Future Directions for DCE-MRI

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1. Introduction

The theory and applications of dynamic contrast enhanced MRI (DCE-MRI) have been well documented, and a number of data acquisition and analysis techniques are readily available and in use for both pre-clinical and clinical studies (reviewed in 1,2). However, there are several aspects that remain to be further investigated, so it is appropriate to consider the status of the field and examine where future research directions may point. In order to initiate a dialogue at this session, we offer the following points as topics for discussion.

2. Making the measurement

2.1 Are all contrast agents created equal? A wide range of contrast agents are currently available (charged or uncharged, large or small, intravascular or extravascular, paramagnetic or superparamagnetic, etc.), but do we have an understanding of, and data on, how to select the optimum agent for a given study?

2.2 The Arterial Input Function Is it important to measure the AIF on an individual basis, or is a population averaged approach reasonable? Do we need to measure AIFs on a more (spatially) local basis, or will a regional measurement suffice? Does the AIF even need to be measured at all? Is there a place for reference region approaches (3,4)?

2.3 From signal intensity to tracer concentration Inherent in all pharmacokinetic models is the need to convert the measured signal intensity time course data into tracer concentration time courses. There has been some disagreement over which technique(s) is(are) most appropriate. In particular, some studies have shown the importance of considering water exchange (5) when making this conversion, while others have indicated that the effects are not present in a typical DCE-MRI study (6). What is an appropriate analytic approach?

2.4 Validation methods (flow phantoms) Are current validation studies helpful or are they a waste of time and resources? Do they actually assist in the design and analysis of studies and assist in adopting a "standardized" DCE-MRI protocol for (e.g.) a multi-site clinical trial?

2.5 Repeatability/Reproducibility Are these limited by measurement error or by physiologic variability? Should every clinical trial incorporate such a substudy?

3. Analyzing the data

3.1 Beyond the Tofts model? Can we rely on parameters returned from models more complex than the Tofts or extended Tofts models? Do more complex models lead to curve fitting instability that place unrealistic requirements on the available SNR?

3.2 Contrast agent diffusion Passive delivery by diffusion of the contrast agent (rather than active delivery by perfusion) almost certainly plays a part in enhancement of voxels that do not have a functioning vascular system. Frequently the vascular status of such sections of tissue are difficult to know *a priori*. How can such diffusion effects be accommodated into current models?

4. What does it all mean?

4.1 Parameter interpretation There is some evidence that v_e is not really the extravascular extracellular volume fraction. This is especially true in regions that are not actively perfused (see comment in section 3.2). Particularly vexing are recent data showing that v_e and the apparent diffusion coefficient have little apparent relationship (7). Also, when, if ever, is $K^{trans}=PS$, or $K^{trans}=F$?

4.2 Prognostic biomarker? Do abnormal values in DCE-MRI actually predict patient outcome? The careful studies in the literature regarding clinical trials appear to offer mixed results.

4.3 Response biomarker? Are DCE-MRI parameters sensitive enough to predict patient response to therapy?

5. Why not just use DCE-CT?

Though dynamic contrast enhanced computed tomography (see, e.g., 8.9) requires ionizing radiation, it provides a number of obvious acquisition and analysis advantages over DCE-MRI. These include high spatial resolution, fast scan time, independence of organ location, a reduced sensitivity to patient motion, and a linear

relationship between measured signal intensity and tracer concentration. The latter, obviously, greatly reduces modeling complexity. What are the relative merits of MRI versus CT for DCE studies?

6. Summary

As the above observations suggest, there are a number of residual DCE-MRI issues that are not clear. We look forward to an exciting discussion of these and other topics that will hopefully yield a number of possible research directions.

7. References

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