Clinical Approach of $T_1$-mapping for Hemodynamic Analysis

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**Abstract**: Our current study concerns $T_1$ measurement and mapping for dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) in clinical settings. The methodology requires rapid, accurate, and reproducible measurements in order to calculate various pharmacokinetic kinetic parameters. We are focusing on methodology, application, and future development of $T_1$ mapping for DCE-MRI. The current study explains the methodology of three $T_1$ measurement methods; variable flip angle (VFA), variable reputation time (VTR), and Look-Locker (LL), respectively. Moreover, for future studies, we discuss the possibility of compressed sensing (CS) and MR fingerprinting (MRF) on $T_1$ mapping. The physical methodology of $T_1$ mapping for hemodynamic analysis will become more and more important in clinical and practical settings.

**Keywords**: Magnetic Resonance Image (MRI), hemodynamic analysis, $T_1$ mapping, dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI)

1. Introduction

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is used to evaluate tumor microvasculature and its acquired kinetics parameters. It requires serial acquired MR imaging data before and after injection of contrast media. The analysis results provide information about the effectiveness or ineffectiveness of treatment, e.g., chemotherapy, and radiation therapy[1].

Tofts et al. reports lead to wide use of clinical quantitative analysis, i.e., tracer kinetic model[2]. Each vendor of MR scanner provide software of hemodynamic analysis for DCE-MRI based on kinetic models[3]. Moreover, the Radiological Society of North America (RSNA) set up a workshop for DCE-MRI in 2007, i.e., the Quantitative Imaging Biomarkers Alliance (QIBA), whose purpose is to define basic standards for DCE-MRI measurements and quality control which are consistent[4]. The guideline shown gives more detail about subject handling, imaging procedure, image post-processing, parametric image formation and analysis, and quality control. Within these reference, since $T_1$ measurement depends on imaging data acquired pulse sequence, it must be accurate to calculate quantitative parameters, e.g., native tissue $T_1$ mapping of pre-contrast agent, gadolinium concentration, arterial input function (AIF), and vascular parameters.

On this article, we discuss methodology, usefulness, application, and future prospects in focusing on $T_1$ mapping methodology required for DCE-MRI.

2. Why must the $T_1$ value be calculated?

The tracer kinetic model is derived by signal change over sequential time converted by kinetic parameters; blood plasma volume ($v_p$), interstitial compartment volume ($v_i$), transfer constant ($K^{trans}$), and efflux rate constant ($k_{ep}$)[5]. Fig. 1 shows the schematic illustration of the kinetic model. Here, concentration of contrast agent (CA) must be calculated. The relationship between concentration of contrast agent and relaxation ratio is linear, but signal intensity (SI) is not. Because the SI affects itself on $T_1$ (or $T_2$) decay, the SI value is at a lower point than the concentration of CA; it is different from spin-echo (SE) and gradient echo (GRE). Accordingly, calculation of $T_1$ relaxation rate lead to the correct on linear relationship in order to evaluate the concentration of CA. $T_1$ value of post-contrast tissue ($T_{1post}$) is calculated with the following equation.

\[
\frac{1}{T_{1post}} = \frac{1}{T_{10}} + R_C C,
\]

Fig. 1 Schematic drawing of a two compartment model presenting exchange of CA between Intravascular Plasma Space (IVPS) and Extravascular Extracellular Space (EES). The kinetic parameters are as follows; flow rate of blood plasma through intravascular space, $F_p$, ratio of blood plasma volume tissue volume $v_p$, ratio of EES volume to tissue volume $v_e$, transfer constant $K^{trans}$, and efflux rate constant $k_{ep}$. There are various parameters in some kinetic model types. The estimation of these parameters needs CA concentration derived from $T_1$ of tissue.
where $T_0$ is the $T_1$ value of pre-contrast tissue, $R_1$ is relativity of CA, and $C$ is the tissue concentration of CA. Now, it becomes possible to estimate each parameter using tracer kinetic models.

3. Methodology and clinical application of $T_1$ calculation

In general, DCE-MRI does not require spatial resolution as temporal resolution. The inversion recovery method is the gold standard, when assessing $T_1$. However, this method would not be suitable in this case because it requires a long measurement time. We selected and describe the three following methods; variable flip angle (VFA), variable TR (VTR), and Look-Locker (LL). In most settings, if $T_0$ is obtained using these $T_1$ calculation methods, $T_1$ can be derived by solving the simultaneous equations from the SI ratio of pre-contrast and post-contrast[3]. Fig. 2 shows $T_1$ calculation and mapping procedure for DCE-MRI.

3.1 Variable flip angle method

VFA method widely is used in DCE-MRI. For this method the $T_1$ is calculated from acquisition data of setting more than two FA using spoiled GRE (SPGR)[6]. SI of SPGR is given by the following equation:

$$S_{\text{pre}} = M_0 \sin \alpha \frac{1 - \exp \left(-\frac{TR}{T_1}\right)}{1 - \exp \left(-\frac{TR}{T_1}\right) \cos \alpha},$$

$$\cdot \arg \left[M_0, T_1\right] = \arg \min_{M_0, T_1} \left(\sum_i \left(S_{\text{pre}}^i - S_{\text{pre}}(\alpha, \theta)\right)^2\right),$$

where $M_0$ is the equilibrium magnetization, TR and FA are each parameters set by the operator, $S_{\text{pre}}$ is the measured signal value, $S_{\text{pre}}$ is the theoretical signal value. With fixed TR and varying $\alpha$, a nonlinear curve fitting procedure can yield estimation parameters of $M_0$ and $T_1$ according to the relationship between SI and FA.

VFA method is suitable in serial data acquisition for motionless organs, e.g., brain, breast, pelvis, and musculoskeletal. Additionally, this method tends to have an effect on $B_1$ inhomogeneity which causes error in quantitative calculations such as $T_1$ mapping. Actual FA needs to be corrected using the application of $B_1$ mapping with a high magnetic field MR scanner[6]. $B_1$ correction would improve difference of local FA into slice section and in-plane[7]. Moreover, because $T_1$ decay effects the result in signal decrease and $T_1$ estimate error, others have made reports concerning the VFA method with $T_1$ correction applied[8].

3.2 Variable TR method

The VTR method is used on application of SE or fast SE (FSE) sequence. This method’s advantage, in comparison with GRE signal, is that SE signal doesn’t have an effect on inhomogeneity of the magnetic field due to apply refocusing pulse, i.e., 180-degree pulse, after excitation pulse. With acquisition on different TRs ($T_{R1}$ and $T_{R2}$) as a double relationship and fixed TE, $T_1$ is described as follows in equation[9]:

$$\begin{align*}
&\text{if } T_{R1} = 2T_{R2}, \\
&\therefore T_1 = \frac{T_{R1}}{\ln \left(\frac{S_i}{S_t}\right)}.
\end{align*}$$

where $S_i$ and $S_t$ are SIs acquired using SE or FSE on the above parameter setting. Here, because $T_1$ is cancel out in above equation (5), the setting value of TE should be extremely short for the suppression of $T_1$ decay effect.

This method’s limitations have a high-velocity signal loss effect when using the SE method[10]. This effect causes an incomplete signal acquisition by rapid flow in the artery and the calculation error of AIF is derived from this. To avoid this problem, it is needed to set at the appropriate slice section. In addition, data acquisition time depends on TR far more than GRE.

3.3 Look-Locker method

LL method is in general used for surveying of the null point at the normal myocardium in order to acquire a high-contrast image in late gadolinium enhancement (LGE)[11]. This method can rapidly measure $T_1$ for one acquisition. After a non-selective inversion pulse, a series of low excitation

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pulses \( \alpha \), which are separated by a short time \( \tau \) during one TR, are applied. Images of each excitation are formed by the segmented sampling of \( k \)-space. The basic data acquisition part is variety, e.g., echo planner imaging (EPI), SPGR, and steady state free precession (SSFP), respectively[12-14].

\[
\frac{1}{T_1} = \frac{1}{T_1} - \frac{\ln(\cos \alpha)}{\tau}
\]  

(6)

The three parameters, \( A \), \( B \), and \( T_1 \), are measured by least-squares fitting at each sampled point \( t_\text{s} \), and \( T_1 \) is ultimately calculated from the equation:

\[
S_{\text{LL}}(t_\text{s}) = A - B \exp \left( -\frac{t_\text{s}}{T_1} \right),
\]  

(7)

\[
[A, B, T_1^\prime] = \arg \min_{A, B, T_1^\prime} \left( \sum_{i=1}^{N_{\text{volumes}}} \left( S_{\text{LL}, i} - S_{\text{LL}, i}(t_\text{s}) \right)^2 \right),
\]  

(8)

\[
\cdot T_1 = T_1^\prime \left( \frac{B}{A} - 1 \right).
\]  

(9)

where \( S_{\text{LL}} \) is the measured signal value, and \( S_{\text{LL}} \) is the theoretical signal value.

This method advantage is feasibility to get directly \( T_1 \) mapping data rapidly at one acquisition to reduce patient loading, e.g., breath holding time. The clinical applications are useful in not only for LGE of heart but enhancement ratio of liver[15]. On the other hand, because the LL method has an affect on \( B_1 \) inhomogeneity as well as the VFA method, it must be collected by another procedure[16]. Moreover, the modified LL inversion recovery method overcomes the problem of incomplete recovery of \( T_1 \) relaxation in the condition of high heart rate[17].

### 3.4 Future prospects

Since appearance of the parallel imaging technique, rapid imaging data acquisition independent of pulse sequences provide benefits in clinical setting[18]. Moreover, data mining has become more and more progressive. Compressed sensing (CS)-MRI is a reconstruction technique from sparse MR data, i.e., few random sampling of \( k \)-space[19]. Previously, there are some reports concerning \( T_1 \) mapping, \( T_2 \) mapping, and DCE-MRI, respectively; the application of accelerated data acquisition maintains the spatial resolution or further improvement of that[20]. The low rank regularization is also significantly used with CS[21]. Thus, it has become important to optimize not only the pulse sequence control but reconstruction from small data acquisition.

In addition to other techniques, we would like to report on MR-fingerprinting (MRF)[22]. This method can measure the parameters of our discussion in here; \( T_1 \), \( T_2 \), \( M_0 \), and off-resonance frequency values, in about 10 seconds. SSFP sequence of varying acquisition parameters such as FA and phase of radio frequency pulses, TR, TE and sampling patterns can be achieved by this method. Moreover, MRF can be reconstructed by the pattern recognition algorithm even if the patient moves. The methodology used in MRF or itself would also be useful in conducting DCE-MRI research.

In conclusion, we describe \( T_1 \) measurement and mapping for DCE-MRI in a clinical approach. Our indicated methods would provide high quality of quantitative hemodynamic analysis by the suitable selection and setting. However, it should be emphasized that DCE-MRI has just begun to be used in the clinical setting. In the future, having a position of basic physical methodology would lead to perfection of DCE-MRI on a practical stage.

### References


