Maria Rosaria Ruggiero, Simona Baroni, Stefania Pezzana, Simonetta Geninatti Crich, Silvio Aime
"EFFECT OF WATER MOBILITY AND MAGNETIC FIELD STRENGTH ON TISSUE AND CELL PROTON T1".

Introduction

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 aim of this project is to develop and validate an innovative diagnostic tool able to report on tumour hallmarks as metabolism deregulation. Briefly, 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.

Methods

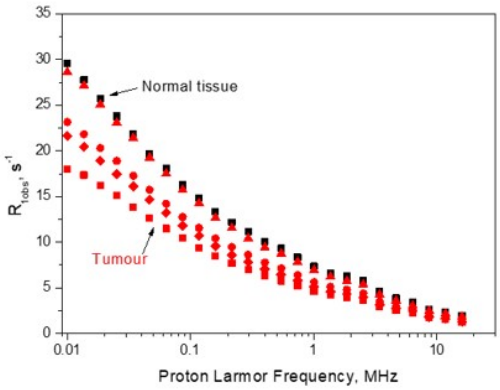
Mouse mammary adenocarcinoma cells(4T1, TS/a, 168farn) were injected in murine muscle himdlimb. *In vivo* measurement of endogenous T_1 were performed in range of low magnetic fields strengths (0.01-10 MHz), using the Fast Field Cycling(FFC)relaxometer technology. Immunofluorescence analysis of different transporters (GLUT1, AQPs, Na^+/K^+ ATPase) will be performed to better understand the biological mechanisms underlying T_1 changes measured.

Results

Longer T_1 values for all adenocarcinoma cell lines were observed at any field when compared to the healthy tissue(fig.2,A). Moreover, significant variations among T_1 values of the different implanted tumours were also observed (fig.2,B). 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, Na^+/K^+ ATPase transporters compared to other cell lines.

Conclusions

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 intra- and extra- cellular compartments which change in depends of tumour grading, aggressivity and metastasis formation.



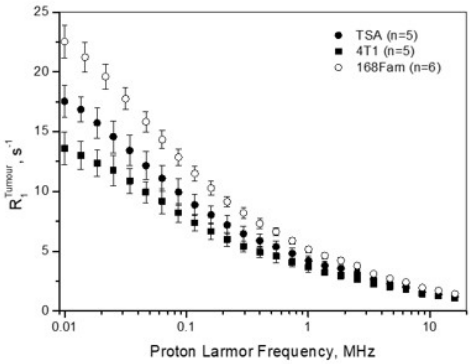


Figure 1, A) Observed relaxation rate as a function of the magnetic field strengths (NMRD profile) of a mouse leg: before (black square, day 0) and after the inoculation of 4T1 cells (red triangle, day 4; red filled circle, day 8; red diamond, day 9; red square, day 11); B) Observed relaxation rate as a function of the magnetic field strengths (NMRD profile) of three different tumor xenografts (4t1: black square; TS/A black filled circle; 168farn: black empty circle)

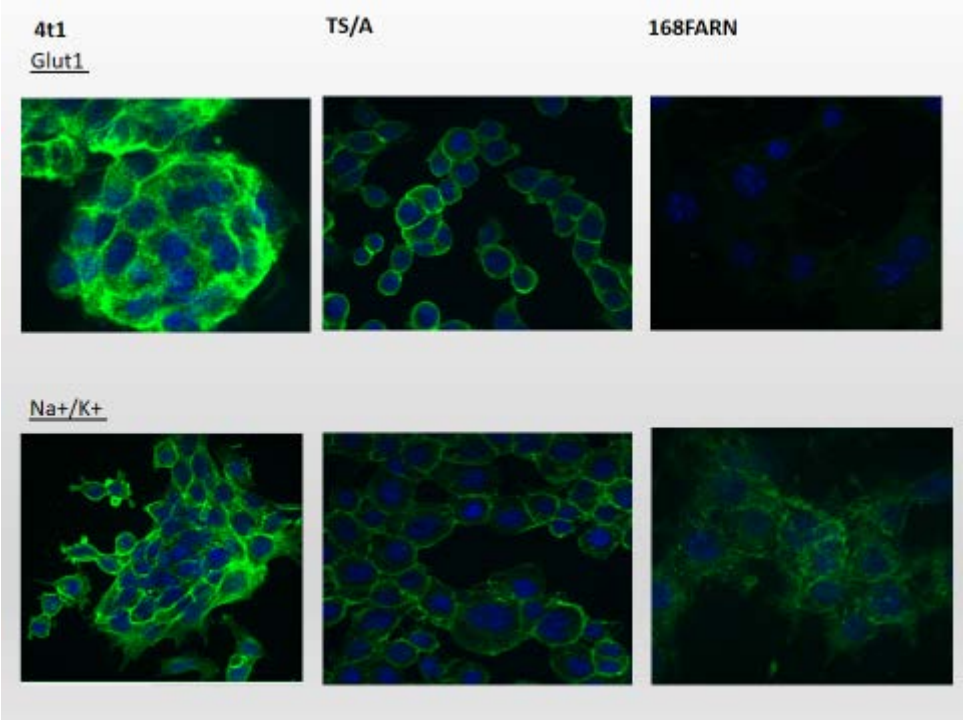


Figure 2: Immunofluorescence images of three different adenocarcinoma cell lines for GLUT1 and NA^{+}/k^{+} TRASPORTERS