Time-resolved fluorescence spectroscopy in differential diagnosis of liver cancer *in vivo*

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This work reports a machine-learning-based approach to interpret time-resolved fluorescence spectroscopy data acquired during optical biopsy of the liver. The approach allowed to differentiate between liver parenchyma and tumor with sensitivity and specificity above 0.91 and 0.79, respectively, providing differential diagnosis of liver cancer (primary malignant tumor, metastases, or benign) with sensitivity and specificity of at least 0.80 and 0.95.

Keywords: time-resolved fluorescence spectroscopy, liver cancer, optical biopsy, machine learning

I. Introduction

Liver cancer is an aggressive and a highly fatal tumor[1]. Proper choice of treatment strategy requires differentiation of primary liver cancer from metastases and benign neoplasms[2]. The diagnostic efficiency of standard diagnostic methods (ultrasound, CT, MRI, PET) depends on the size and types of the tumor, as well as on the hepatic parenchymal disease. Therefore, histological and cytological analysis of a biopsy sample obtained with a percutaneous needle biopsy (PNB) remains the gold standard for the diagnosis of liver cancer. The introduction of optical techniques into the PNB diagnostic procedure has allowed us to increase its diagnostic efficiency[3,4]. The time-resolved fluorescence spectroscopy (TRFS) technique has a high sensitivity to metabolic shifts in biological tissues. The application of machine learning (ML) to data processing can provide a more accurate diagnosis and help in the selection of an individual treatment strategy. In our work, we suggested that the reprogrammed metabolism of various types of liver cancer can be detected by TRFS and classified using ML.

II. Methods and Materials

The fluorescence lifetime optical biopsy system[4] included a TCSPC system (Becker&Hickle, Germany) based on a SPC-130-EMN photon counting board, HPM-100-40 detectors, and a 375 nm BDL-SMN laser. Fluorescence emission detection range was 445 ± 25 nm. Optical signals were recorded through the 1 mm original fine-needle optical probe compatible with the standard equipment for the puncture biopsy procedure – a 17.5G Chiba-type biopsy needle. The clinical study involved 25 patients with different diagnoses: 6 hepatocellular carcinoma (HCC), 6 nodular hyperplasia (NH), and 13 metastases (MTS). After preprocessing the data, the following 4 parameters of TRFS were selected, which were used in as inputs the ML: fluorescence intensity (I_f), the amplitude of the short decay component (α_1), short fluorescence lifetime (τ_1) and long fluorescence lifetime (τ_2). The developed model utilizes random forest (RF), support vector machine (SVM), and logistic regression (LR) methods.

III. Experimental Results and Discussion

At the first stage of ML application, we developed a classifier for the differentiation of liver parenchyma from different types of liver cancer. The RF algorithm showed the best values of sensitivity (Se) and specificity (Sp). We obtained the following evaluation criteria values when differentiating between two classes (normal liver/tumor): liver/NH (Se = 0.96 ± 0.04; Sp = 0.85 ± 0.07), liver/HCC (Se = 0.96 ± 0.01; Sp = 0.82 ± 0.05) and liver/MTS (Se = 0.91 ± 0.04; Sp = 0.79 ± 0.08).

At the second stage, we solved the problem of classifying tumors into different types. Similar to previous case, the RF algorithm showed the highest efficiency. As expected, HCC is detected with the highest Se and Sp, since this type of tumor has the most pronounced metabolic shifts towards glycolysis (Se = 0.87 ± 0.07; Sp= 0.95 ± 0.01). Our approach also demonstrates good results in detecting NH (Se= 0.84 ± 0.09; Sp= 0.95 ± 0.03), while the lowest indicators of accuracy were achieved for MTS (Se= 0.80 ± 0.10; Sp= 0.99 ± 0.01). Most likely, this is due to liver metastases are too heterogeneous and may have different metabolism.

The proposed ML approach to processing TRFS data obtained from liver optical biopsy reveals the potential of the technology as a promising tool in the early diagnosis of liver cancer allowing for development of individual treatment strategies.

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