Time resolved luminescence microscopy for optical metabolic imaging and oxygen sensing

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Correlated imaging of phosphorescence and fluorescence lifetime parameters of metabolic markers is a challenge for direct investigating mechanisms related to cell metabolism and oxygen tension. A large variety of clinical phenotypes is associated with mitochondrial defects accomplished with changes in cell metabolism. In many cases the hypoxic microenvironment of cancer cells shifts metabolism from oxidative phosphorylation (OXPHOS) to anaerobic or aerobic glycolysis, a process known as "Warburg" effect. Also during stem cell differentiation a switch in cell metabolism is observed. Mitochondrial dysfunction associated with hypoxia has been invoked in many complex disorders such as type 2 diabetes, Alzheimer´s disease, cardiac ischemia/reperfusion injury, tissue inflammation and cancer.
Cellular responses to oxygen tension have been studied extensively, optical imaging techniques based on time correlated single photon counting (TCSPC) to detect the underlying metabolic mechanisms are therefore of prominent interest. They offer the possibility by inspecting fluorescence decay characteristics of intrinsic coenzymes to directly image metabolic pathways. Moreover oxygen tension can be determined by considering the phosphorescence lifetime of a phosphorescent probe. The combination of both fluorescence lifetime imaging microscopy (FLIM) of coenzymes like NADH and FAD and phosphorescence lifetime imaging microscopy (PLIM) of phosphorescent dyes could provide valuable information about correlation of metabolic pathways and oxygen tension.
Within this presentation the basic mechanisms and relations of FLIM, PLIM and cell metabolism will be discussed and clinically relevant applications will be demonstrated. This includes investigations on Alzheimer´s related diseases and tumour diagnosis.

Publications:

[1] **A. Rück**, C. Hauser, S. Mosch, and S. Kalinina, "Spectrally resolved fluorescence lifetime imaging to investigate cell metabolism in malignant and nonmalignant oral mucosa cells", Journal of Biomedical Optics 19(9), 096005 (2014).
[2] S. Kalinina, J. Breymayer, P. Schäfer, E. Calzia, V. Shcheslavskiy, W. Becker, and **A. Rück**, "Correlative NAD(P)H-FLIM and oxygen sensing-PLIM for metabolic mapping", J. Biophotonics 1–12 (2016) / DOI 10.1002/jbio.201500297 (2016).