FFC-NMRD RELAXOMETRY FOR EARLY DETECTION AND CHARACTERIZATION OF *EX-VIVO* MURINE BREAST CANCER

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Breast Cancer is a multifactorial disease, considered a major public-health issue worldwide. It is the most diffuse cancer among women and the treatment outcome is strongly influenced by the possibility to detect it at a very early development stage and to evaluate the metastatic potential. Quick and detailed diagnostic tests able to provide a detailed characterization of tumor are still needed in order to further improve the chances of curing this disease. It evolves through a multistep progression process, starting from epithelial simple hyperplasia, to atypical hyperplasia, to carcinoma in situ (CIS) and finally to metastatic carcinomas. Herein, Balb-NeuT mice at different ages (7, 15, 21 and 30 weeks) have been used [1]. They are transgenic mice in which breast cancer spontaneously develop in all mammary glands and closely recapitulate human breast cancer development. The onset of cancer is triggered by the overexpression of the activated form of the rat ErbB2 (Her/2-neu) oncogene, whose amplification is typically observed in 20–30% of human breast. In this work, for the first time, it has been reported that Fast Field Cycling Nuclear Magnetic Resonance Dispersion (FFC-NMRD) profiles can be used for the detection of cancer in murine breast tissues biopsies [2]. In particular, from the analysis of longitudinal water relaxation time (T_1) at variable magnetic field (FFC relaxometry), it has been possible to detect the presence of tumor in NeuT mice at a very early stage (7-weeks) when the disease is not detectable by common high resolution MRI and shows minimal and not diffuse histological modifications. Tumor progression is strongly correlated with significant changes in T_1 values and of the overall shape of NMRD profiles (Fig.1A). By fitting with a line the log/log NMRD profiles, it has been possible to quantify the slope of the curve. This parameter is strongly correlated to the tumor stage (Fig.1B). In particular, the slope is small in healthy control (ca. 0.1) and it increases at late stages of tumor (up to *ca.* 0.35 for 30weeks NeuT mice).
In addition, ^{14}N-quadrupolar peaks (^{14}N-QPs) have been analyzed. They are not present in healthy mammary tissue (Fig.1A) but are clearly detectable in presence of the tumor, at all stages of development. Therefore, the presence of ^{14}N-QPs is an early biomarker of tumor onset.
In such a way, NMRD profiles can be suitable for i) making detectable breast tumor at a very early stage (by investigating the presence of ^{14}N-QPs) and ii) making possible to assess tumor stage (by investigating the overall NMRD profile shape). Importantly, both the information can be gained without the administration of exogenous contrast agents.

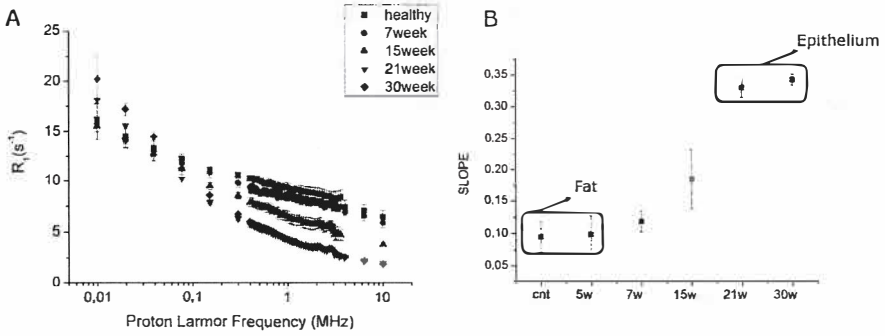

Fig. 1. (A) NMRD profiles of ex vivo breast tissue of NeuT at different stages (7, 15, 21 and 30 weeks) compared with healthy mice. (B) Slope of NMRD profiles at different stages of NeuT.

References

[1] E. Quaglino, F. Cavallo, *Immunol. Lett.*,**80**, 75 (2002).
[2] E. Di Gregorio, G. Ferrauto, S. Lanzardo, E. Gianolio, S. Aime S. *Sci Rep.*, **9**, 4624 (2019).