Intraoperative detection of brain tumors with infrared spectroscopy and coherent antistokes Raman scattering

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Intra-operative histochemical assessment of tissue could significantly improve the prognosis of the patient by reducing the need for further surgeries. Such an assessment can be made with optical biopsies using infrared spectroscopy. Infrared spectroscopy is an analytical technique that yields unique molecular and biochemical information about tissues while being very fast and not requiring exogenous labels. As new portable instruments are available now this technique can be stationed in the operating room for quick evaluation of tissue.

Freshly resected tissue of glioblastoma of more than 200 patients and non-neoplastic control tissue from 19 epilepsy surgery resections were investigated with infrared spectroscopy. Tumor and control specimens were obtained from adult patients. Spectroscopic measurements were performed in the OR using a Bruker Alpha spectrometer. Very small samples of resected tissue (volume less than five mm^3) were spectroscopic evaluated without any sample preparation. Spectra of GBM show, in comparison to normal tissue, stronger signals of phosphate groups of RNA. Furthermore, the spectra reveal a lower content of glycolipids for GBM. Several other variations can be observed in spectral regions, which are assigned to COO-C groups. The study revealed that three marker signals exist, which allow a classification of the tissue. In comparison to standard histological methods, the overall accuracy of the spectral classification was 92%. The spectroscopic based information about tissue could be obtained within few minutes which is faster than the instantaneous section histology.

Coherent anti-Stokes Raman scattering (CARS) microscopy reveals morphological and chemical information. It allows the delineation of brain tumors based on the contrast generated by the lower lipid content of neoplastic tissue. If analyzing tissue sections, a comparison with histological staining enables the precise matching between CARS images and pathological evaluation.

Together with CARS fluorescence and second harmonic generation can be excited by the same optical set up. We used the multimodal imaging to show that the identification of glioblastoma tumors and infiltrates is possible on living mouse brain tissue and on native human biopsies at single cell level [1]. For glioblastoma, both CARS signal intensity and cell morphology constitute objective parameters that allow discerning normal and neoplastic tissue structures.

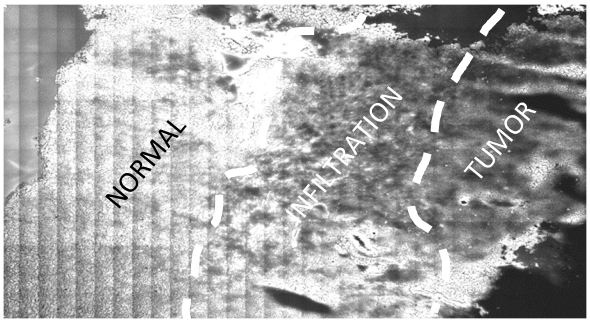

Fig. 1. CARS image: cryosection of a gliobastoma multiforme specimen. The CARS image displays the solid tumor and an infiltrative region. The normal and neoplastic tissue can be distinguished on the basis on CARS signal intensity and the tumor boundaries identified. The CARS intensity value in tumor, infiltration and normal tissue calculated falls in separated ranges and constitutes a reliable parameter for delineation of infiltrative tumor borders.

The results of this study demonstrate the potential value of the molecular information obtained directly from tissue. Since infrared spectroscopy and CARS rely on the intrinsic biochemical differences between pathological and normal tissues, these techniques are poised to guide decision marking during surgery within an appropriate timeframe and to make intra-operative treatment decisions more accurate.

Literature

[1] O. Uckermann, R. Galli, S. Tamosaityte, E. Leipnitz, K.D. Geiger, G. Schackert, E. Koch, G. Steiner, M. Kirsch, PLOS One **9**(9), e107115, (2014).