DCE-MRI Measurement Challenges

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1. Introduction

Quantitative dynamic contrast enhanced MRI (DCE-MRI) requires 1) serial measurement of the signal intensity time course in a tissue of interest before, during, and after the injection of a paramagnetic contrast agent, 2) the time course of the contrast agent concentration in the blood plasma from a nearby feeding vessel, and 3) a pharmacokinetic model to analyze the data (1,2). The model is then fit to the time course data to extract physiologically meaningful parameters. Unfortunately, there are challenges at every step: converting the measured signal intensities to concentration of contrast agent (as required for pharmacokinetic analysis), developing (or selecting) an appropriate model, and interpreting the output parameters. Within each of these steps are a number of sub-steps, many of which have the ability to contribute error to the overall analysis. In this presentation, we will explore the theory of four current measurement challenges in DCE-MRI and attempt to summarize the current state of the art as provided by the literature.

2. Current Acquisition Challenges

2.1 Spatial versus Temporal Resolution

The two most common applications of DCE-MRI are to 1) report quantitatively on tissue properties including blood vessel perfusion and permeability as well as volume fractions within heterogeneous lesions, and 2) provide clinically relevant insights into lesion enhancement. While these two are related, the requirements of the data to perform these applications may be quite different. In order to perform the first application, the temporal sampling rate must be high enough to characterize the uptake portions of signal intensity curves from both the tissue of interest and a feeding vessel. Unfortunately, this is at odds with the requirements of high-spatial resolution data. We will discuss the relative merits of high spatial resolution versus high temporal resolution data and allude to keyhole techniques that may deliver both simultaneously.

2.2 Arterial Input Functions

Directly related to the temporal resolution needs, is the requirement to characterize the rate of change of concentration of contrast agent in the blood plasma, the so-called arterial input function (AIF). This time course is needed for analysis with most currently existing pharmacokinetic models and, because it changes so rapidly, images have to be acquired on the order of a few seconds. Unfortunately, this leads to poor signal-to-noise and/or poor spatial resolution. One of the utilities of DCE-MRI is to probe lesion heterogeneity, so having to acquire data rapidly to characterize the AIF significantly limits the power of the technique. While many investigators have attempted to measure the AIF in individual patients, others have explored alternative paths such as using an average AIF obtained from a sub-population (3), assuming a model AIF (4), or using a reference region model (5,6). In this presentation we will discuss the benefits and drawbacks of each approach.

2.3 From signal intensity to contrast agent concentration

Pharmacokinetic analysis cannot be performed directly on the signal intensity time courses measured in a DCE-MRI study; they must be converted to concentration of contrast agent time courses. In most models, the tissue extravascular space is assumed to be a well-mixed, homogeneous compartment; or, equivalently, the system remains in what is typically called the fast exchange limit (FXL) with respect to the water exchange between two regions. Some investigators, noting that in most tissues, most water is intracellular, and since the common Gadolinium chelates cannot access this intracellular water directly, water exchange between the extravascular extracellular space and the extravascular intracellular space must be incorporated into analytic models under certain circumstances (7). Similar comments apply to water exchange between the intravascular and extravascular spaces when using an intravascular agent (8). However, some careful studies have indicated that this effect is not terribly common in many DCE-MRI applications (9). We will discuss the theory of water exchange and then review the literature on both "sides" of this important issue.

2.4 When to scan?

As stated above, one of the central goals of DCE-MRI is to obtain information on tissue vascular status. One of the applications of these data is to assess treatment response. For such a study, DCE-MRI data must be acquired before and during the course of therapy. This raises the practical and very relevant question of when scans should be performed after the onset of treatment. This is, ultimately, determined by a combination of the rapidity with which the treatment induces changes on diseased vasculature, combined with DCE-MRI's sensitivity to the induced change. Determining the optimal time to image during treatment is a matter of great import, so we will present and discuss several instructive examples from the literature.

3. Discussion

In this presentation we will review four key measurement challenges in DCE-MRI: 1) choosing the temporal and spatial resolution of the data, 2) measuring the AIF, 3) converting from measured signal intensity to the concentration of contrast agent, and 4) determining when best to scan a patient during a longitudinal study. It is hoped that by the conclusion of the presentation, the attendee will have a reasonable understanding of the problems and potential solutions in these four areas and be able to know where to look in the literature for further information and guidance.

4. References

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5. Acknowledgements