Fluorescence Lifetime Macroimaging: Interrogation of Tumors on Macroscale

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While laser scanning fluorescence lifetime imaging (FLIM) is a powerful approach for cell biology, its small field of view (typically less than 1 mm) makes it impractical for imaging of large objects that is often required for biomedical applications. In this talk, we present a system that allows to perform both fluorescence and phosphorescence lifetime imaging (FLIM/PLIM) on macroscopic samples as large as 18 mm with a lateral resolution of 15 µm. We verified the performance of the system by doing FLIM of endogenous metabolic cofactor reduced nicotinamide adenine dinucleotide (phosphate), NAD(P)H, and genetically encoded fluorescent protein mKate2 in a mouse tumor *in vivo.* Moreover, by using PLIM we managed to observe the oxygen status of healthy and tumor areas in live animals. We used the genetically encoded sensor TR23K based on the red fluorescent protein TagRFP and chromoprotein KFP linked by 23 amino acid residues (TagRFP-23-KFP) containing a specific caspase cleavage DEVD motif to monitor the activity of caspase-3 in tumor xenografts by means of fluorescence lifetime imaging-Forster resonance energy transfer during chemotherapy with paclitaxel. Time-resolved macroscopic imaging proves to be a nice method not only for exploration biological processes *in vivo* in the whole tumor, but also for drug screening, facilitating the development of new anticancer agents as well as improvement of chemotherapy efficiency and its adaptation for personal treatment.

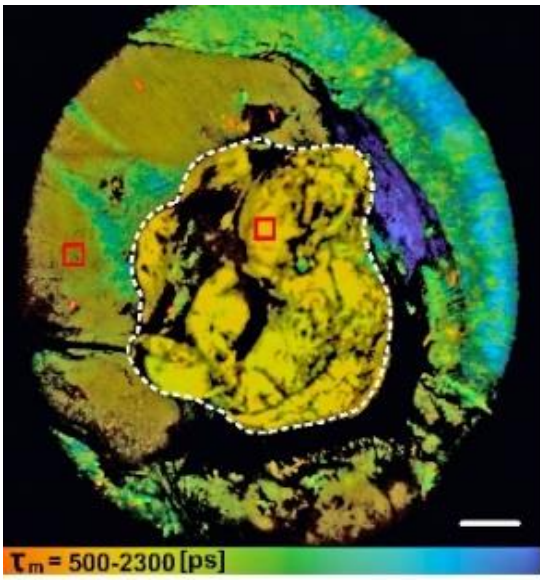

Fig. 1: Macroscopic fluorescence lifetime image of mouse tumor (within dashed ROI). Autofluorescence of NADH (exc. 375 nm, det. 450/50 nm detection) was measured. Average lifetimes τ_m within tumor tissue are shorter than the surrounding muscle tissue.