Hierarchical Mixed Effect Models for the Analysis of a Longitudinal Dynamic Contrast-Enhanced MRI Oncology Studies

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Imaging in clinical oncology trials provides a wealth of information that contributes to the drug development process, especially in early phase studies. Standard analysis of such data is performed by summarizing each scanning session as a single kinetic parameter — such as median K^{trans} across all voxels in the tumor region of interest.

Inspired by mixed-effects models that are frequently used in the analysis of clinical trials, we propose to analyze all voxel time courses from all scans and across all subjects simultaneously in a single model. Kinetic parameters from the usual nonlinear regression model are decomposed into unique components associated with factors from the longitudinal study; e.g., treatment, patient, and voxel effects. A Bayesian hierarchical model provides the framework.

Hypothesis testing at the study level for an overall treatment effect is straightforward and the patient- and voxel-level parameters capture random effects that provide additional information at various levels of resolution to allow a thorough evaluation of the clinical trial.

The proposed method is validated with two cancer studies, where the subjects were imaged before and after treatment with novel chemotherapy, demonstrating the clinical potential of this method to longitudinal oncology studies.