Novel imaging strategies preclinical: molecular readouts/ pathway imaging: MRI versus other modalities

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MR imaging and spectroscopy provide extensive quantitative morphological and functional information that combined with high spatial resolution make this modality a true workhorse for diagnostic radiology. On the other hand, traditional nuclear imaging modalities such as SPECT and PET and more recently optical imaging have intrinsically higher sensitivity and can detect imaging probes administered in tracer concentrations. Therefore, these imaging techniques are currently methods of choice for molecular imaging that provide information regarding expression status of molecular targets and/or metabolic and signaling pathways. Adapting MR imaging and spectroscopy to this new class of molecular imaging applications is a challenging but potentially very rewarding problem.

Several novel highly sophisticated imaging strategies have been developed for MR molecular imaging in preclinical small animal systems. One group of MR imaging applications relies on some form of signal amplification through the use of targeted paramagnetic or superparamagnetic contrast agents, water exchange, or enzyme reactions to generate MR detectable product molecules. Molecular imaging targets, such as several classes of cell surface receptors found in tumors, can be endogenous and tissue specific. Exogenous molecular targets that function as reporter genes can be incorporated in the cell population of interest and used to study activation of specific pathways.

MR spectroscopy is widely used in clinical and preclinical studies to measure concentration of metabolites present in relatively high concentrations *in vivo*. There is a significant interest in the development of MR spectroscopy molecular markers that can be used for *in vivo* detection of physiological processes. One important example includes prodrug activation for cancer therapy. MR imaging can be used to follow the delivery of a prodrug enzyme to the tumor, and MR spectroscopy can be used to detect the conversion of the parent prodrug to its active form by the specific enzyme that is either expressed by or pretargeted to the tumor cells.

Clinical translation of MRI methods that have been developed and validated in preclinical models will require significant effort as multiple problems related to optimal targeting, toxicity and immunogenicity of the imaging probes have to be solved before clinical translational. While traditional nuclear imaging technologies and novel optical imaging techniques provide excellent sensitivity and can use tracer concentrations of the imaging probe, MRI has several important advantages such as high spatial resolution, no radiation exposure, true three-dimensional imaging, and the ability to provide unique morphological and functional information that can be of key importance for diagnostic applications.