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Planar Waveguide NMR Gradients (B_0 and B_1) for spatiotemporal Investigations of Anticancer Drug Concentration in 3D Cancer Cell Cultures

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ABSTRACT

Despite the progression in cancer therapeutic approaches, cancer is still the leading cause of death worldwide with a steadily increasing incidence rate. In Jordan, CRC is the most common type of cancer among men and the second most common among women, while being one of the most accruing cancers in Germany.

The difficulties in cancer treatments arise from the poor correlation between in vivo and in in vitro anti-cancer drug testing results and cancer cells resistance to chemotherapy, which are attributed to the heterogeneity of cancer cells, and the interaction of cancer cells with non-cancerous cells in the tumor microenvironment (TME). In addition to, the several mechanisms, that governs DNA damages repair, epigenetics, epithelial to mesenchymal transition (EMT).

Cell culture techniques have been developed to construct in vitro multicellular cancer spheroids (MTCS) that mimic cell-cells interaction and the cellular organization in the TME. They also illustrate the proliferation gradient of solid tumors, and the nutrition and gas supply to cancer cells at different depth in the spheroid. Therefore, they are considered an excellent in vitro cancer model to study the efficiency and to investigate the penetration depth of the anti-cancer materials.

Nuclear Magnetic Resonance (NMR) spectroscopy is a reliable analytical method that gives comprehensive and rich chemical information, along with high speciation performance. It is one of the major noninvasive tools for metabolomics, therefore it has been utilized to study the metabolic profiling of freshly isolated- non-destructed tissues, and living in vitro cellular models.

A micro-imaging technique for real-time NMR investigations is developed to study the penetration depth, rate, and effective diffusion coefficients of anti-cancer materials through cancer spheroids. This technique is based on our patented invention of planar waveguide micro slot NMR detector with on board thermal regulator integrated and a microfluidic device. Based on this innovative development, we are able to perform real-time magnetic resonance spectroscopic imaging (MRSI) on a living synthetic tissue constructed in micrometer scale to monitor drug penetration and diffusion, while providing spectroscopic information about the production and degradation of metabolites in picomoles concentrations.

