Implementation and Applications of Hyperpolarized C-13 MRI in Medicine

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The development of technology that applies Dynamic Nuclear Polarization to generate hyperpolarized ^{13}C agents and a dissolution process that prepares them for injection into living subjects means that it is now possible to investigate applications to in vivo systems. The prototype polarizer that was designed in Malmo, Sweden (1-5) has been shown to provide a >10,000 fold signal enhancement for detecting ^{13}C probes of endogenous, nontoxic, non-radioactive substances such as pyruvate and to have the potential for monitoring fluxes through multiple key biochemical pathways such as glycolysis, the citric acid cycle and fatty acid synthesis. Preliminary studies that were performed in a whole body MR scanner in rat kidney and in tumors have confirmed that ^{13}C-1 labeled pyruvate is delivered to tissues and converted to alanine, lactate and bicarbonate with a spatial distribution and time course that varies according to the tissue of interest.

There is already considerable evidence that in vivo metabolic imaging is important for the characterization and evaluation of response to therapy for cancer. Patient studies using ^{1}H MR spectroscopic imaging have demonstrated that there are distinct metabolic signatures between normal tissue and tumor. High-grade brain tumors are distinguished by the presence of lactate and lipid, with increasing levels of these metabolites being associated with poor outcome for patients with newly diagnosed lesions. Evidence for lactate being a marker of aggressiveness for prostate cancer has come from ex vivo measurements of human biopsy samples. The application of hyperpolarized ^{13}C pyruvate MR to pre-clinical models of these cancers have confirmed the presence of elevated lactate in late stage tumors and demonstrated reductions in lactate in response to therapy. Other applications being pursued in a number of different research groups are the evaluation of cardiac viability and assessment of broader range of neurological diseases.

The implementation of C-13 imaging as a routine methodology on clinical scanners requires a number of hardware and software modifications. While many systems are able to obtain single channel multi-nuclear data, fast imaging applications are currently directed primarily towards obtaining proton images. The ability to follow dynamic changes in multiple metabolites means that spectroscopic imaging and frequency selective imaging approaches are of interest. In addition to considering the timing of delivery of the agent to the tissue of interest, strategies used for data acquisition need to be adjusted to take account of signal decay due to T1 and metabolic activity, as well as taking account of the fact that polarization is used up at each excitation. A number of different approaches are being developed but it is clear that parallel imaging, in conjunction with echo planar, spiral or other rapid k-space sampling strategies are going to be important for designing appropriate pulse sequences for human applications. The construction of a volume resonator for C-13 transmission and multi-channel, multi-nuclear radiofrequency coils for reception will be needed to take advantage of such techniques. Taken in conjunction with the consideration of polarizing different agents, it is clear that there is a broad potential for addressing clinical applications and that this is likely to be the source of many new technological advances.

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