APPLICATION OF $^{19}$F MAGNETIC RESONANCE IMAGING FOR THE STUDY OF DRUGS EFFICACY EX VIVO

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Oncology is the major beneficiary of pre-clinical and clinical applications of $^{19}$F NMR. $^{19}$F nuclei is used in pharmaceutical investigations of anti-cancer drugs because $^{19}$F stabilizes drugs and is responsible for interactions with intracellular microenvironment, thus drugs efficacy.

The aim of our study was to apply $^{19}$F Magnetic Resonance Imaging at 9.4 T (Cross Cancer Institute, Edmonton, Canada) to observe drug efficacy. We labeled Herceptin (Trastuzumab, Genentech Inc., San Francisco, CA) with fluorine in the form of perfluorocarbon (PFCE, perfluoro-15-crown-5-ether). For the study we selected human breast cancer cell line MCF-7 with stable positive over-expression of HER-2 protein. On the cell surface HER-2 is recognized as Herceptin receptor. As control we used Human mammary epithelial cells (HMEC). The three dimensional cell cultures were established using Hollow Fiber Bioreactor (HFB, FiberCell System Inc., Frederick, MD). $^{19}$F MRI was used for visualization of the cellular uptake of new fluorine labeled Herceptin.

We observed that the oil-water emulsion of Herceptin with PFCE was more efficient than Herceptin alone in MCF-7 culture. Normal (HMEC) cells did not respond to any treatment. A significant correlation between duration of treatments and MCF-7 cells viability was observed. $^{19}$F signal intensity increased due to $^{19}$F uptake, however the cells that were successfully treated were no longer possible for viability assays with trypan blue. The use of HFB device allowed high-density 3-D cell cultures in the reproducible experimental setup and provided controlled conditions during biochemical and MR study.