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INTRACELLULAR WATER LIFETIME AS A TUMOUR BIOMARKER BY FFC-RELAXOMETRY

M. R. Ruggiero,[‡] S. Baroni,[‡] S. Pezzana, ,[‡] S. Geninatti Crich,[‡] G. Ferrante,[†] S. Aime[‡]

[‡]University of Turin, Turin, Italy
[†]Stelar, Mede (PV) Italy
E-mail: ruggiero.mr@gmail.com

Diagnostic tools have a key role in the phenotyping of complex, heterogeneous and multifactorial diseases like cancer. They have a fundamental role also for the selection of a personalized therapy, to increase the chance of success and reduce the side effects. Magnetic resonance imaging (MRI)is one of most useful imaging modalities in the field of oncology. However, at the magnetic field strength of the currently available MRI scanners, changes in endogenous longitudinal relaxation times (T_1) do not appear sensitive enough to report on peculiar aspect of the tumour stage. The alternative diagnostic approach herein proposed is based on the in vivo measurement of endogenous T_1, in range of low magnetic fields strengths (0.01-10 MHz), using the Fast Field Cycling(FFC)relaxometer technology. Our hypothesis is that the osmosis and metabolism driven movement of free water molecules across membranes (that affects cell volume and shape), may represent an intrinsic and extremely sensitive reporter of the metabolic state. The measurement of the intracellular water lifetime (τin) may bring relevant information on the ongoing metabolism of the tumour cell. The analysis of measurements of T_1 (performed using the FFC-relaxometry) at different fields using the NMR "shutter-speed" model (model that keep in count the extra/intra-cellular compartment and the exchange water between them) allows to determine the τin. Mouse mammary adenocarcinoma cells (4T1, TS/a, 168farn) were injected in murine muscle himdlimb. In vivo measurements of endogenous T_1 were performed using the FFCrelaxometer technology. Immunofluorescence analysis of different transporters (GLUT1, AQPs, Na^+/K^+ ATPase) will be performed to better understand the biological mechanisms underlying T_1 changes measured. Longer T_1 values for all adenocarcinoma cell lines were observed at any field when compared to the healthy tissue. The observed T_1 increase was directly proportional to the tumor size increase. Moreover, significant variations among T_1 values of the different implanted tumours were also observed. The elongation of the intracellular water T_1 as well as an overall increase of the cellular volume in tumour cells could be accounted in terms of the augmented metabolic activity and the consequent increase in the local concentration of the produced metabolites. The most aggressive 4T1 cells display an overexpression of GLUT1, AQPs, Na^+ /K^+ ATPase transporters compared to other cell lines. From these preliminary results we can conclude that T_1 of tumour tissues (in particular at low magnetic fields) may act as reporter of the different water content in the tumor mass and its mobility through intraand extra- cellular compartments which change in depends of tumour grading, aggressivity and metastasis formation.

References

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