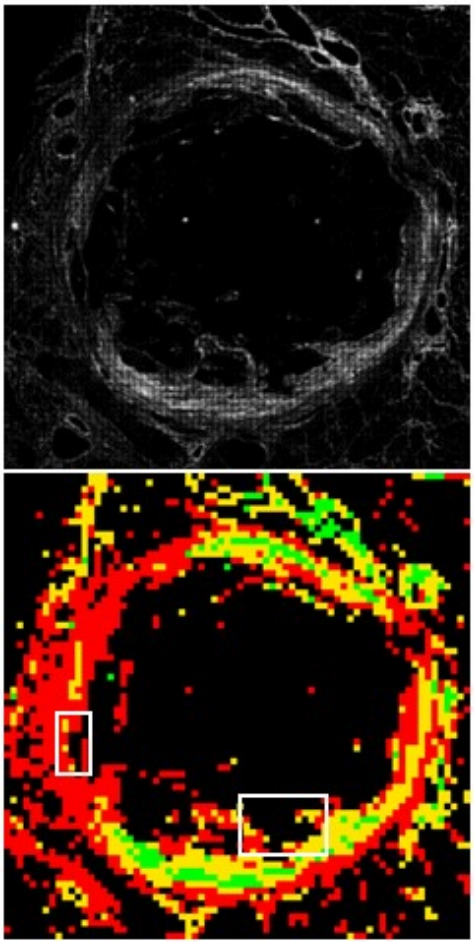

Figure 1. (Top) Tiled SHG image of a thyroid nodule capsule consisting of 72x72 individual SHG image tiles and covering an area of 8x8 mm. (Bottom) A map of SHG image tiles attributed to 3 different K-means clusters with designated cancer cell invasions.

Second harmonic generation (SHG) microscopy has become a technique of choice for label-free microscopic imaging of various biological structures. SHG is a non-linear optical process, where illumination light is frequency-doubled upon its interaction with ordered non-centrosymmetric material. Among biological materials, the strongest harmonophores are collagen, microtubules, and myosin in the order of decreasing efficiency of SHG. SHG imaging thus allows for detailed visualization of collagen arrangement in the extracellular matrix. Collagen structure appears to be remodelled in various pathological situations such as cancer, fibrosis, and connective tissue disorders. Since those changes can be detected with SHG imaging, and SHG does not require extraneous labels, it is a viable addition to traditional diagnostic methods based on the inspection of stained histological sections.

Since its inception and up until not so long ago SHG imaging was performed by employing laser scanning microscopy. Recently, it was demonstrated that the speed of acquisition can be significantly increased in the wide-field configuration that in combination with mechanical scanning enables fast imaging of macroscopic sample areas [1][2]. In the present work, we exploit this opportunity of fast measurement to accumulate SHG images of large sample areas (Figure 1) and investigate the possibility to detect cancerous changes in thyroidal tissue sections. SHG images of collagen structures in thyroid nodule capsule were quantitatively analysed using first, second and higher order statistics based on grey level co-occurrence matrix (GLCM) in combination with a variant of unsupervised machine learning for image segmentation according to the calculated texture parameters. K-means clustering revealed areas of collagenous capsule with presumably different extent of cancer-associated collagen remodelling. This designation not only dubbed the assignment of the sites of cancer cell invasion but also provided an indication of less obvious areas of possible inflammation or cancer cell invasion occurring on a different section of a voluminous thyroid nodule. Overall, SHG imaging of thyroidal nodules in tandem with automated data analysis presents an illustrative example of an objective approach that could be auxiliary to the established pathological analysis.

Key words: second-harmonic generation. wide-field imaging, collagen, machine-learning.

Literature

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