

# HYPERPOLARIZED $^{13}\text{C}$ MAGNETIC RESONANCE SPECTROSCOPIC IMAGING OF BREAST CANCER

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## Abstract

Breast cancer is one of the leading causes of cancer-related deaths in women worldwide, owing largely to metastatic disease. However, this disease lacks personalized treatment plans due to an incomplete understanding of the microenvironmental forces driving tumorigenesis and corresponding prognostic markers. Dysregulated metabolism has been identified as an emerging hallmark of cancer, with ample observations that malignant tumors exhibit upregulated glycolysis and increased conversion of pyruvate to lactate regardless of oxygen availability. Additionally, tumor lactate levels have been significantly positively correlated with the development of distant metastases. The advent of hyperpolarized  $^{13}\text{C}$  magnetic resonance spectroscopic imaging (MRSI) has enabled real-time assessment of the conversion of pyruvate to lactate in vivo. This aim of this work was to improve the accuracy and precision of metabolic quantification with hyperpolarized  $^{13}\text{C}$  MRSI in order to compare in vivo glycolytic rates in murine breast cancer models of different metastatic potential. This work involved several technical advances to increase hyperpolarized  $^{13}\text{C}$ -labeled metabolite SNR in the breast cancer tumors and to improve the accuracy and precision of metabolic imaging measures. A number of studies in this work were also designed to characterize the repeatability of quantitative hyperpolarized  $^{13}\text{C}$  metabolic measures, a little-explored metric in the field of hyperpolarized  $^{13}\text{C}$  MRI. With the culmination of all technical advances enabling reliable metabolic imaging and quantification, a final study comparing glycolytic metabolism in two murine breast cancer models of different metastatic potential was performed. The tested quantitative imaging measures

of pyruvate-to-lactate conversion displayed a trend towards increased values in the more metastatic tumor model compared to a tumor model of metastatic dormancy, although this result was not significant for the given study population size. Therefore, the technical advances in this work, and the results of the breast cancer study presented herein, suggest promise for in vivo assessment of glycolytic metabolism with hyperpolarized  $^{13}\text{C}$  MRSI in breast cancer models. Furthermore, augmenting glycolytic measures with metabolic rates of complementary pathways may help to develop a more well-rounded understanding of in vivo energy metabolism in breast cancer in the future.