EVIDENCE FOR THE ROLE OF INTRACELLULAR WATER LIFETIME AS A TUMOUR BIOMARKER OBTAINED BY IN VIVO FIELD-CYCLING RELAXOMETRY

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Conventional diagnostic magnetic resonance imaging (MRI) techniques have focused on the improvement of the spatial resolution by using high magnetic fields (1-7 T). High field allows the visualization of small tumour mass but lacks to give a precise evaluation of tumour grading and metastatic potential. Recently, we showed that the intracellular water lifetime 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, ranging from 0.2 to 200 mT [1,2]. A fast exchange through cell membranes indicates a high metabolic rate and thus a high activity of the tumor cells. Thus it is possible to measure the high metabolic pressure by an enhance water exchange with the exterior of the cell. Therefore, intracellular water lifetime can be considered an important tumour biomarker directly depending on the rate of cell proliferation, cell migration and in responding to external stimuli as hypoxia or extracellular acidosis. Moreover, currently tumour responses to therapy are monitored primarily by imaging evaluating essentially the decrease of tumor size. This approach, however, lacks sensitivity and can only give a delayed indication of a positive response to treatment. In our 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.

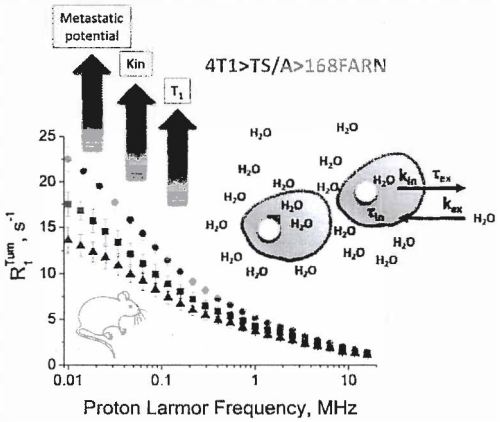

Fig. 1. NMRD profiles of the tumour tissues grown on hind limbs: 4T1 (▲), TS/A (■), and 168FARN (●).

References
[1] Ruggiero et al., *Angew Chem Int Ed Engl* **57**, 7468-7472 (2018).
[2] Ruggiero et al., *Molecular Physics* **117**, 968-974 (2019).