Netiesinė multimodalinė poliarimetrinė mikroskopija melanomos diagnostikai ir prognostikai, naudojant mašininį mokymąsi

Machine learning-aided nonlinear multimodal polarimetric microscopy for human melanoma diagnostics and prognostics

Martynas Riauka¹, Viktoras Mažeika¹, Vincas Urbonas^{2,3}, Edvardas Žurauskas^{4,5}, Lukas Kontenis⁶, Kamdin Mirsanaye⁷, Leonardo Uribe Castano⁷, Mykolas Mačiulis¹, Mehdi Alizadeh⁷, Vitalijus Karabanovas⁸, Ričardas Rotomskis⁸, Virginijus Barzda^{7,9}

¹Laser Research Centre, Faculty of Physics, Vilnius University, Saulėtekio Av. 3, Vilnius LT-10222, Lithuania ²Laboratory of Clinical Oncology, National Cancer Institute, Santariškių St. 1, 08406 Vilnius, Lithuania ³Department of Medical Oncology, National Cancer Institute, Santariškių St. 1, 08406 Vilnius, Lithuania

⁴National Centre of Pathology, P. Baublio St. 5, LT-08406, Vilnius, Lithuania

⁵Department of Pathology, Forensic Medicine and Pharmacology, Faculty of Medicine, Vilnius University, M. K.

Čiurlionio St. 21/27, LT-03101, Vilnius, Lithuania

⁶Light Conversion, Keramikų St. 2B, LT-10234, Vilnius, Lithuania

⁷Department of Chemical and Physical Sciences, University of Toronto Mississauga,

3359 Mississauga Rd. North, Mississauga, L5L 1C6, Canada

⁸Biomedical Physics Laboratory, National Cancer Institute, P. Baublio St. 3b, LT-08406 Vilnius, Lithuania

⁹Department of Physics, University of Toronto, 60 St. George St., Toronto, M5S 1A7, Canada

martynas.riauka@ff.vu.lt

Nonlinear multimodal polarimetric microscopy (NMPM) is a technique allowing extensive analysis of cellular and extracellular components in hematoxylin and eosin-stained (H&E) as well as unstained histological sections of biopsy tissue.

The processes of carcinogenesis and metastasis affect both the exctracellular matrix (ECM) and the cellular components of the tissue. The ECM is comprised mostly of collagen, which is a non-centrosymmetric material and is known to generate second harmonic (SHG) signals, dependent on the polarization of the incoming laser light [1]. SHG signal analysis is performed in the framework of the double Stokes-Mueller polarimetry (DSMP) formalism. It has been shown that such analysis coupled with machine learning is suitable for breast [2] and lung [3] cancer diagnostics.

In this work, H&E-stained histological sections of melanoma were investigated. The samples corresponded to different types and stages of melanoma and analysis included two more modalities, i.e. multiphoton excitation fluorescence (MPEF) as well as third-harmonic generation (THG). In the MPEF channel, eosin-stained ECM is observed whereas hematoxylin-stained cell nuclei are highlighted in the THG channel [4].

Data from all three channels was investigated by means of texture analysis, statistical testing and the combination of both supervised and unsupervised machine learning. Additionally, for the analysis of nuclear morphology a segmentation algorithm was developed and the morphological features were examined using deep learning.

It was shown that the analysis can be applied for tasks, such as tumor margin delineation, differentiation of tumorous and inflammatory regions, identification of type and staging of melanoma and also has a potential of recognizing the cases of rapidly spreading melanoma.



Figure 1. Human melanoma histological section.
Brightfield image (a) and machine learning-classified three channel map superimposed on the brightfield image (b). Green color corresponds to normal tissue, whereas yellow and red highlights the inflammatory and tumorous regions. Red line corresponds to the tumor margin, as identified by a pathologist.

Key words: Stokes-Mueller polarimetry, nonlinear multimodal microscopy, texture analysis, nuclei segmentation, machine learning, neural networks, melanoma, digital histopathology.

Literature

- Samim M, Krouglov S, Barzda V. Double Stokes Mueller Polarimetry of Second-Harmonic Generation in Ordered Molecular Structures. J Opt Soc Am B (2015) 32:451–60.
- Mirsanaye, K.; Uribe Castaño, L.; Kamaliddin, Y.; Golaraei, A.; Augulis, R.; Kontenis, L.; Done, S.J.; Žurauskas, E.; Stambolic, V.; Wilson, B.C.; et al. Machine Learning-Enabled Cancer Diagnostics with Widefield Polarimetric Second-Harmonic Generation Microscopy. Sci. Rep. 2022, 12, 10290.
- Mirsanaye, K., Uribe Castano, L., Kamaliddin, Y., Golaraei, A., Kontenis, L., Zurauskas, E., R. Navab, K. Yasufuku, M.-S. Tsao, B. C. Wilson, V. Barzda (2022). Unsupervised determination of lung tumor margin with widefield polarimetric second-harmonic generation microscopy. Sci. Rep. 12, 20713.
- A. Tuer, D. Tokarz, N. Prent, R. Cisek, J. Alami, D. J. Dumont, L. Bakueva, J. Rowlands, and V. Barzda, "Nonlinear multicontrast microscopy of hematoxylin-and-eosin-stained histological sections," J. Biomed. Opt. 15(2), 026018 (2010)