Biomedical applications of terahertz solid immersion microscopy

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A number of terahertz (THz) imaging and spectroscopy techniques were proposed for biomedical purposes, i.e. for label-free differentiation of tumors and healthy tissues of different localizations: colon [1,2], breast [3,4], skin [5–7], brain [8,9] etc. Nevertheless, some problems are inherent to THz technology. We can note absence of efficient waveguides for the delivery of THz radiation and limited spatial resolution of THz imaging systems. The problem of low spatial resolution is especially important in biomedical applications of THz imaging as some tissue elements and structures have sub-wavelength dimensions. Several approaches had been already proposed for obtaining sub-wavelength resolution of THz imaging. Among them are near-field scanning-probe imaging [10], THz digital holography or synthetic aperture synthesis [11,12], which however require high-power sources, sensitive detectors or sophisticated computations. Another group of methods utilize effects of electromagnetic field localization in the shadow side of a mesoscale dielectric object, i.e. photonic jet effect [13,14] and solid immersion (SI) phenomenon [15,16]. SI microscopy implies focusing of an electromagnetic wave into the evanescent field volume behind a high-index material. In our work we propose SI microscopy assembly achieving 0,15λ resolution for handling and imaging of biological objects and soft tissues.

Developed SI lens include three optical elements: aspherical lens, forming converging beam with good aberrational correction in paraxial field [17], truncated sphere concentric to converging beam and a moveable plane window for biological tissue depositing. Truncated sphere and window were made of high-refractive index material (HRFZ-Si). Silicon window allows to deposit biological samples on the top of it during the scanning in X-Y directions. Favourable combination of aspherical singlet and HRFZ-Si truncated sphere provide 0,15λ resolution which was estimated theoretically using FDTD (finite-difference time-domain) simulations, and experimentally by means of continuous wave imaging of test object with step-like reflectivity distribution [18]. In order to demonstrate sub-wavelength resolution of SI lens for THz imaging of bioloigical objects and tissues we developed experimental setup based on backward wave oscillator as a continuous wave source of THz radiation and Golay cell coupled with mechanical chopper as a broadband detector.

We applied THz SI microscopy to study several types of biological objects and tissues, namely: leaf blades of such plants as mint [19] or poinsettia, artificially grown 300 μm tissue spheroids [20] and freshly excised human tissues of different localizations. In order to prevent tissue dehydration and i.e. minimize changes in THz properties during the measurements we embedded them into a gelatin slab. Gelatin embedding allows to conserve specimens for THz measurements for a long time after the excision. Fig. 1 demonstrate THz imaging of human breast tissue *ex vivo* obtained for the wavelength λ=500 μm. The specimen is formed by dense fibrous connective tissues with large single fat cells and their groups embedded into it. Though fat cells have sub-wavelength scales according to considered THz wavelength, they are clearly observed on the THz image 1(a).

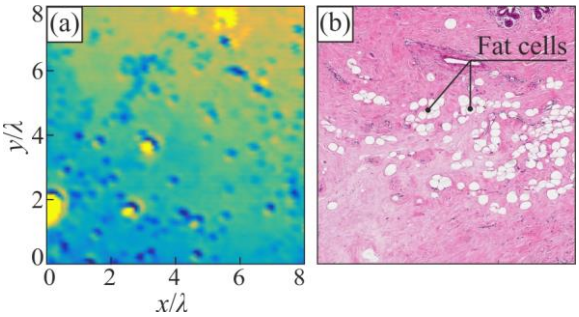

Fig. 1. THz SI microscopy of human breast tissue: (a) THz image observed on λ=500 μm; (b) histological photo.

Described configuration of THz SI microscopy provides the best of the known spatial resolution among SI imaging techniques 0,15λ. It also allows for handling of soft biological tissues during the measurements, thus making THz SI imaging technique a prospective tool for studying sub-wavelength scale inhomogeneity of biological objects.

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