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Analysis of Cancer Metabolism by Imaging Hyperpolarized Nuclei: Prospects for Translation to Clinical Research

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A major challenge in cancer biology is to monitor and understand cancer metabolism *in vivo* with the goal of improved diagnosis and perhaps therapy. Because of the complexity of biochemical pathways, tracer methods are required for detecting specific enzyme-catalyzed reactions. Stable isotopes such as ^{13}C or ^{15}N with detection by nuclear magnetic resonance provide the necessary information about tissue biochemistry, but the crucial metabolites are present in low concentration and therefore are beyond the detection threshold of traditional magnetic resonance methods. A solution is to improve sensitivity by a factor of 10,000 or more by temporarily redistributing the populations of nuclear spins in a magnetic field, a process termed *hyperpolarization*. Although this effect is short-lived, hyperpolarized molecules can be generated in an aqueous solution and infused *in vivo* where metabolism generates

products that can be imaged. This discovery lifts the primary constraint on magnetic resonance imaging for monitoring metabolismâ€”poor sensitivityâ€”while preserving the advantage of biochemical information. The purpose of this report was to briefly summarize the known abnormalities in cancer metabolism, the value and limitations of current imaging methods for metabolism, and the principles of hyperpolarization. Recent preclinical applications are described. Hyperpolarization technology is still in its infancy, and current polarizer equipment and methods are suboptimal. Nevertheless, there are no fundamental barriers to rapid translation of this exciting technology to clinical research and perhaps clinical care.

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