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Intraoperative diagnosis of malignant brain gliomas using terahertz pulsed spectroscopy and optical coherence tomography

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An intraoperative diagnosis of malignant brain gliomas remains a challenging problem of modern neurosurgery [1]. A complete resection of glioma is the most important factor, determining an efficiency of its treatment [2]; while an incomplete resection, caused by inaccurate detection of the tumor margins, increases a probability of its recurrence. The existing methods of the intraoperative neurodiagnosis of tumors are plagued with limited sensitivity and specificity, some of them remains laborious, time-consuming and/or rather expensive. Therefore, development of novel methods for the intraoperative diagnosis of gliomas relying on modern instruments of medical spectroscopy and imaging is a topical problem of medicine, physics, and engineering [3,4].

In our research, we studied a potential of terahertz (THz) pulsed spectroscopy (TPS) [5–9] and optical coherence tomography (OCT) [10–12] in the intraoperative diagnosis of brain tumors, with a strong emphasize on brain gliomas.

First, we performed *in vitro* THz spectroscopy of human brain gliomas of different grade. In order to fix tissues for the THz measurements, we applied the gelatin embedding, which allows to preserve tissues from hydration/dehydration; thus, sustaining the THz dielectric response of tissues unaltered for a long time after the surgery. We applied the laboratory TPS setup to study *in vitro* the refractive index and the amplitude absorption coefficient of intact tissues and gliomas. We observed significant differences between the THz characteristics of normal and pathological tissues of the brain [13]. This highlights a potential of THz technology in the label-free intraoperative diagnosis of brain tumors. Particularly, THz imaging and microscopy [14] can be applied for the intraoperative detection of the tumor margins in order to ensure its gross-total resection. Furthermore, the single-point THz spectroscopy and reflectometry could be integrated into modern neuroprobes, which are based on sapphire shaped crystals and yields combining the THz waveguiding [16,17] with diagnosis, aspiration and laser coagulation of brain tissues [18–20].

Second, we studied intact tissues and gliomas of the brain using OCT. For each tissue class, we analyzed a slope of the OCT signal in a depth. This slope reveals statistical difference between healthy and pathological tissues of the brain [10], which could be further emphasized using modern wavelet-domain denoising of OCT data [12]. Thus, the results of our study showcase a potential of OCT in intraoperative neurodiagnosis of brain gliomas.

Thereby, this work yields preliminary analysis (feasibility test), which aims to objectively uncover strengths and weaknesses of TPS and OCT from the viewpoint of their use in intraoperative diagnosis of human brain tumors before committing to a full-blown study involving measurements and analysis of a large amount of tissue sample, both *ex vivo* and *in vivo*.

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