First results of computer-enhanced optical diagnosis of bladder cancer

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Introduction

Bladder cancer is the sixth leading cancer cause worldwide. Non-muscle invasive tumors can be diagnosed and treated endoscopically. Based on biopsies alone, pathologists cannot determine the spatial organization of specimens, their relationship with each other, or their complete removal.

Methods

To extend white light cystoscopy as the gold standard for bladder cancer detection, diagnosis and removal of small or flat lesions, new image-based technologies have been investigated. These include a stereo-cystoscope for improved orentation and navigation, computation of 2D and 3D panoramic images for extended visualization and documentation, as well as label-free fiber-based fluorescence-lifetime imaging (FLIM) and Raman-spectroscopy in combination with statistical data analysis.

Results

FLIM-images are fitted in each pixel with a double-exponential decay model of various samples samples classified by a pathologist into healthy, healthy, inflammation, high-grade tumor. A well-defined difference between healthy and tumor cells us achieved, hence fluorescent spectral analysis can successfully distinguishes normal cell from carcinoma.

Raman data sets were decomposed into endmember loadings and scores by vertex component analysis without further pre-processing. The results represent the spectra and concentrations of the most dissimilar components. The observed changes together with typical bands of proline and hydroxyproline point to elevated content of fibrous proteins such as collagen

Simultaneous visualization of a 2D and 3D bladder panorama together with images and data of suspicious findings, as e.g. from FLIM and Raman data of tumorous lesions can strongly enhance an examination´s completeness as well as lesion documentation, since these can now be related to their correct anatomical context.

Conclusion

Combining all these technologies, cystoscopy can will be further enhanced to include new diagnostic possibilities.

Raman Spectroscopy to Characterize Bladder Tissue for Multidimensional Diagnostics of Cancer in Urology

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Introduction

Fiber optic Raman spectroscopy offers label-free identification of cancer in the bladder under in vivo conditions. However, state-of-the art Raman technology does not enable to scan the entire bladder wall. Our innovative approach within the project Uro-MDD is to combine panoramic image reconstruction of white light cystoscopy and fluorescence lifetime imaging to define regions of interest for Raman-assisted diagnostics.

Methods

Control and cancer specimens were prepared from ten human bladder resections ranging in size from 5-10 mm. Raman images were registered at 785 nm excitation in the sequential acquisition mode at 250 µm step size. Raman data were decomposed into endmember loadings and scores by vertex component analysis without any prepocessing. The results represent the spectra and concentrations of the most dissimilar components that can be used as input for supervised classification models.

Results

First results of an ongoing study are presented. Raman spectra of control bladder tissue are dominated by spectral contributions of proteins with alpha helical structures whereas Raman spectra of cancer tissue show proteins with different secondary structures typical for fibrous proteins. Other components in the tissue specimens were assigned to optimal cutting tempeature (OCT) medium and phthalocyanine. The first component was expected because OCT medium was used to embed tissue samples prior to freezing. The second component is consistent with photodynamic therapy treatment (PCT) of the patient before surgery.

Conclusion

The Raman data demonstrate how to obtain specific molecular information from resected bladder specimens. Such Raman images can be used in a clinical setting to determine cancer margins and the resection status. Fiber probes are under development to translate the technique to in vivo screening.

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Metabolic Imaging by Simultaneous FLIM of NAD(P)H and FAD

Abstract: We describe a metabolic imaging system[1] based on simultaneous recording of lifetime images of NAD(P)H and FAD. The system uses one-photon excitation by ps diode lasers, scanning by galvanometer mirrors, confocal detection, and two parallel TCSPC FLIM recording channels[1]. Two lasers, with wavelengths of 375nm and 410 nm, are multiplexed to alternatingly excite NAD(P)H and FAD. One FLIM channel detects in the emission band of NAD(P)H, the other in the emission band of FAD. For both channels, the data analysis delivers images of the amplitudes of the decay components, a1 and a2. We show that these are robust parameters to characterize the metabolic state of cells. FLIM results obtained from excised human-bladder tissue were in perfect agreement with histology.

Keywords: NAD(P)H, FAD, Metabolic Imaging, FLIM

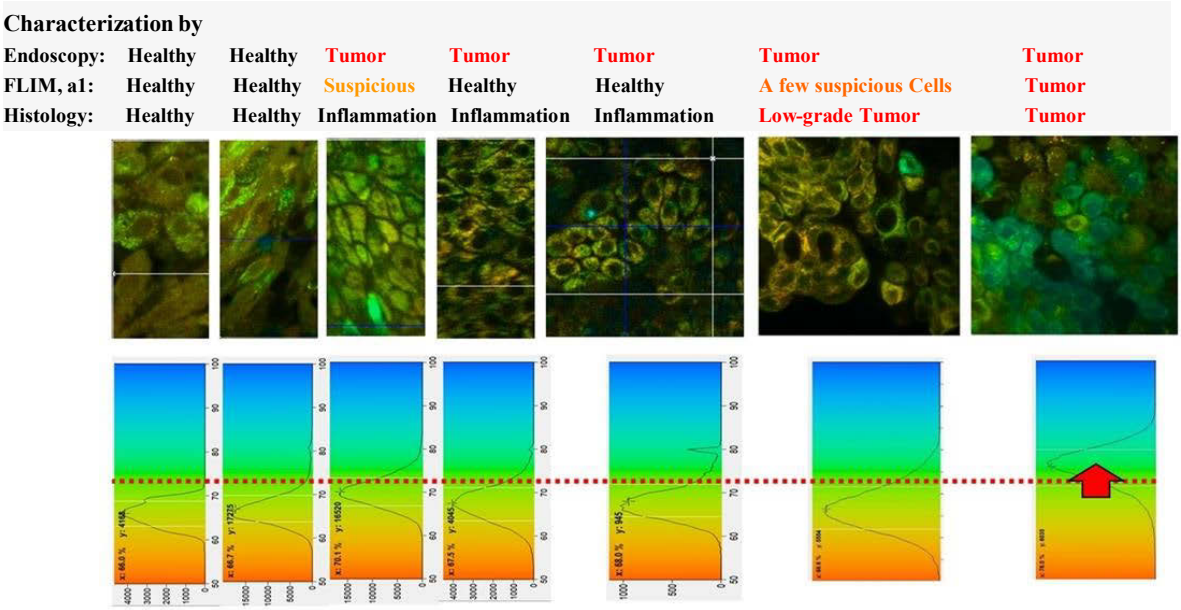

Figure: Comparison of endoscopy, NAD(P)H FLIM, and histology results

References

[1] M.N. Pastore, H. Studier, C.S. Bonder, M.S. Roberts, Non-invasive metabolic imaging of melanoma progression. Exp. Dermatol. 26, 607–614 (2017)
[2] W. Becker, The bh TCSPC Handbook. 8th edition (2019). Available on www.becker-hickl.com. Please contact bh for printed copies.

Characterization of the Measurement Setup for Polarization-sensitive Imaging in Medicine

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The intraoperative visualization of nerve fibers within the white matter of the human brain is still an unsolved problem in neurosurgery. Precise information about the location and orientation of fiber bundles is essential for preserving neural functionality. Today, diffusion tensor imaging is the gold standard for preoperative MRI fiber tracking and plays an important role in surgical planning. But due to brain shift during surgery the precise spatial correlation gets lost. Polarization-sensitive imaging has already shown its potential in providing relevant information on the structural details of fibrous tissue, such as the density and orientation of the nerve fibers. However, due to the technical complexity of hitherto existing polarization imaging systems this method has been restricted to in vitro applications until now. Furthermore, current research in the field of biomedical polarization imaging focuses on the transmission mode, which excludes in vivo application from the outset. We are pursuing a different approach and have constructed a new measurement setup in reflection mode. Since this research work differs from the current state of the art, a clearer understanding of the underlying theory of physical optics for the interpretation of polarization signals from a diffuse backscattering sample needs to be developed. Here, we publish the characterization of our measurement setup including all relevant parameters and properties. The designed methods for characterizing the camera and the light source are described in detail. Based on this, the system can be validated and it can be shown that reflection-based polarization imaging is possible. This could be a first step towards enabling intraoperative polarization imaging in neurosurgery.