A multimodal approach to non-invasive diagnosis of basal cell carcinoma: a pilot study

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September 27-October 1 2021
Basal-Cell Carcinoma (86.8%)

Melanoma (9.4%)

Squamous Cell Carcinoma and other malignant skin tumors (3.8%)
Micrographs of a basal-cell carcinoma (BCC)

Characteristic histomorphologic features: peripheral palisading, myxoid stroma, artefactual clefting, nodular pattern

BCC

Nodular basal-cell carcinoma
>50% of all BCC

Superficial basal-cell carcinoma
~10% of all BCC

Morpheiform basal-cell carcinoma
aggressive form of BCC

H&E stain

Benign Neoplasm

Images of neoplasms

Macro photographs
Motivation

Early diagnosis, effective prevention and treatment of skin BCC after irradiation or surgery provide a favorable outcome in 85-95%.

Medical intervention at later stages gives hope for a positive result in only 60% of clinical cases.

Multimodal approach in combination with optical clearing increases the effectiveness of methods of optical diagnostics of cancer.
Objective

The development of modern multimodal diagnostics including a combination of high-resolution ultrasound examination and optical methods: Raman spectroscopy, backscattered diffuse reflectance spectroscopy, and optical coherence tomography (OCT) with biocompatible optical clearing agents.
Materials and Methods:

- Ten volunteers with slightly pigmented skin (II phototype) with BCC and benign neoplasms
- Three healthy volunteers with highly pigmented skin (VI phototype)
- Digital Video Dermatoscope DE300 Firefly (tpm taberna pro medicum GmbH, Germany)
- DUB SkinScanner (tpm taberna pro medicum GmbH, Germany) with ultrasound probes with frequencies of 33 and 75 MHz, scanning depths of 6 and 3.2 mm and longitudinal resolution of 48 and 21 μm, respectively
- Raman spectrometer QE65000 equipped with 785-nm diode laser (Ocean Optics, USA) and probe (f = 7.5 mm)
- Multichannel reflectance spectrometers USB4000-UV-VIS and NIRQUEST with a fiber-optic probe QR400-7-VIS-NIR (Ocean Optics, USA) and a spectral range of 400-2100 nm
- Optical coherence tomograph GAN930V2-BU (Thorlabs, USA) with a center wavelength of 930 nm, longitudinal and lateral resolutions of 6 and 7.32 μm, respectively
- 70%-glycerol solution as an optical clearing agent
Results:

Real photo of BCC  
Macro-photo

Volunteer #2: Superficial BCC

High-resolution ultrasound examination

33 MHz  75 MHz  Healthy skin
Volunteer #4: pigmented BCC

Real photo of BCC
Macro-photo

High-resolution ultrasound examination

33 MHz
75 MHz
Healthy skin

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Volunteer #3: Pigmented benign neoplasm

Real photo of BCC

Macro-photo

High-resolution ultrasound examination

33 MHz

75 MHz

Healthy skin
Volunteer #1: Nodular solid BCC

Volunteer #3: Benign neoplasm

Volunteer #4: Pigmented BCC

OCT scanning
Volunteer #1:
Nodular solid BCC

42 days after radiotherapy

Healthy skin site
Volunteer #6: non-pigmented BCC

OCT examination with optical clearing (OC)

Before OC

After 10-min OC using 70% glycerol solution
Diffuse reflectance spectra

Volunteer #1:
Nodular solid BCC

Real photo of BCC
Macro-photo

VIS-NIR spectra
NIR spectra
Diffuse reflectance spectra

VIS-NIR spectra

NIR spectra
Raman examination

Average Raman spectra and standard deviation of basal cell carcinoma (BCC), and normal skin (NORM)

Multimodal Optical Diagnostics of Cancer, Edited by Valery V. Tuchin, Jürgen Popp, and Valery Zakharov, Springer Nature, Cham, Switzerland, 2020, pp. 3-106 (https://doi.org/10.1007/978-3-030-44594-2)
Raman examination

Wavenumber, 1/cm

Raman, a.u.

Nodular solid BCC
Healthy skin
BCC after irradiation

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Conclusion

- Thus, the sizes of neoplasms were evaluated using ultrasound examination, and their internal structure was visualized using OCT in combination with OC.

- Diffuse reflectance can extract physiological parameters such as hemoglobin content, oxygen saturation, and tissue microarchitecture.

- Raman spectroscopy is helpful for determining lipid, nuclear, and protein content.

- Our results demonstrate the ability of these modalities to quantitatively assess tissue biochemical, structural, and physiological parameters that can be used to determine tissue pathology.
Acknowledgement

The reported study was funded by RFBR and INSF, project number 20-52-56005, RFBR, project number 20-32-90043 and the grant under the Degree of the Government of the Russian Federation No. 220 of 09 April 2010 (Agreement No. 075-15-2021-615 of 04 June 2021).
Thank you for your attention!