Dynamic Contrast Enhanced Perfusion
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Introduction

Dynamic contrast enhanced magnetic resonance imaging (MRI) methods, both relaxivity ($T_1$) and susceptibility ($T_2$ and $T_2^*$) based approaches, have demonstrated the potential to measure important characteristics of tissue structure and function in both pre-clinical and clinical applications. Studies that assess changes in tissue $T_1$ following the administration of a paramagnetic contrast agent (CA) are commonly termed dynamic contrast enhanced MRI (DCE-MRI; reviewed in, e.g., [1]), whereas those relying on $T_2$ and $T_2^*$ changes are referred to as dynamic susceptibility contrast MRI (DSC-MRI; reviewed in, e.g., [2]). As the CA traverses through the vasculature and into the extravascular space, it alters the $T_1$, $T_2$ and $T_2^*$ relaxation rates of tissue water and therefore the measured MR signal intensity. The resultant signal intensity time courses can be related to changes in tissue CA concentration and, by fitting the acquired data to an appropriate pharmacokinetic model, physiological parameters can then be derived. The analysis of DCE-MRI yields parameters that relate to the extravasation rate of the CA (denoted by the parameter $K^{\text{trans}}$) and the volume fractions of the underlying tissue compartments (e.g. extravascular extracellular volume fraction). The goal of a DSC-MRI study is to track the first pass of a CA through a tissue’s vasculature and characterize its hemodynamic status through such parameters as the blood volume, blood flow, and mean transit time. In this lecture we will discuss the physical and physiological basis of DCE- and DSC-MRI as well as describe quantitative methods of obtaining and analyzing such data. Particular emphasis will be placed on the topics described below.

Relationship between MRI signal change and contrast agent concentration

As indicated above, quantitative DCE-MRI and DSC-MRI methods depend on the reliable characterization of the relationship between the CA induced signal intensity change and the concentration of the CA in the tissue. However, since MRI is measuring the influence of the CA on the relaxation properties of water and not the CA itself, the measured signal intensity is also dependent upon physical phenomena such as CA induced (and geometry dependent) susceptibility gradients and water exchange between tissue compartments. While this dependency may complicate the interpretation of MRI signals it also provides an opportunity to indirectly assess sub-voxel tissue features such as vascular tortuosity, cellular spacing and water exchange rates.
Data acquisition

In order to observe the signal changes induced by the injected CA, heavily $T_1$, $T_2$ or $T_2^*$-weighted images must be acquired before, during, and after the CA injection. As with any MRI imaging protocol, trade-offs exist between tissue coverage, temporal resolution, spatial resolution, and signal to noise. The kinetic models used to analyze such data typically require rapid sampling of the dynamic datasets and this often restricts the choice of pulse sequence and its associated parameters. As many quantitative dynamic MRI methods require simultaneous measurements of the CA induced signal changes in an artery and a tissue of interest, the selected data acquisition approach should be able to reliably detect a wide range of CA concentrations. An oft reported source of error, high CA concentrations can present as $T_2^*$ induced signal suppression in DCE-MRI studies or signals near the noise-floor in DSC-MRI studies. Furthermore, in the case of DSC-MRI, the choice of pulse sequence can substantially alter the sensitivity of the extracted parameters to specific vascular populations, a feature that underlies the basis of the vessel size imaging approach. Finally, to improve the reliability of the derived parameters recent DCE-MRI and DSC-MRI studies propose the use pulse sequences that enable the simultaneous acquisition and separation of contrast-agent induced $T_1$ and $T_2^*$ changes.

Arterial Input Function

The selection of a suitable AIF is particularly important for quantification of DCE-MRI and DSC-MRI derived kinetic parameters. Ideally, the AIF would be measured for each voxel in an image, but since this is impractical, the most common way to select an AIF is to arbitrarily select a global concentration time curve that is measured from a voxel(s) located in or near major arterial vessels and exhibit kinetic patterns consistent with arterial delivery such as early contrast enhancement, high amplitude and rapid wash-in/out kinetics. Several challenges make quantification of the AIF difficult, including a breakdown of the assumption of a linear relationship between relaxation rate change and CA concentration and partial volume effects. To overcome this limitation several investigators have explored the use of phase-image derived AIFs as phase changes within vessels demonstrate improved linearity with contrast agent concentration. For organs with multiple arterial input sources, automated methods are being used to identify local AIFs in an attempt to further improve the reliability of the derived kinetic parameters.

Kinetic Models

Mathematical models for CAs have been developed that describe the introduction, distribution, and clearance of the agent within the body. The appropriate description of CA passage through tissue can reveal insights into its physiologic parameters such as blood flow, vessel wall permeability, and volume fractions of tissue compartments. There continues to be a great interest in refining existing models in an attempt to more accurately describe and incorporate the physical and physiological factors that influence the acquired MRI
signals and to simplify the extraction of the kinetic parameters of interest. For example, the effects of water exchange, CA diffusion and vascular contributions can be incorporated into conventional DCE-MRI models. While a conventional kinetic model exists for DSC-MRI studies of brain tissue with an intact blood brain barrier, the extravasation of CA in brain tumors and in all organs outside the brain greatly confounds the application of this model to such data and has necessitated the further development of more sophisticated signal and kinetic models. Recent advancements in DSC-MRI kinetic models have also enabled the voxel-wise assessment of flow and capillary transit time heterogeneity.

Discussion

At the completion of this seminar, the attendee should have 1) a basic knowledge of the foundations of DCE-MRI and DSC-MRI theory and acquisition methods; 2) insight into physical and physiological factors that influence such measures; and 3) an understanding of the basis for current questions and unresolved issues of interest to DCE-MRI and DSC-MRI investigators.

References