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DEVELOPING A MULTIMETHODOLOGICAL APPROACH TO CANCER BIOPSY

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РАЗРАБОТКА МУЛЬТИМЕТОДОЛОГИЧЕСКОГО ПОДХОДА К БИОПСИИ РАКА

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Considering recent advances in the field of cancer diagnostics, the authors, researchers from National Research Tomsk State University, outline their perspective of developing a multimethodological approach to visualizing cancer on a macro-, meso-, micro- and nanoscale level. Additionally, this work provides an overview of contemporary cancer diagnostic methods/techniques.
Keywords: Cancer, microscopy, spectroscopy, tomography, method development.

Advances in cancer therapy depend on the precise assessment of tumor morphology, localization, progression, invasion and metastasis [1, 2]. Therefore modern cancer biopsy/diagnosis must be supported by the development and improvement of high-resolution imaging techniques for the visualization of tumor characteristics (internal cell morphology, cell-cell interactions, cell-extracellular matrix interactions, etc.) on a macro-, meso-, micro- and nanoscale level. Here, we present a brief overview of the state-of-the-art cancer diagnostic techniques as well as an outline of our (future) research in the field.

Based on a variety of optical, electromagnetic, X-ray and spectral methods cancer diagnostics can be divided into the following categories: microscopic techniques; spectroscopic techniques; and tomographic techniques [3–17] (see Table 1).

Modern microscopic techniques for diagnosing cancer include: 2D optical microscopy (OM); scanning probe microscopy (SPM); transmission electron microscopy (TEM); scanning electron microscopy (SEM); laser scanning confocal microscopy (LSCM); and two-photon excitation microscopy (TPEM) [3–12].

Recent spectroscopic techniques applied in cancer research encompass Fourier transform infrared spectroscopy (FTIRS) and Raman spectroscopy [13–15].

State-of-the-art tomographic techniques used in cancer diagnostics comprise of (X-ray) computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) [16–25].

However, most contemporary cancer research studies are centered on a single diagnostic method/technique. Currently we are focused on developing a next generation methodology for visualizing cancer cell and tumor characteristics. Our main aim is to provide a multimethodological approach for cancer biopsy on a macro-, meso-, micro- and nanoscale level.

T a b l e 1

Overview of cancer diagnostic methods/techniques

Diagnostic method /technique	**Scale of measurement**	**Application**	**Principle of operation**	**Ref.**
2D optical microscopy (OM)	**Macro- till mesoscale** Resolution: 0,01 mm^2	Only tissue/cell surface imaging; With staining histo- and cytological structures are visible.	Light reflection; fluorescence	[18, 19]
Scanning probe microscopy (SPM)	**Nanoscale** Resolution: Atomic step/near-atomic size.	Cell surface morphology, cell–cell interactions, cytoskeleton organization, cell growth rates, and cell-extracellular matrix interactions.	Interatomic forces between imaging probe and specimen	[3, 20]
Transmission electron microscopy (TEM)	**Micro- and nanoscale** Resolution: Atomic step/near-atomic size.	Cell surface and/or internal structures	Electron diffraction	[7, 21]
Scanning electron microscopy (SEM)	**Micro- and nanoscale** Resolution: Atomic step/near-atomic size.	Cell surface and/or internal structures	Electron diffraction	[8, 22]
Laser scanning confocal microscopy (LSCM)	**Micro- and nanoscale** Resolution: Atomic step/near-atomic size.	Cell surface and/or internal structures	Laser diffraction	[9–11, 23]
Two-photon excitation microscopy	**Macro- till nanoscale** Resolution: Atomic step/near-atomic size.	Imaging of intact thick tissues such as brain slices, embryos, whole organs, and of live animals (in vivo imaging)	Photon excitation, fluorescence	[12, 24]

Fourier transform infrared spectroscopy (FTIRS)	**Macro- till nanoscale** Resolution: Better than 1 cm^{-1}	An imaging tool for distinguishing between benign and malignant tumors in tissue samples of breast, colon, lung and prostate along with cervical cytology or biopsies.	Infrared excitation, Fourier transform	[13, 14]
Raman spectroscopy	**Macro- till nanoscale** Resolution: up to 1 μm	Imaging of differences between normal and neoplastic living cells. Confocal Raman spectroscopy has also been applied to construct maps of lung carcinoma cells, and glioma cells, showing the distribution of nucleic acids, cell membrane lipids and proteins in both of these cell types.	Inelastic photon scattering	[15]
(X-ray) Computed tomography (CT)	**Macro- till microscale** Resolution: 1 mm^3; for 3D-digital X-ray microtomography up to 1 μm.	Integrin imaging	X-ray attenuation	[17, 18]
Magnetic resonance imaging (MRI)	**Macro- till microscale** Resolution: 1 mm^3	3D whole body/ tissue imaging	Magnetic resonance	[18]
Positron emission tomography (PET)	**Macro- till microscale** Resolution: 0,5 cm^3	Imaging of cancer metabolism	Positron-electron annihilation	[18, 25]

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