

Metabolic FLIM and oxygen PLIM: Luminescence lifetime imaging on the way to clinical diagnosis

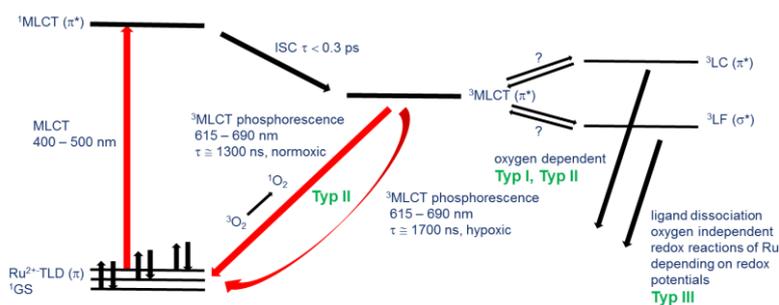
A. Rueck

University Ulm, Core Facility Optical Microscopy N24, Albert-Einstein-Allee 11, 89081
Ulm, Germany: e-mail: angelika.rueck@uni-ulm.de

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Simultaneous metabolic and oxygen imaging is a promising idea to follow up therapy response, disease development and to determine prognostic factors. A common property during tumor development is altered energy metabolism, which could lead to a switch between oxidative phosphorylation (OXPHOS) and glycolysis. The impact of this switch for theranostic applications is significant. FLIM of metabolic coenzymes, as NAD(P)H and FAD, is now widely accepted to be the most reliable method to determine cell metabolism and different algorithms are actually proved to get reproducible results. During treatment also oxygen consumption has to be taken into account to understand treatment responses. The phosphorescence lifetime of newly developed drugs is able to indicate local oxygen changes. For this, simultaneous imaging of phosphorescence and fluorescence lifetime parameters was implemented.

Dyes based on ruthenium (II) coordination complexes, were used for PLIM. For example, TLD1433 (Theralase Inc. 1945 Queen St E, Toronto, ON M4L 1H7) possess a variety of different triplet states, which enables complex photochemistry and redox reactions. TLD1433 can be used as a phosphor to follow up local oxygen concentration and consumption during treatment.



Jablonski diagram of TLD1433

Within this presentation correlated luminescence lifetime imaging will be presented, applications will be demonstrated and pitfalls discussed. With respect to the last point the different redox pairs involved in cell metabolism (as FAD/FMN) will be revalued.

Publications:

[1] S. Kalinina, J. Brey Mayer, 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).

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[3] Kalinina S, Brey Mayer J, Reeß K, Lilge L, Mandel A, Rück A, “Correlation of intracellular oxygen and cell metabolism by simultaneous PLIM of phosphorescent TLD1433 and FLIM of NAD(P)H,” J. Biophotonics. e201800085 (2018).