Tumor Response Assessment using Dynamic Contrast-Enhanced MRI
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Dynamic contrast enhanced MRI, or DCE-MRI refers the use of rapid T1-weighted MRI imaging before and during IV administration of gadolinium-based contrast agents. DCE-MRI belongs to a family of imaging techniques that monitors the time-dependent passage of exogenous contrast agents into tissues. While DCE-MRI has been performed to assess the status of a variety of disease states, including inflammatory conditions, the most prominent use of DCE-MRI is in oncologic imaging, where it can be used to diagnose and characterize malignant tumors from surrounding tissues. DCE-MRI has most notably been used as a method for detecting alterations in tumor vascularization following treatment with targeted anti-vascular and anti-angiogenic compounds.

In the setting of vascular-targeted anti-tumor therapies, DCE-MRI offers a methodology for more functional assessment of early tumor response to treatment. In a variety of studies, including cohorts of patients with advanced renal cell carcinoma, hepatocellular carcinoma, glioma, non-small-cell lung cancer, and others, DCE-MRI has demonstrated physiologic changes in tumors treated with anti-angiogenic agents. DCE-MRI has also proven useful as a means of assessing the spectrum of anti-vascular effects in early stage studies of vascular disruptive agents.

Equally important, DCE-MRI has demonstrated the ability to effectively quantify the vascular “phenotype” of tumors. Numerous studies have documented the relationship between DCE-MRI metrics and tissue-based markers of angiogenesis, such as microvessel density (MVD), CD-40 expression, and others. These tissue markers have consistently been shown to be a surrogate for tumor biologic behavior, and have been used as predictive biomarkers in therapeutic response modeling. As such, baseline (pre-treatment) non-invasive tumor vascular phenotyping by DCE-MRI has the potential as serve as a predictor of clinical response for established anti-vascular therapies.

Several trends in DCE-MRI acquisition and analysis have emerged which are expected to increase the ability of clinical and scientific investigators to utilize DCE-MRI, especially the option for non-Cartesian k-space acquisition strategies. These provide opportunities for retrospective post-processing to optimize temporal resolution without requiring sacrifices in spatial resolution or volumetric coverage typical with Cartesian based rapid imaging methods. These altered k-space trajectories improve the quality of imaging in the setting of respiratory motion, and offer the option for retrospective respiratory gating of DCE-MRI image sets.

In addition, more novel analytic approaches that move beyond the tradition two-compartmental tumor model provide additional avenues for DCE-MRI analysis. Multi-compartment modeling approaches have enabled investigators to gauge the effects of tumor therapies not just on flow and vascular permeability, but also tumor vascular volume fraction as well as the dynamics of water exchange. Such modeling requires more complex computation methods, but may allow for more robust analysis of the tumor vascular micro-environment, and its alteration in response to local or systemic therapies.

Challenges in the application of DCE-MRI in oncologic studies remain. Large volume DCE-MR imaging remains difficult to achieve in representative human populations. Quantitative reproducibility, though demonstrated to be adequate in the hands of skilled...
investigators, may be lacking in larger-scale multi-site studies. In a subset of clinical subjects, the safety of gadolinium administration remains an issue.

As alternative methods for evaluating the tumor vascular microenvironment by MRI (such as arterial spin-labeling and multi-B value diffusion weighted imaging) or by PET (such as RGD-peptide imaging) emerge, defining the value, applicability, and generalizability of DCE-MRI in tumor response assessment remains a unique challenge for the imaging community.