Terahertz spectroscopy of blood plasma as a promising method for diagnosing of thyroid cancer

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***Abstract*—Using terahertz time domain spectroscopy (THz TDS), the dielectric properties of liquid and lyophilized blood plasma of patients with thyroid nodules were studied for the first time. THz absorption and refraction were compared with the data of biochemical analysis of blood plasma; a correlation with the concentration of glucose, protein, and some tumor miRNAs were revealed. Thus, the sensitivity of THz TDS to thyroid cancer was confirmed in the frequency range from 0.05 to 1.6 THz.**

I. INTRODUCTION

Over the past decades, thyroid cancer has been the most common endocrine tumor. The starting point of thyroid cancer is the thyroid nodule formation [1]. Despite the wide range of methods used, there is a need to improve the preoperative diagnosis of thyroid nodules.

THz methods have proven their sensitivity to the determination of structural changes in tumor tissues [2, 3]. However, the use of THz in vivo for the study of nodular thyroid diseases is impossible due to the high absorption of THz radiation by tissues. In contrast, blood sampling is minimally invasive and easy to obtain, making it attractive to explore for thyroid cancer biomarkers, for example, miRNAs [1, 4]. We have previously shown the applicability of THz TDS for the diagnosis of experimental liver cancer [5]. The object of this paper is to demonstrate the possibilities of THz TDS of human blood plasma for diagnosing of thyroid cancer.

II. RESULTS

Using the THz TDS method in the range from 0.05 to 1.6 THz, we studied samples of dry and liquid blood plasma for 3 groups: tumor (5), nodus (5) and healthy (7). Two pellets (“thick” and “thin”) were made from each dry plasma sample. The thickness was measured with a micrometer as well as using the technique based on the delay of the re-reflected THz pulse. The weight and thickness of the thick pellets were in the range of 21.1-26.2 mg and 0.75-1.11 mm, respectively. The weight and thickness of the thin tablets were 9.3-13.2 mg and 0.385-0.565 mm, respectively. Liquid plasma samples were placed in a cell (Bruker Optics, USA) with two identical polystyrene windows. The thickness of the liquid layer was 120 ± 5 μm. The transmission of the blood serum was analyzed after normalization to the signal passing through the distilled water in the same cell, measured regularly in turn with the serum [5]. Based on the measurements, the absorption and refraction spectra were obtained [6]. The averaged results of the absorption coefficient of dry plasma for 3 groups are shown in the figure 1. Averaging the spectral characteristics by groups revealed that THz makes it possible to separate not only samples with nodular diseases from healthy ones, but also to differentiate patient’s plasma with thyroid tumor and thyroid nodus. The absorption spectra for each sample correlate with biochemical analysis, which suggests that changes in the content of protein and glucose may be associated with pathological processes occurring in the human body during oncology (see Fig. 2).

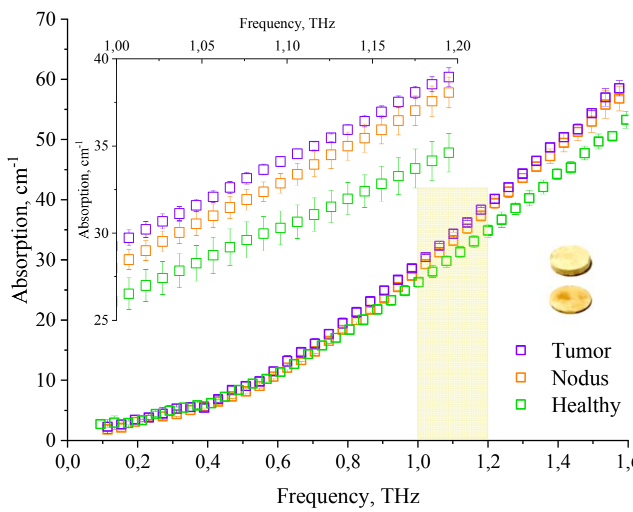

Fig. 1. The absorption coefficient of dry plasma in the range of 0.05-1.6 THz. Green squares - plasma pellets of healthy people, orange squares plasma of people with nodus, purple squares - plasma of people with thyroid tumor.

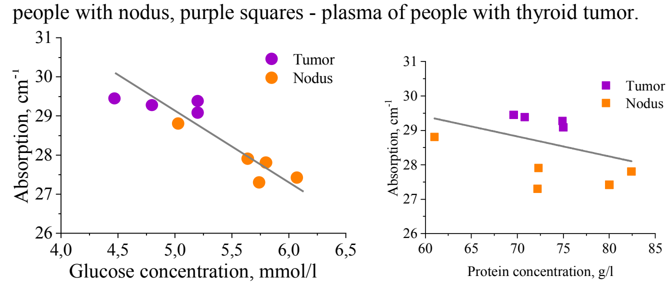

Fig. 2. The dependence of the absorption coefficient at 1 THz on glucose (left) and protein concentration (right) in the samples

The Pearson's correlation (R=0.62, $p<0.05$) was also revealed between the absorption coefficient at 1THz and cancer biomarker miRNA-146b (see Fig. 3). It was shown that miR-146b, along with a set of other microRNAs, are overexpressed in tumours versus hyperplastic nodules [7]. MiR-146b was analyzed in fine-needle aspiration samples by real-time PCR [8].

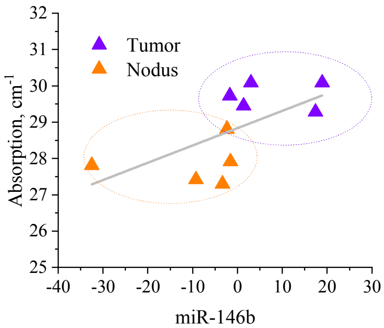

Fig. 3. The dependence of the absorption coefficient at 1THz on the concentration of thyroid tumor marker miR-146.

The use of dimensionality reduction techniques is needed to visualize data structure and make exploratory data analysis. We tried several popular dimensionality reduction methods like principal component analysis, multidimensional scaling, and UMAP [9]. The results from these methods agree well. The supervised machine learning algorithms namely Support Vector Machine (SVM) and perceptron have confirmed the difference between the THz spectra of blood plasma samples with thyroid cancer from healthy ones (Fig. 4).

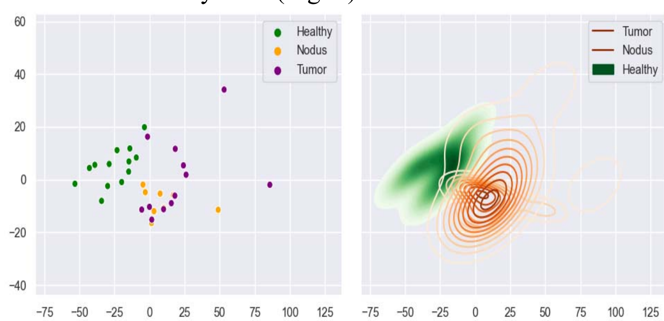

Fig. 4. Left: A projection of data to the 1st and 2nd principal components; Right: data distribution density of tumor and nodus groups together versus healthy group.

To separate tumor and nodus groups an additional analysis was performed. Thick and thin tablets was separated and UMAP, kernel PCA, and MDS methods were applied. There is a good separability of tumor and nodus thin tablets with the UMAP and PCA with Radial Based Function (RBF) kernel (Fig. 5), while thick tablets are not divided perfectly.

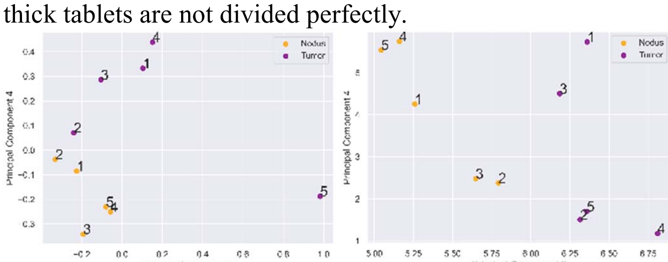

Fig. 5. A projection of thin tablets THz spectra by RBF kernel PCA method (left) and UMAP method (right).

Averaging absorption spectra of liquid plasma normalized to water spectrum are shown in Fig. 6.

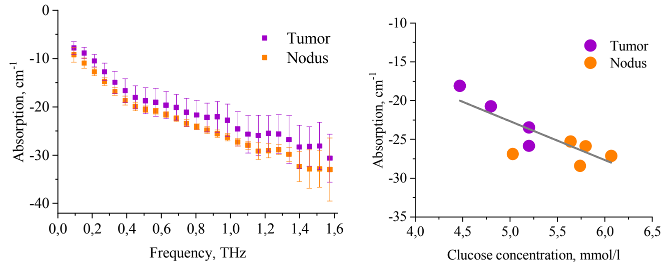

Fig.6. Averaging absorption difference spectra of liquid plasma (left) and the dependence of the absorption coefficient at 1 THz on glucose concentration (right) in the samples.

There is a significant difference in absorption spectra between the tumors and nodus groups. As well as in the case of dry plasma, there is a correlation between the absorption at 1 THz and the content of glucose and protein in the blood plasma.

III. Summary

In this work, we have proposed a THz-TDS for studying of dry and liquid human blood plasma with thyroid cancer and without it. The repeatability of the results for samples of different aggregate states indicates the sensitivity of THz spectroscopy to small changes in the concentration of substances in the blood plasma. Thus, THz spectroscopy of blood plasma can be a promising method for diagnosing of thyroid cancer.

The work was supported by the RFBR (project no.17-00-00275 (17-00-00270, 17-00-00186), by the Ministry of Science within the State assignment FSRC «Crystallography and Photonics» RAS in part of equipment. The work was performed under the government statement of work for ISPMS Project No. III.23.2.10

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