

Simulations of Perfusion Signals of Pulsed Arterial Spin Labeling MRI

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Purpose : A pulsed arterial spin labeling (PASL) signal usually depends on several parameters. The objective of this study was to determine the optimal parameters using simulation for perfusion signals of PASL magnetic resonance imaging (MRI).

Materials and Methods : Perfusion signals, $\Delta M/M_{0b}$, derived from the Bloch equation were evaluated in regard to the four most important parameters in PASL MRI: the tissue-to-blood coefficient (λ), the longitudinal relaxation time of blood (T_{1b}), the arterial transit delay from the application of tag (δt), and the magnetic field strength (B_0). The simulation was conducted with Mathematica software.

Results : First, perfusion signals differed depending on the value of λ in brain tissue. The maximum signal, $\Delta M/M_{0b} = 0.390$, was obtained at an inversion time (TI) = 1.53 sec for gray matter on 3T MRI. Second, perfusion signals were reduced with increasing δt . The maximum signal, $\Delta M/M_{0b} = 0.526$, was obtained at TI = 2.1 sec for $\delta t = 0.5$ sec. Finally, perfusion signals increased with increasing B_0 . The maximum signal, $\Delta M = 1.15$, was obtained at TI = 1.52 sec for 3T MRI.

Conclusion : We reported that the optimized TI values were obtained to provide the highest PASL signals. It is very important that optimized TI values be used to obtain high-quality perfusion signals using PASL MRI.

Index words : Perfusion

Arterial spin labeling

Bloch equation

Cerebral blood flow

Introduction

Perfusion is a physiological parameter that refers to the delivery of oxygen and nutrients to tissues via the flow of blood (1). Cerebral blood flow (CBF) is

generally quantified in terms of milliliters of blood per gram of tissue per second ml/g/sec (2). Perfusion measurements provide information regarding tissue viability and function, and are therefore of fundamental significance in the fields of medical research and clinical diagnostics.

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Arterial spin labeling (ASL) perfusion (3), which involves an endogenous tracer on MR images, is one of the techniques used for perfusion imaging without injection or inhalation of contrast agent or radioisotopes (4). Generally speaking, a perfusion-weighted image gathered by this technique is derived from the subtraction of two successively acquired images: one with, and one without, the proximal labeling of arterial water spins after a short delay time (5). The water employed as a tracer in ASL is largely free-diffusible.

Most ASL approaches in common use employ either pulsed labeling (PASL) with an instantaneous spatially selective saturation or inversion pulse (6), or continuous labeling (CASL), most typically via flow-driven adiabatic fast passage (7). In both of these approaches, arterial spins are tagged outside the imaging slice. Tagged spins are then permitted to flow into the slice of interest, and the image is acquired. The control image is acquired without tagging, and the signal difference between the two scans provides perfusion-weighted imaging (PWI) to estimate a quantitative CBF (8). Several PASL methods, including EPI and signal targeting with alternating radiofrequency (RF) (EPSTAR) (9, 10), flow sensitive alternating inversion recovery (FAIR) (11, 12), and proximal inversion with a control for off-resonance effects (PICORE) (7), have been proposed. Recently, additional, better PASL methods have been proposed, such as the double inversion of both tagged and reference images (DIPLOMA) (13) and improved arterial spin labeling methods (IDOL) (14).

PASL signals generally depend on several parameters (15). First, the tagging efficiency of RF pulse (α) is a key

factor in improving PASL signals. The second parameter is the tissue-to-blood partition coefficient (λ). Knowledge of λ is usually required for the quantification of CBF. λ changes during development of the brain and varies regionally in it, even among different gray matter structures, owing to variations in brain water content. In addition, λ would be expected to vary with the hematocrit, owing to changes in blood water content. The impact of using an incorrect value will result in errors in the quantifications of CBF. Third, the arterial transit delay time (δt) can affect measurements of the PASL signal. The transit delay for the flow of blood from the tagging region to the imaging slices in humans is not small compared with the T_1 blood, and varies significantly across voxels, creating a variable attenuation of the ASL signal (7, 16); thus resulting in errors in the calculated CBF. Intravascular tagged blood that is flowing through the imaging slices and destined to perfuse more distal tissue can induce very large-amplitude focal artifacts in the difference signal that do not represent perfusion of the imaging slices (17). Finally, the longitudinal relaxation time of blood (T_{1b}) and magnetic field strength (B_0) are other factors.

The objective of this study was to determine optimal parameters using simulation for perfusion signals of PASL MRI. Perfusion signals, $\Delta M/M_{0b}$, derived from the Bloch equation were evaluated with the four most important parameters in PASL MRI: λ , T_{1b} , δt , and B_0 . Although α is an important factor in acquisitions of high signals in ASL perfusion MRI, we did not include it in this simulation because perfusion signals are only linearly scaled by it.

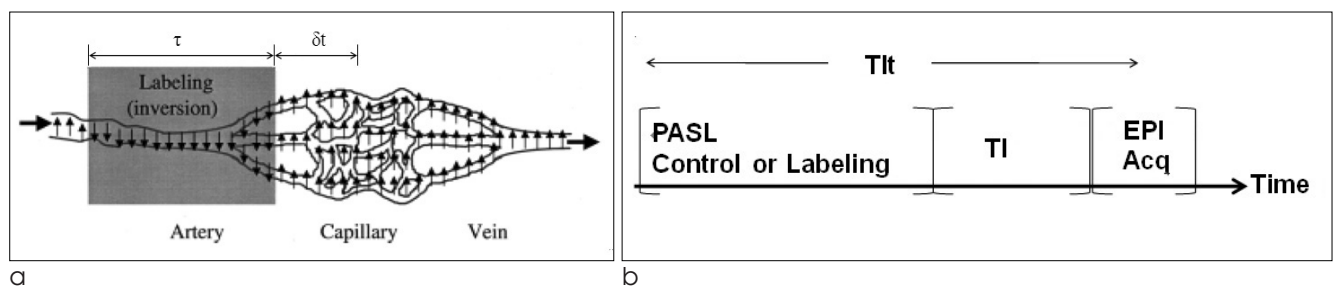


Fig. 1. Schematic illustration of the labeling of the spins in the arteries (1a) and schematic of the PASL pulse sequence (1b).

τ is the duration of the arrival of labeled water molecules at the tissue.

δt is the delay of water molecules between arterial labeling and exchange into tissue.

Tlt is the total labeling delay time, which is the time interval from the center of the labeling radiofrequency pulse and the center of the excitation pulse.

Theory

PASL perfusion is based on the phenomenon of the inversion of signals. Fig. 1a is the schematic illustration of the labeling (inversion) of the spins in the arteries. The proton spins of blood flow to the arteries. The Bloch equation for tissue water, including flow, can be described as follows Eq. [1] :

$$\frac{dM(t)}{dt} = \frac{M_0 - M(t)}{T_1} + f(M_a - M_v) \quad [1]$$

in which M_0 is the amplitude of the fully relaxed signal, f is the cerebral blood flow ($\text{ml g}^{-1}\text{s}^{-1}$), T_1 is the longitudinal relaxation time of water in tissue (sec), and $M(t)$, $M_a(t)$, and $M_v(t)$ are the magnetizations of water in tissue, arterial blood, and venous blood, respectively. Assuming that water is freely diffusible, $M_v = M/\lambda$ and $M_a = M_0/\lambda$, in which λ is the brain-blood partition coefficient (ml/g).

In PASL, the arterial blood is tagged near the imaging slice by inversion, and sequential images are acquired in which blood is alternately inverted and not inverted. We refer to these as tag and control states, respectively. Subtraction of the tag from the control images then leaves a difference signal, ΔM which is based on a general kinetic model for PASL signals (18):

$$\Delta M(TI_t) = 2M_0^0 \alpha \frac{f}{\lambda} (TI_t - \delta t) e^{-\frac{TI_t}{T_{1b}}} \cdot q, \delta t < t < \tau + \delta t \quad [2]$$

$$q = \frac{e^{\left\{ \frac{1}{T_{1b}} - \left(\frac{1}{T_1} + \frac{f}{\lambda} \right) \right\} (TI_t - \delta t)} - 1}{\left\{ \frac{1}{T_{1b}} - \left(\frac{1}{T_1} + \frac{f}{\lambda} \right) \right\} (TI_t - \delta t)} \quad [3]$$

in which M_{0b} is the relaxed magnetization of arterial blood, α is the inversion efficiency, T_{1b} is the T_1 of arterial blood (sec), δt is the arterial transit delay (ATT, sec) from the application of the tag to the first arrival of tagged blood in the imaging slice, τ is the time width of the tag (sec), and T_1 is the longitudinal relaxation time of water in tissue. TI_t is the total labeling delay time. The timing diagram schematic of the PASL pulse sequence is provided in Fig. 1b.

The q-factor is a correction factor for the fact that the rate of decay of the tag switches from that of blood to the tag by flow. If we assume that blood water exchanges instantly and completely with tissue water upon reaching the capillary bed, and that tissue water follows single-compartment kinetics, then the q-factor is represented as Eq.[3]. A typical CBF value is 60 mL/100 mL/min, providing a rate constant of 0.01 s^{-1} . The rate constant for the clearance of tagged water by T_1 decay is $1/T_1$, or approximately 1.1 s^{-1} . Thus, the clearance of the tag is dominated by T_1 decay, and clearance by flow is likely to be insignificant. The q-factor is dimensionless and typically has a value near 1. If $T_{1b} = 1.6 \text{ sec}$, T_1 for gray matter is 0.9 sec , $f = 0.01 \text{ sec}^{-1}$, $\lambda = 0.9$, $\delta t = 1.0 \text{ sec}$, and $TI_t = 1.3 \text{ sec}$ -which are the general parameters used at 3T (7) are assumed, the q-factor value is approximately 0.94. That is, it approaches 1 in accordance with the parameter values.

It is important to note that the expressions provided here for the difference signal assume that the parameters (δt , τ , T_{1b} , etc.) are uniform across each voxel, which is certainly not the case. The actual signal is an average across heterogeneous populations of vessels and tissues, but we begin with these simple expressions to determine how well they describe the experimental data and provide insights into the relevant contrast mechanisms.

Table 1. Values of Parameters Used in Four Simulations

Simulation	Parameters	λ (ml/g)	T_{1b} (sec)	δt (sec)	M_{0b} (T)
λ effect	$1.05(\lambda_{gm}) / 0.86(\lambda_{wm}) / 0.95(\lambda_{wb})$		1.6	0.7	3.0
T_{1b} effect		1.05	1.4 (1.5T) / 1.6 (3T) / 2.2 (7T)	0.7	3.0
δt effect		1.05	1.6	0.5 / 0.7 / 0.9	3.0
M_{0b} effect		1.05	1.4 (1.5T) / 1.6 (3T) / 2.2 (7T)	0.7	1.5 / 3.0 / 7.0

For all simulations, $\alpha = 1$.

λ_{gm} , λ_{wm} , and λ_{wb} : the tissue-to-blood partition coefficient for gray matter, white matter, and whole brain, respectively. T_{1b} : blood longitudinal relaxation time. δt : the arterial transit delay time. M_{0b} : the strength of magnetic field.

Materials and Methods

To determine how to change the q-factor and the corresponding magnetization signal for each of the parameter, we simulated (M/M_{0b}) and the q-factor based on Eq. [2] and [3]. Mathematica 7.0 (Wolfram Research Inc., IL, USA) software was used to simulate these parameters. Values of the parameters employed in the four simulations are shown in Table 1.

a. Tissue-to-blood partition coefficient λ effect on the q-factor and $\Delta M/M_{0b}$

To evaluate the effect of λ on the q-factor and (M/M_{0b}) , λ was varied according to brain tissue (19). For the well-perfused tissue, the incompleteness was no more than 1%. Therefore, the coefficient of tissue in brain would be only slightly affected by errors in the assumed perfusion (20). Parameter values to simulate λ were $\lambda_{gm} = 1.03$ ml/g, $\lambda_{wm} = 0.86$ ml/g, and $\lambda_{wh} = 0.95$ ml/g for gray matter, white matter, and whole brain,

respectively. The range of TI was $0 \sim 5.0$ sec. Other factors except for λ were fixed as $\alpha = 1$, $T_{1b} = 1.6$ sec, $\delta t = 0.7$ sec, and $T_1 = 0.977$ sec. The simulation was assumed to be 3T.

b. Blood longitudinal relaxation time T_{1b} effect on the q-factor and $\Delta M/M_{0b}$

To evaluate the effect of T_{1b} on the q-factor and (M/M_{0b}) , the q-factor was evaluated for T_{1b} values of 1.4, 1.6, and 2.2 sec for 1.5T (21, 22) 3.0T (22, 23), and 7T (22, 24) MRI. The range of TI was from 0 to 5 sec. (M/M_{0b}) was simulated using the simulation result of the q-factor. Factors except for T_{1b} values were fixed as $\alpha = 1$, $\delta t = 0.7$ sec, and $\lambda_{gm} = 1.03$ ml/g. The factor λ was used the value of gray matter in the brain. T_{1b} values were 1.4 sec, 1.6 sec, and 2.2 sec, for 1.5T, 3.0T, and 7.0T respectively.

c. Arterial transit delay δt effect on the q-factor and $\Delta M/M_{0b}$

To evaluate the effect of δt on the q-factor and

Table 2. The Maximum Value of Perfusion Signals and Inversion Time at the Maximum Value

	λ Effect	T_{1b} Effect	δt Effect	M_{0b} Effect
$\Delta M/M_{0b} / TI$ (sec)	λ_{gm}	0.390 / 1.53	1.4	0.351 / 1.48
	λ_{wm}	0.341 / 1.58	1.6	0.390 / 1.53
	λ_{wb}	0.365 / 1.55	2.2	0.481 / 1.64

* λ_{gm} , λ_{wm} , and λ_{wb} : the tissue-to-blood partition coefficients for gray matter, white matter, and whole brain, respectively. Unit of T_{1b} and δt are sec and the unit of M_{0b} is Tesla.

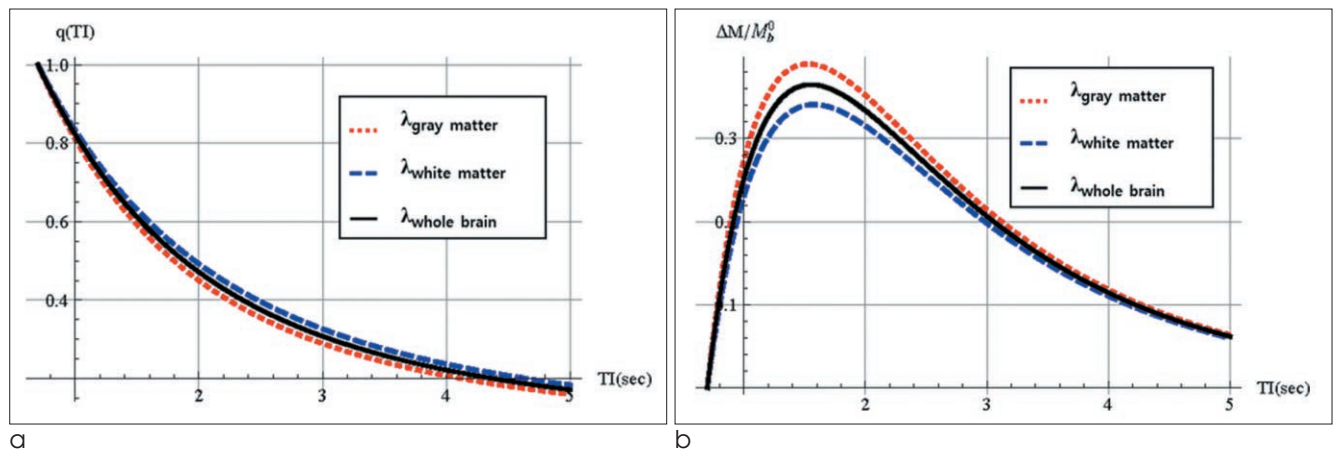


Fig. 2. Simulation results of the q-factor (2a) and perfusion signals (2b) depended on three different values of tissue-to-blood partition coefficient (λ).

Whole brain (Solid line), gray matter (Dotted line), and white matter (Dashed line)

Other parameters were used for $T_{1b} = 1.6$ sec, $\delta t = 0.7$ sec, and $\alpha = 1$ at 3T.

(M/M_{0b} , the q-factor was evaluated for δt values of three different cases, which were 0.5, 0.7, and 0.9 sec. The range of TI was from 0 to 5 sec. (M/M_{0b} was simulated using the simulation results for the q-factor. Factors except for the δt values were fixed as $\alpha = 1$, $T_{1b} = 1.6$ sec, and $\lambda_{gm} = 1.03$ ml/g. The factor λ was used the value of gray matter in the brain. The simulation was assumed to be 3T.

d. Strength of the magnetic field M_{0b} effect on the q-factor and ΔM

The strengths of the magnetic field also do not affect the q-factor because there is no M_{0b} term in Eq. [2]. Therefore, M_{0b} simulated only the difference in magnetization. We considered the three different magnetic field strengths of 1.5T, 3.0T, and 7T in regard to our ASL perfusion MRI. In this simulation, we also took into consideration the longitudinal relaxation time of blood values (23). T_{1b} values were 1 sec, 1.3 sec, and 1.5 sec, for 1.5T, 3.0T, and 7.0T respectively. Other factor values were $\alpha = 1$, $\delta t = 0.7$ sec, $\lambda_{gm} = 1.03$ ml/g, and T_{1b} values were assumed to be 1.4 sec, 1.6 sec, and 2.2 sec, for 1.5T, and 3.0T, and 7.0T, respectively.

Results

The maximum value of perfusion signals and the corresponding inversion time are shown in Table 2.

a. Tissue-to-blood partition coefficient λ effect on the q-factor and $\Delta M/M_{0b}$

Fig. 2 shows the simulation results of the q-factor (2a) and $\Delta M/M_{0b}$ (2b) in accordance with λ for gray matter, white matter, and whole brain. All three q-factor lines showed a similar pattern of monotonic decrease with increasing TI values. The q-factor was least, with the largest λ for all TI ranges.

$\Delta M/M_{0b}$ shown in Fig. 2b was dramatically varied with varying λ . $\Delta M/M_{0b}$ was increased with increasing λ or decreasing the q-factor. $\Delta M/M_{0b}$ was progressively increased with increasing TI, reached a broad maximum at TI ~ 1.7 sec, and declined with further increases in TI for all three different tissues. The maximum values of $\Delta M/M_{0b}$ were 0.390 at TI = 1.53 sec for gray matter, 0.365 at TI = 1.55 sec for whole brain, and 0.341 at TI = 1.58 sec for white matter.

b. Blood longitudinal relaxation time T_{1b} effect on the q-factor and $\Delta M/M_{0b}$

Fig. 3 shows the simulation results of the q-factor (3a) and $\Delta M/M_{0b}$ (3b) depended on the T_1 of blood for three different magnetic strengths for the gray matter in the brain. All three q-factor lines evidenced a similar pattern of monotonic decrease with increasing TI values. The q-factor was largest with the largest T_{1b} for all TI ranges.

$\Delta M/M_{0b}$ shown in Fig. 3b increased progressively with increasing TI, reached a broad maximum at TI ~ 1.7 sec, and then declined with further increases in TI.

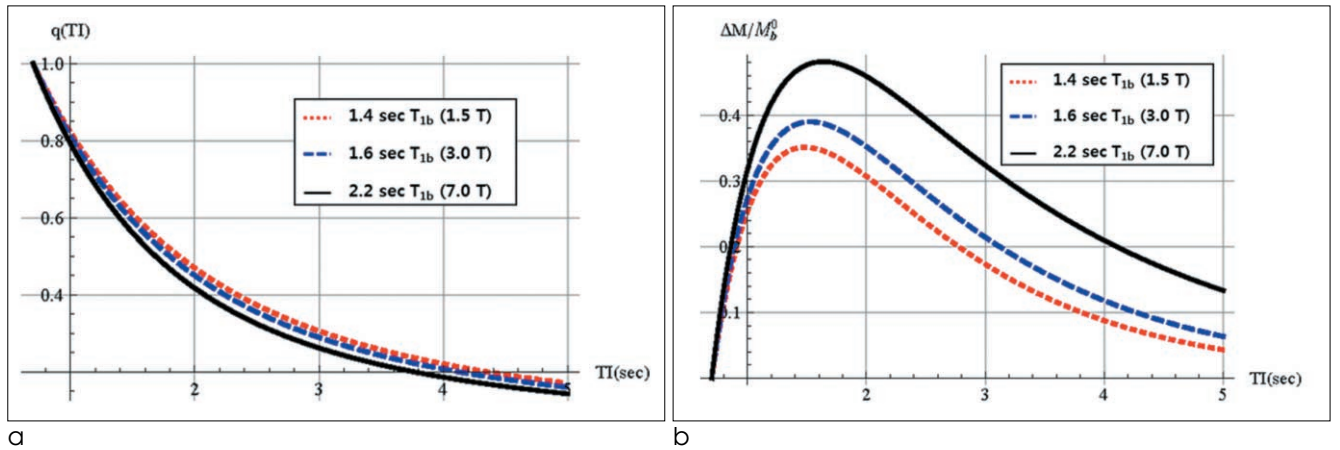


Fig. 3. Simulation results of the q-factor (3a) and perfusion signals (3b) depended on the longitudinal relaxation time of blood (T_{1b}) T_{1b} at 1.5T (Dotted line), at 3T (Dashed line), and at 7T (Solid line) Other parameters were used for $\lambda_{gm} = 1.05$ ml/g, $\delta t = 0.7$ sec, and $\alpha = 1$ at 3T. T_{1b} values were 1.4 sec, 1.6 sec, and 2.2 sec, for 1.5T, 3.0T, and 7.0T respectively.

Perfusion signals were increased with increasing T_{1b} , as anticipated. The maximum values of $\Delta M/M_{0b}$ were 0.351 at $TI = 1.48$ sec for $T_{1b} = 1.4$ sec (1.5T), 0.390 at $TI = 1.53$ sec for $T_{1b} = 1.6$ sec (3T), and 0.481 at $TI = 1.64$ sec for $T_{1b} = 2.2$ sec (7T).

c. Arterial transit delay δt effect on the q-factor and $\Delta M/M_{0b}$

Fig. 4 shows the simulation results of the q-factor (3a) and $\Delta M/M_{0b}$ (3b) depended on δt for gray matter in the brain at 3T. All three q-factor lines evidenced a similar pattern of monotonic decrease with increasing TI value. The q-factor was largest with the largest δt for all TI ranges.

$\Delta M/M_{0b}$ shown in Fig. 4b increased progressively with increasing TI, reached a broad maximum at $TI \sim 1.7$ sec, and declined with further increasing TI. Perfusion signals were reduced with increasing δt . The maximum values of $\Delta M/M_{0b}$ were 0.526 at $TI = 2.1$ sec for $\delta t = 0.5$ sec, 0.464 at $TI = 2.3$ sec for $\delta t = 0.7$ sec, 0.410 at $TI = 2.5$ sec for $\delta t = 0.9$ sec.

d. Strength of magnetic field M_{0b} effect on ΔM

Fig. 5 shows the simulation results of ΔM depending on M_{0b} for 1.5, 3.0, and 7.0T for the gray matter in the brain. ΔM increased progressively with increasing TI, reached a broad maximum at $TI \sim 1.7$ sec, and declined with further increasing TI values. Perfusion signals were increased with increasing B_0 , as anticipated. The maximum values of ΔM were 0.593 at $TI = 1.48$ sec for 1.5T, 1.154 at $TI = 1.52$ sec for 3T, and 2.557 T at $TI = 1.60$ sec for 7T.

T, and 2.557 T at $TI = 1.60$ sec for 7T.

Discussion

For improved CBF quantification using ASL MRI, several parameters must be optimized to reduce systematic errors. In this paper, we attempted to optimize four parameters: the tissue-to-blood coefficient (λ), the longitudinal relaxation time of blood (T_{1b}), the arterial transit time (δt), and the of magnetic field strength (M_{0b}) by simulating the q-factor and the perfusion signals of PASL MRI to determine the optimum labeling time (TI). Based on the simulation

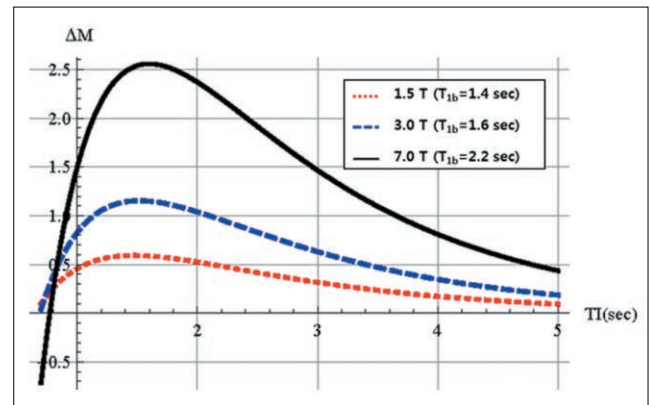


Fig. 5. Simulation results of perfusion signals (5) depended on the strength of the magnetic field (M_{0b}). 1.5T (Solid line), 3T (Dotted line), and 7T (Dashed line) Other parameters were used for $\lambda_{gm} = 1.05$ ml/g, $\delta t = 0.7$ sec, and $\alpha = 1$. T_{1b} values were 1.4 sec, 1.6 sec, and 2.2 sec, for 1.5T, 3.0T, and 7.0T, respectively.

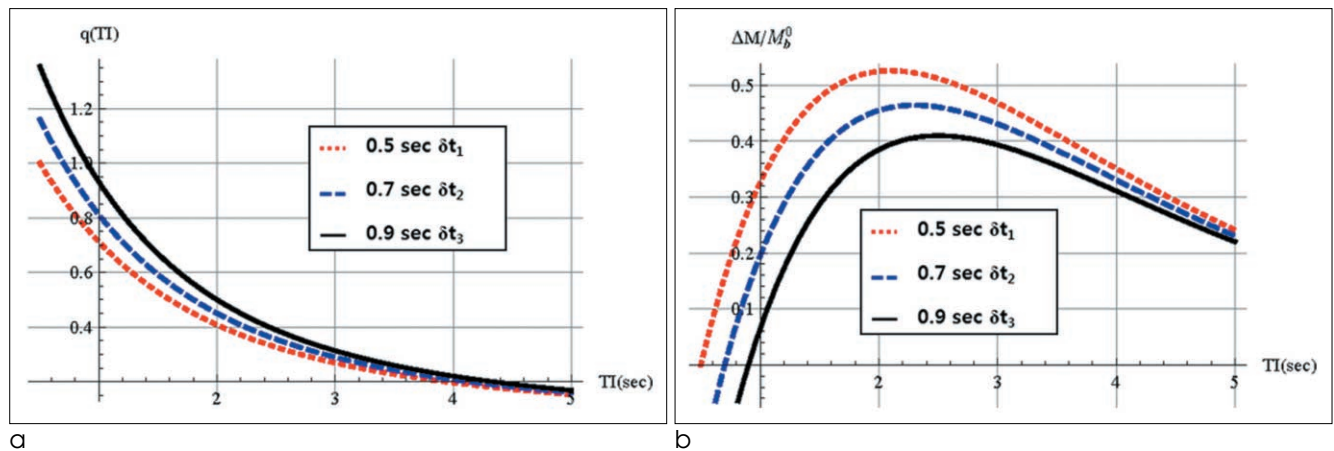


Fig. 4. Simulation results of the q-factor (4a) and perfusion signals (4b) depended on the arterial transit delay (δt). δt at 0.5 sec (Solid line, Black), at 0.7 sec (Dotted line, Red), and at 0.9 sec (Dashed line, Blue) Other parameters were used for $\lambda_{gm} = 1.05$ ml/g, $T_{1b} = 1.6$ sec, and $\alpha = 1$ at 3T.

results, we can optimize the TI values with the highest perfusion signals (23, 25).

a. Tissue-to-blood partition coefficient λ effect on the q-factor and $\Delta M/M_{0b}$

The first simulation was the estimation of the q-factor and $\Delta M/M_{0b}$ against TI depending on λ . Variations in λ occur in accordance with the water contents in brain tissues, including the white matter and gray matter. The q-factor was not dependent on the state of the brain tissues. However, the perfusion signals, $\Delta M/M_{0b}$, depended on brain tissues. Perfusion signals were at a maximum at TI = 1.53 sec for the gray matter. Perfusion signals in the gray matter were 1.14 times greater than that in white matter, due primarily to λ . The error for white matter may be greater than that for gray matter (26).

b. Blood longitudinal relaxation time T_{1b} effect on q-factor and $\Delta M/M_{0b}$

The second simulation was the estimation of the q-factor and $\Delta M/M_{0b}$ against TI depending on T_{1b} . The q-factor did not depend greatly on T_{1b} . However, perfusion signals, $\Delta M/M_{0b}$, were dependent on T_{1b} . Perfusion signals were at a maximum at TI = 1.64 sec for $T_{1b} = 2.2$ sec. The early part of the signal curve was weakly sensitive to T_{1b} . T_{1b} increases as hematocrit increases (27–29). Perfusion signals in the $T_{1b} = 2.2$ sec (7T) were 1.37 times greater than in $T_{1b} = 1.4$ sec (1.5T). Perfusion signals at 7T are increased by the increase in T_{1b} . However, a loss in perfusion signals can occur as the result of a reduction in T2 and tagging efficiency loss.

c. Arterial transit delay δt effect on the q-factor and $\Delta M/M_{0b}$

The third simulation was the estimation of the q-factor and $\Delta M/M_{0b}$ against TI depending on δt . The q-factor values were reduced with increasing TI for any δt . Because the signals rose rapidly after the delay, measurements at only one delay could potentially be strongly sensitive to variations in δt across the imaged plane. As a result, at any single time delay, the perfusion signal could evidence large errors. The quantification of CBF can be depended greatly upon the value of the transit delay.

d. Strength of magnetic field M_{0b} effect on q-factor and ΔM

The last simulation was the estimation of ΔM against TI for three magnetic field strengths. The three q-factor curves had identical values because relaxed magnetization cannot affect the q-factor. The signal increase at higher field strengths was due primarily to the elongated T1. The maximum perfusion signal increased by approximately 51% at 3.0T compared to 1.5T. The perfusion signal at 7.0T would be approximately 431% greater than that seen at 1.5T. The signal is dependent on magnetic field strength and is greater at higher field strengths, due to the longer T1. In the case of ΔM for magnetic field strength as shown in the above result, it is possible to obtain high perfusion signals at high field strengths as the impact on TI. Additionally, however, because the amount of spin polarization increases with increases in M_{0b} . Therefore, when multiplied by ΔM and M_{0b} , the overall impact is significantly greater. Additionally, pseudo-continuous ASL (pCASL) and velocity-selective ASL (VSASL) are other types of PASL. We can also optimize those methods based on the simulation in this work

Conclusion

In this paper, we reported the optimized TI values for several conditions to obtain the highest perfusion signal for PASL MRI. Both the q-factor and perfusion signals depended strongly on the longitudinal relaxation time of blood and the arterial transit delay. The tissue-to-blood coefficient affected the perfusion signals, but not the q-factor. Based on our results, it is important to select the optimized TI value by estimating the values of the longitudinal relaxation time of blood and the arterial transit delay.

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동맥 스핀 라벨링 자기공명영상의 펄스 관류 신호의 시뮬레이션

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목적: PASL (Pulsed ASL) 자화 신호에 영향을 주는 주요 4개의 인자들에 대한 평가를 컴퓨터 시뮬레이션으로 알아보고 높은 PASL 자화 신호를 얻기 위하여, 최적화된 인자들의 값을 알아본다.

대상 및 방법: PASL 자화 신호를 평가하기 위해서 Bloch 방정식을 바탕으로 PASL 자화 신호에 영향을 주는 주요 4개의 요소; tissue-to-blood coefficient (λ), blood longitudinal relaxation time (T_{1b}), arterial transit delay (δt), strength of magnetic field(M_{0b}) 에 대해서 Wolfram 사의 Mathematica 7.0을 이용하여 비교·분석하였다.

결과: 첫 번째, λ 의 경우, 3T에서 gray matter가 inversion 시간이 1.53초일 때, 값이 0.390로 가장 컸다. 두 번째로 δt 시간의 경우, 3T에서 inversion 시간이 2.1초에서 0.526로 가장 큰 값을 가졌다. 마지막으로 M_{0b} 는 3T에서 inversion 시간이 1.52 초에서 1.15 로 가장 큰 값을 보였다.

결론: 시뮬레이션을 통하여 최적화된 inversion 시간으로 높은 PASL 신호를 가진 관류 영상을 얻을 수 있다.

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