

## INTRACELLULAR WATER LIFETIME AS A TUMOUR BIOMARKER FOR DIAGNOSIS AND THERAPY OUTCOME BY FFC-RELAXOMETRY IN BREAST CANCER

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The diagnostic power of Magnetic Resonance Imaging in tumour phenotyping could be improved observing the marked decrease of  $T_1$  in biological tissues at low magnetic field strength. It is well known that the  $T_1$  of a given tissue changes as a function of the applied magnetic field strength. In particular, the lower is the magnetic field the higher is the differences among tissues. Known as “ $T_1$ -dispersion”, this phenomenon is a marker of disease and it is invisible to conventional, fixed-field MRI scanners. The Fast Field-Cycling (FFC)-NMR is the only practicable way of measuring it. An overall increase of water content together with an impairment in water exchange across membranes have fundamental role in this behaviour. The measurement of the intracellular water lifetime ( $\tau_{in}$ ) *in vitro* and *in vivo* may bring relevant information on the ongoing metabolism of the tumour cell, as report on the pathological status, grade and therapeutic outcome. The measurement of  $\tau_{in}$  was performed *in vitro* and *in vivo* on murine adenocarcinoma cell line (4T1). Different doses of doxorubicin have been tested before the  $T_1$  measurement. The data were analysed using two-site exchange (2SX) model in which the Bloch equations are modified to describe two-compartments (intra and extracellular) in which water exchange modulates the observed relaxation behaviour. The most striking result from the fitting procedure is the observation of a significant  $\tau_{in}$  increase after the first treatment due to the slower tumour metabolism caused by doxorubicin, that it was not observed on the corresponding doxorubicin resistant cell line. Recently, [1] we showed that the  $\tau_{in}$  represents a hallmark of tumour tissue cells status that can be easily monitored by measuring  $T_1$  at different and relatively low magnetic field strengths. Currently, tumour responses to therapy are monitored primarily by imaging evaluating essentially the decrease of tumour size. This approach, however, lacks sensitivity and can only give a delayed indication of a positive response to treatment. In this study, we propose the use of FFC-NMR to provide relevant information about response to treatment by monitoring changes of water exchange rates through cell membranes that are directly dependent on the metabolism alterations caused by the chemo- or radio-therapy.

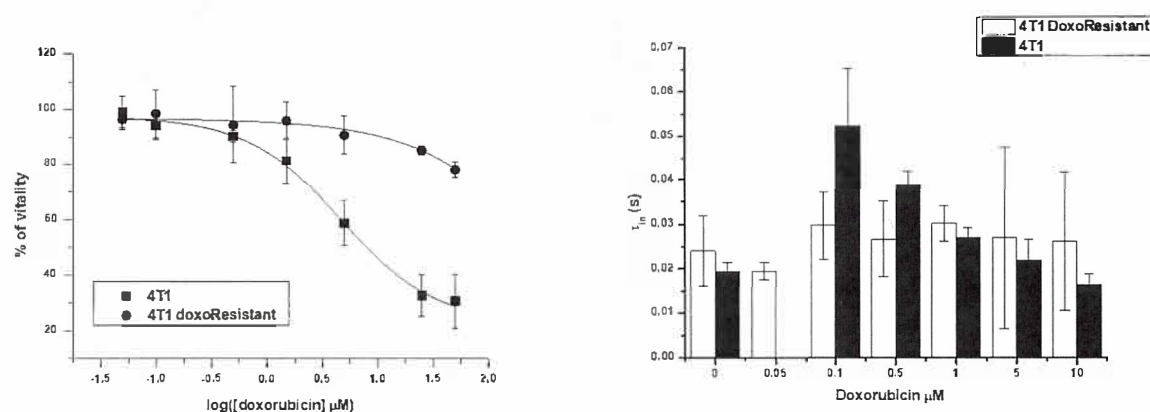


Figure 1: Left, Toxicity of Doxorubicin on 4T1 and 4T1 resistant: Right,  $\tau_{in}$  values at different concentration of drug.

References:

[1] MR Ruggiero, et al., *Angew. Chem. Int. Ed. Engl.*, (2018).