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The Physics & Chemistry of Molecular Imaging[1]

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MRI contrast agents have become an important diagnostic tool in clinical medicine. The most popular and widely-used agents over the past 30 years have been small chelates of Gd3+ that act as T1 shortening agents after IV administration. These small molecule agents in general lack tissue specificity, quickly enter all extracellular space, and do not respond to changes in physiology or biology. A goal of our lab over the past few years has been to develop newer types of agents for measuring important physiological parameters such as tissue pH, hypoxia or enzyme activity. The recent discovery of a Zn2+-responsive Gd-complex has allowed monitoring of insulin secretion from pancreatic beta-cells and Zn2+ secretion from prostate, both in response to glucose. A second new imaging contrast mechanism based on chemical exchange saturation transfer (CEST) is rapidly gaining popularity for detecting in vivo proton exchange processes. Many endogenous proteins and small metabolite molecules have been detected and several new exogenous paramagnetic agents (paraCEST) have been designed that "respond" to specific biological events. Finally, one of the newest areas of molecular imaging applied to biology and medicine is dynamic nuclear polarization (DNP), a process by which electron spin polarization is transferred to nuclear spins at low temperature. This process increases the sensitivity of 13C, 15N and other insensitive NMR nuclei by a factor of 10,000 or more thereby offering the exciting possibility of imaging metabolic pathways in real time in humans. Basic physics and chemistry principles have been used to improve the sensitivity of DNP to the point where clinical applications of DNP are rapidly becoming a reality. Examples of the first human metabolic imaging experiments performed in Dallas will be presented.

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