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Terahertz express diagnostics of complications caused by COVID-19

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A spectrometer based on silicon nanosandwiches has been proposed to detect complications caused by COVID-19. Operating in the mode of a balanced photodetector, the silicon nanosandwich is both a source of terahertz irradiation and a receiver of reflected and/or radiated from biological tissue. It has been demonstrated that recording the current-voltage characteristics of a silicon nanosandwich made it possible to analyze changes in the thyroid gland, thereby determining the degree and nature of changes caused by the COVID-19 disease..

Keywords: silicon nanosandwich, terahertz irradiation, current-voltage characteristic, COVID-19.

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Introduction

Coronavirus epidemic was the main problem. According to the Johns Hopkins University website, about 5 million disease cases were recorded in Russia and about 170 million cases were recorded worldwide by the end of May 2021[1]. Despite the significant success in coronavirus vaccine development, the virus is still mutating and the emergence of new strains which are able to bypass the obtained immunity cause major concern. Therefore, the problem of COVID-19 diagnostics and complication treatment is of utmost interest.

Recently, medicine starts to extensively use terahertz (THz) radiation. THz radiation extends within the wavelength range from dozens of micrometers to some millimeters (spectral range from 100 GHz to 30 THz). The main benefits of THz radiation are, first, its non-ionization — due to low radiation quanta energy, and, second, — significant influence on the essential biological reaction processes. Despite the fact that THz radiation intensity is reduced significantly when going through skin surface (the intensity is reduced by a factor of tens of thousands at a depth of several micrometers), its therapeutic efficacy is an undeniable fact [2]. In addition, preliminary study was carried out in the field of COVID-19 patient treatment which showed that early application of THz radiation allows to reduce the patient's stay time in the intensive care unit by 4−8 days; to reduce radiation and pharmaceutical load on the patient and mechanical ventilatory support time by 4−8 days; increase the opportunity of favorable prognosis in patients with risk factors [3].

The main problem in using THz radiation is the fact that Earth's atmosphere does not pass electromagnetic waves in the wavelength range corresponding to THz radiation, which means that there are no natural sources. The artificial sources provided constitute free-electron lasers, traveling-wave tube lamps or weak incoherent radiation sources. To detect THz radiation, liquid helium cooled low-noise bolometers have to be used. Nevertheless, semiconductor and high-temperature superconductor nanotechnology progress allowed to get compact solid-state devices which are capable of emitting and detecting in the THz wavelength band [4].

These discoveries made it possible to use the potential of a spectral range which has been inaccessible before. Since THz radiation passes freely through such materials as plastics, ceramics , wood, paper, building structures, and clothing, which is more important, the use of THz-radiation detector gates instead of the existing X-ray detector gates for people and cargo control is a promising security area. Some European countries already use GHz radiation. The use of THz radiation for personal identification is one of the most promising areas. This method is based on the fact that DNA oligonucleotide structure has absorption and radiation spectra in the specified range. Currently, a lot of investigations are carried out for DNA sequencing using THz radiation [5–7]. Moreover, according to the DNA absorption and radiation spectra, cancer disease diagnostics methods are being developed [8]. It has been shown that spectral response characteristics of normal and cancer cells differ in the THz wavelength band [9]. The authors of the paper have previously studied the capability of disease diagnostics by analysis of THz response of biological tissue. The main focus was made on the detection of response at frequencies corresponding to DNA oligonucleotides demonstrated by Fischer [10] and on possible epigenetic changes caused by various pathologies, for example, cytosine methylation manifested at about 1.7 THz [8]. Response amplitudes demonstrated an important role of DNA oligonucleotides in the early identification of various diseases. In the previous research, all volunteers had recovered from COVID-19, and response from different parts of body was compared. This paper offers to address the opportunity of express identification of complications caused by COVID-19 by

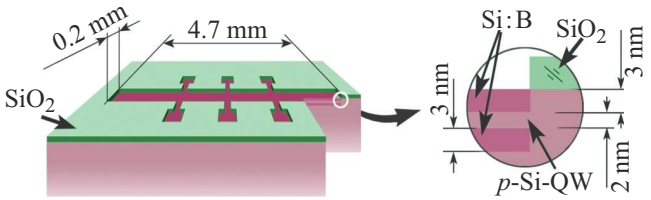

Figure 1. SNS diagram with typical dimensions.

means of spectral response of the biological tissue exposed to THz radiation. Response amplitude changes were studied six months after the previous COVID-19. It should be noted that presentation of results for one volunteer is due to their similarity with other test persons. In addition, this research made a special focus on thyroid gland, and the next investigations will be focused on other organs. Parallel thyroid gland research was carried out at the Almazov National Medical Research Center, Saint Petersburg, which also participates in other research activities where this spectrometer had been successfully used. According to the research carried out by the Almazov Center, thyroid gland is highly vulnerable to changes after the previous COVID-19, and relative changes in it are approximately the same for all patients.

1. Materials and methods

To achieve the goals of this research, a silicone nanosandwich (SNS) was used as a THz radiation source, which consisted of p type ultra-narrow quantum well (p-Si$-$QW), limited by δ barriershighly boron-doped ($5 \cdot 10^{21}\,\mathrm{cm}^{-3}$) on n-Si (100) surface where high carrier mobility is achieved (Figure 1) [2,11]. These p-Si$-$QW are formed on n-Si (100) substrates during preliminary oxidation and subsequent short-term boron diffusion from gas phase [2,11]. It has been shown that boron atoms in δ barriers form trigonal dipole centers (B^+-B^-) as result of negative-U-reaction: $2B^0 \rightarrow B^+ + B^-$ [11] whose crystallographically oriented sequences form edge channels responsible for conductivity in p-Si$-$QW. Two-dimensional hole density, $3 \cdot 10^{13}\,\mathrm{m}^{-2}$, was defined by recording field Hall dependencies [11]. Moreover, it has been shown that p-Si$-$QW edge channels in longitudinal current conditions are efficient THz and GHz radiation sources due to the presence of negative-U dipole boron centers (Figure 2) [11]. Radiation characteristics may be controlled both by stabilized source-drain current variation and by integration of microresonators for various wavelengths into the SNS edge channels. The presence of THz and GHz radiation from SNS was confirmed using various experimental procedures [2], and FTIR spectroscopy has shown that variation of characteristics of microresonators integrated into Si$-$QW edge channels can change modulation frequency and depth of GHz radiation which modulates THz response of the biological object [2].

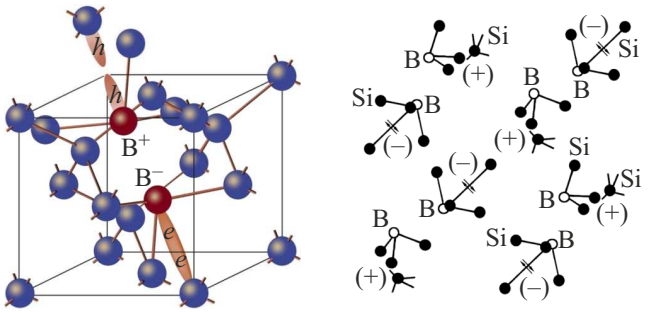

Figure 2. Dipole trigonal boron center (B^+-B^-) with negative correlation energy and dipole boron center chains in β barriers limiting $p-$Si$-$QW.

As previously mentioned, THz-radiation variables may be controlled by varying source$-$drain current for which a stabilized current source (Keithley 6221) was used during the experiment. To record longitudinal voltage variation, a nanovoltmeter (Agilent 34420A) was used. The experiments used a stabilized source-drain current range from -3.504 to $3.504\,\mu$A with interval 8 nanoamperes to achieve maximum resolution with minimum amount of noise. To synchronize the devices, National Instruments Lab View software was used. In order to obtain more accurate values, 20 measurements were made in each point, then averaging was carried out.

To study the complications caused by COVID-19, thyroid gland was studied. For this, the emitter was directed towards the test area at about 1 cm from skin, then SNS started to emit and simultaneously receive THz and GHz-radiation reflected and/or emitted by the biological tissue. Thus, for the purpose of this research, the device was used in balanced photodetector mode. THz–GHz radiation generation and receipt mechanism is based on the Faraday quantum effect [11].

2. Results and discussion

A volunteer who had been exposed to COVID-19 was studied during the research. When the disease was confirmed by PCA test,the patient's thyroid gland behavior was observed during the period from one month to six months from the date of ultimate recovery. In this research, the thyroid gland absorbs and reflects the source radiation. According to Bragg's criterion, the emission received from the thyroid contains a pronounced frequency corresponding to the resonator dimensions which may be represented by lobes, parathyroid glands and nodules. We interpret the observed changes in the typical thyroid dimensions as COVID-19 consequences, though thyroid is highly vulnerable to changes by its nature. A special focus is made on the range from 2.5 to 3.5 THz which contains DNA oligonucleotide emission spectra [10]. The volunteer's DNA contains dominating guanine - cytosine bonds which are manifested in peaks at 2 and 2.8 THz (Figure 3, a).

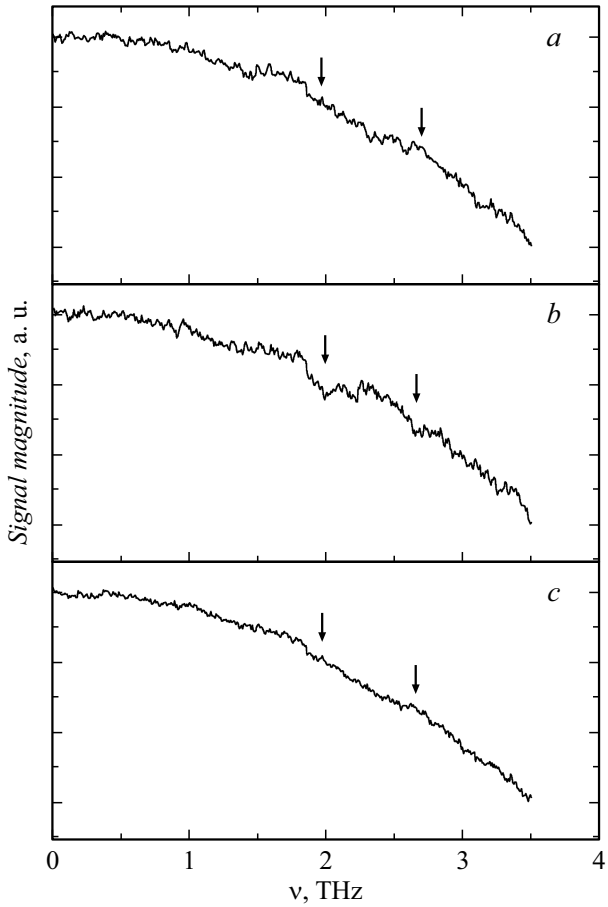

Figure 3. Terahertz response from the patients thyroid gland: *a* — after month, *b* — six months after COVID-19, *c* — six months after COVID-19 with preliminary 15 min THz irradiation.

Amplitudes of these peaks are retained even after six months which indicates the changes in thyroid caused by COVID-19 (Figure 3, *b*). Figure 3, c shows the data after repeated THz irradiation which indicate that even short irradiation during 15 min is able to produce a therapeutic effect and to flatten these peaks. therapeutic effect is not addressed herein, but it was studied together with the Almazov Center and were published in [3]. Thus, this express method based on THz radiation may be used for Covid complication analysis.

Longitudinal voltage U_{xx} KHC was measured during the experiment in source−drain stabilized longitudinal current passage conditions I_{ds}. As previously stated, the edge channel which is an efficient THz radiation source consists of pixels containing a single carrier and having typical dimensions $16.6\,\mu\text{m} \times 2\,\text{nm}$. Between the measurement channels, 124 pixels connected in parallel are located. The whole system is in Earths magnetic field, therefore we can assess, using the Faraday equation, the generation current in the edge channel when additional energy $h\nu$ is introduced due to the biological tissue response in magnetic flux change conditions $\Delta\Phi$ which corresponds to capture of single magnetic flux quanta [12]:

$$I_{gen} = \frac{\Delta E}{\Delta\Phi} = \frac{h\nu}{\Phi_0}.$$

For capture of single power lines in quantum interference area for a pair of carriers in the adjacent pixels in electron-electron interaction suppression conditions, $\Delta\Phi = \Phi_0 = h/2e$ relationship is true [11]. Thus, if the generation current is known, we can assess the incident radiation frequency within the Faraday quantum effect [11]:

$$\nu = \frac{I_{gen}\Phi_0}{h}.$$

The obtained data show that in the 2.8 THz region, there is a valley whose half-width corresponds to $\Delta I_{gen} = 10\,\text{nA}$ (Figure 3). And the change in the generation current was defined according to the edge channel containing 62 pairs of pixels connected in parallel and measured longitudinal voltage. Using this value, relative changes in the thyroid gland volume may be assessed. According to the preliminary calculations using the Faraday ratio, longitudinal dimensions of the thyroid changed by 1.6 mm which shows relative change in the volume by three percents. The thyroid volume restores almost completely within six months. Moreover, by analyzing current-voltage curve modulation in this frequency band, we can define typical dimensions of „microresonators“formed in the thyroid gland during Covid complications — spots and nodules. Using the ratios stated above, the typical dimensions of two types of formed thyroid nodules were determined, respectively, 0.8−1.0 mm and $200-400\,\mu\text{m}$.

Conclusion

SNS based spectrometer is presented combining the THz frequency band emitter and THz radiation response receiver properties. This spectrometer was used for analysis of Covid complications manifested as the change in thyroid dimensions and formation of various thyroid nodules. Further study of the behavioral features of SNS current-voltage curve spectral peaks recorded during THz response from the biological tissue is of high interest for the development of the personalized diagnostics and treatment methods.

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Compliance with ethical standards

All procedures performed within the human subject research were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and later amendments or comparable ethical standards.

Informed voluntary consent was obtained from all participants involved in the research.

Conflict of interest

The authors declare that they have no conflict of interest.

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