Assessment of tumour response to chemiotherapy by In vivo fast field cycling relaxometry

S. Geninatti Crich[1], MR Ruggiero[1], S Baroni[1], S. Rapisarda[1], S Aime[1]
[1]*University of Torino, Molecular Biotechnology and Health Sciemces, via Nizza 52, Torino (Italy). simonetta.geninatti@unito.it*

Conventional diagnostic magnetic resonance imaging (MRI) techniques have focused on the improvement of the spatial resolution by using high magnetic fields (1-7T). High field allows the visualization of small tumour mass but lacks to give a precise evaluation of tumour grading and metastatic potential. However, there is widespread opinion that, at low magnetic field strength, the marked increase of R_1 observed in biological tissues might be beneficial towards improving the diagnostic potential of MRI in tumour phenotyping. Recently,[1,2] 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. 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. 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 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. To this purpose mammary tumour bearing mice (obtained by the hindlimb intramuscular injection of breast adenocarcinoma 4T1 cells) have been treated with different dosed of doxorubicin. FFC-NMR profiles have been acquired before and after drug administrations by evaluating whether the toxic effect of the administered drug can be assessed by changes in T_1 values.

Acknowledgments

This work was supported by the CA15209 COST Action (EURELAX) and has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 668119 (project "IDentIFY")

References

[1] MR Ruggiero, S Baroni, S Pezzana, G Ferrante, S Geninatti Crich, S Aime, Evidence for the role of intracellular water lifetime as a tumour biomarker by in vivo Field-Cycling relaxometry, *Angew Chem Int Ed Engl*, **2018**, 57, 7468-7472

[2] Ruggiero, S Baroni, S Aime, S Geninatti Crich Relaxometric investigations addressing the determination of intracellular water lifetime: a novel tumour biomarker of general applicability *Molecular physics* **2018**, https://doi.org/10.1080/00268976.2018.1527045