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Relaxometry of Cancer: effect of water mobility and magnetic field strenght on tissue and cell proton T_1

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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 (1-7T). High field allows the visualization of small tumour mass but lacks to give a precise evaluation of tumour grading, oxygenation, pH and metastasization. The presence of hypoxic or necrotic regions as well as the interstitial pressure are important hallmarks of the disease as they may affect the type of therapy to be chosen. This work aims at developing an innovative diagnostic strategy, based on the measurements of NMRD profiles with Fast Field Cycling FFC-NMR to obtain quantitative information on tumour characteristics, due to different water content and mobility, that is invisible to standard MRI. In fact, 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 pathology. Cell volume regulation is important in determining the rate of cell proliferation, in aiding cell migration and in responding to external stimuli as hypoxia or extracellular acidosis. Moreover, upregulation of transporters as GLUT1 or/and Na^+/H^+ exchangers promoted by hypoxia, and acidosis are necessary for the formation of an invasive cancer.

In this work, the use of FFC-NMR as reporter of hydrodynamic cellular volume changes has been assessed primarily by comparing cells (mammary adenocarcinoma) grown in normo- or hypoxic conditions and in "hypo-and hyper-osmotic" solutions. Then the same cell types have been injected in the leg muscle to generate a tumour xenograft suitable for "in vivo" studies. The Stelar SPINMASTER-FFC-NMR relaxometer herein used is equipped, for the first time anywhere in the world, with a 40mm 0.5T magnet with a dedicated 11 mm detection coil allowing to acquire FFC-NMR profiles "in vivo". Due to the technical limitations the position to implant tumour cells has to be, for the moment, at the mouse legs. Preliminary results show significant differences in FFC-NMR profiles (both "in vitro" and "in vivo") reporting on different tumour characteristics. Cell swelling, caused by hypoxia or necrosis, increases both the amount of cytoplasmatic water and its mobility causing the increase of T1 of tumour tissues. We can conclude that FFC relaxometry may be a paradigm-shifting technology which will generate new, quantitative disease biomarkers, directly informing and improving clinical diagnosis, treatment decisions and monitoring in oncology. Despite this prototype FFC-NMR instrumentation is not endowed with spatial resolution, fundamental knowledge that will be obtained, will open the route for the development of new diagnostic horizons in oncology until now uncharted and easily transferable to the increasing number of FFC-MRI scanners already present around in the world.