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Parameter Estimation in Arterial Spin Labeling MRI: Comparing the Four Phase Model and the Buxton Model with Fourier Transform

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Abstract—**This paper presents a comparison between two algorithms that analyze and extract brain perfusion parameters from pulsed arterial spin labeling (ASL). One algorithm is based on the Four Phase Single Capillary Stepwise (FPSCS) model, which divides the time course of the signal difference between the control and labeled image into four phases. The other algorithm utilizes the Buxton model and Fourier transformation (FTB). Both algorithms are implemented on MATLAB to extract the bolus arrival time (BAT) and the cerebral blood flow (CBF). Current results show that the FTB algorithm has similar estimations of the BAT and CBF compared to the FPSCS model with generally faster processing speeds.**

Keywords—**Magnetic Resonance Imaging, Arterial Spin Labeling, bolus arrival time, cerebral blood flow**

I. INTRODUCTION

Magnetic Resonance Imaging (MRI) is one of the leading modalities in clinical human brain imaging. In addition to being invasive, the methods to enhance a healthy human brain image using MRI and contrast agents are prevented by the blood brain barrier. Arterial Spin Labeling (ASL) is a non invasive method that uses blood water that is tagged with radio frequency (RF) pulses to pass through the blood brain barrier and can be used to study perfusion parameters in the human brain. ASL is currently being researched and improved upon with hopes of fully integrating this new method into clinical applications.

The perfusion data from ASL MRI gives a measure of the effectiveness of the blood circulation to provide oxygen and nutrients to the tissue and the ability to remove waste products. Three important factors in perfusion measurements are cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT) [1], and bolus arrival time (BAT). Measurement of perfusion is useful for studying pathological conditions (such as Alzheimer's, tumors, and sickle cell disease).

Many algorithms have been published for extracting these parameters for MRI uses. This study will focus on two algorithms. The first algorithm is the Four Phase Single Capillary Stepwise (FPSCS) model [2]. This model divides the time duration of the tagged blood in the region of interest (ROI) and takes into account the arrival time of labeled blood water at the region of interest, transit time through the arteries of the region, and the duration of the bolus of labeled spins. This algorithm provided improvements in temporal dependency and computation efficiency. The FPSCS model is the current algorithm being implemented in many ASL studies.

The second algorithm estimates brain perfusion parameters by utilizing Fourier Transform [4]. This algorithm uses the previous Buxton model [3] and applies a Fourier transform to extract the BAT and CBF. The Fourier Transform of the time series was compared with a non-linear least square fitting algorithm and it provided accurate information on the BAT and CBF for both, macro and micro vascular signal curves.

Both algorithms showed promising results, but they were not compared together using the same brain image. The purpose of this research is to compare the FPSCS model and the FTB model with the same brain image and determine if the FTB model has similar accuracy and efficiency.

II. THEORY

This section describes the two algorithms that will be examined in this research.

FPSCS Model

The Pulsed ASL (PASL) signal is analyzed by taking the difference between the untagged (control) and tagged images.

$$\Delta M(t) = M^{ctrl}(t) - M^{tag}(t, f, PS) \tag{1}$$

where t = time, f = blood flow, and PS = capillary permeability

The time duration of the PASL signal is divided into four phases with respect to the arrival time of labeled blood water at the region of interest (t_a or BAT), transit time through the arteries of the region (t_{ex}), and the duration of the bolus of labeled spins (τ) [2].

Phase 1: Transit Phase

$$\Delta M(t) = 0 \tag{2}$$

The tagged blood has not reached the arteries yet in this phase. Since the tagged blood is not present in the ROI, the signal difference is zero.

Phase 2: Arterial Phase ($t_A < t \leq T_{ex}$ where $T_{ex} = t_A + t_{ex}$)

$$\Delta M(t) = 2\alpha M_0 f e^{-R_{1b}t} \min(t - t_A, \tau) \quad (3)$$

where M_0 = equilibrium magnetization, α = labeling efficiency, f = CBF, and R_{1b} = longitudinal relaxation rate of water in blood.

In this phase, the tagged blood is in the arteries. The min function returns the smaller of the two arguments.

Phase 3: Arterial-Capillary Transitional Phase ($T_{ex} < t \leq T_{ex} + \tau$)

$$\Delta M_a(t) = 2\alpha M_{0a} f e^{-R_{1b}t} \min(T_{ex} + \tau - t, t_{ex}) \quad (4)$$

$$\Delta M_c(t) = 2\alpha M_{0a} f e^{-R_{1b}t} \int_{t_{cl}}^{t} e^{-PS_v(t'-T_{ex})} dt' \quad (5)$$

$$\Delta M_e(t) = 2\alpha M_{0a} PS_v f \bullet \int_{t_{cl}}^{t} \int_{Tex}^{t'} e^{-PS_v(t_c - T_{ex}) - R_{1b}(t_c + t - t') - R_{1e}(t' - t_c)} dt_c dt' \quad (6)$$

where $PS_V = PS/v_{cw}$, $t_{cl} = \max(T_{ex}, t - \tau) = T_{ex}$, R_{1e} is the longitudinal relaxation rate of water in in the extravascular space, and V_{cw} is the capillary blood water volume per unit volume of tissue. The min function returns the smaller of the two arguments.

$$\Delta M(t) = \Delta M_a(t) + \Delta M_c(t) + \Delta M_e(t) \quad (7)$$

This phase takes into account that only part of the tagged blood has reached the capillary bed, which is why there is still contribution in the arterial space ($\Delta M_a(t)$). The amount of labeled water in the capillary bed includes contributions from both the intracapillary ($\Delta M_c(t)$) and the extracapillary space ($\Delta M_e(t)$).

Phase 4: Capillary Phase ($t > T_{ex} + \tau$)

$$\Delta M(t) = \Delta M_c(t) + \Delta M_e(t) \quad (8)$$

All of the labeled blood has entered the capillary bed; therefore, equations (5) and (6) describe $\Delta M_c(t)$ and $\Delta M_e(t)$ respectively, and $t_{cl} = \max(T_{ex}, t - \tau) = t - \tau$.

FTB Model

The signal difference between the control and tagged image is modeled as follows [4]:

$$\Delta M(t) = Heaviside(t - t_A) \bullet 2 \bullet \frac{M_0 \bullet f \bullet e^{-t \bullet R_{1b}}}{(R_{1b} - R_{1e})} \bullet \left(e^{-(t - t_A) \bullet (R_{1e} - R_{1b})} - 1\right) \quad (9)$$

This model is based on the previous Buxton model [3]. A Fourier transform is applied to equation 9:

$$\Delta \hat{M}(\omega) = 4 \bullet M_0 \bullet f \bullet \frac{R_{1b} \bullet R_{1e} - \omega^2}{\left(R_{1e}^2 + \omega^2\right) \bullet \left(R_{1b}^2 + \omega^2\right)} \bullet e^{-t_A \bullet R_{1b}} \bullet e^{-I * t_A \bullet \omega} \quad (10)$$

By setting the frequency to zero ($\omega = 0$)

$$\Delta \hat{M}(0) = 4 \bullet \frac{M_0 \bullet f}{R_{1e} \bullet R_{1b}} \bullet e^{-t_A \bullet R_{1b}} \quad (11)$$

The only two unknown values are CBF and BAT since values M_0, R_{1app}, and R_{1b} are already given parameters. By analyzing the phasor domain, the following equation is given:

$$\varphi\left(\Delta \hat{M}(\omega)\right) = t_A \bullet \omega \quad (12)$$

By taking the phase angle of the signal and dividing it by the frequency at that moment, the BAT can be determined.

III. METHODOLOGY

The two algorithms discussed were implemented in MATLAB. Two brain images will be analyzed and processed for each algorithm. One brain image has 6 time samples and the other brain image contained 13 time samples. Two types of analysis were conducted. The first analysis was to analyze the brain image pixel by pixel in a ROI and determine the BAT and CBF for that individual pixel. The second analysis takes the average of the ROI and generates one pixel for each time sample, and the average signal intensity curve is analyzed.

Brain Images

Volunteers were scanned at a 4T MR unit (Bruker Medical Systems, Best, Erlangen) using an 8-channel head array coil. Interleaved tagged and control images were acquired using a fast 3D-GRASE sequence. Three-dimensional images were collected at 13 different TI times (from 70 to 2600 ms) with TR=3000 ms and echo time of 23.28 ms. The k-space data matrix was 128 x 34, with a field of view of 300 x 150 mm (in plane resolution, 2.34 x 8.82 mm), and slab thickness of

100 mm (slice thickness 4.7 mm). Twenty two axial slices were acquired to covers the entire hemispheric areas of brain. These images only provided the control and labeled images. These images were subtracted in order to get the difference in signal intensity.

Model 1: The FPSCS Model

This MATLAB program has been previously implemented and tested. This program requires the following parameters to be inputted into the program for processing: the dimensions of the brain image (length, width, slice, and time), time samples (in seconds), the brain image, and a mask to show the ROI and cover the rest of the image. The program will calculate and extract certain parameters such as signal intensity for each pixel at different time samples, estimated arrival time, estimated bolus duration, etc. These values are then inputted into text files for further processing by an outside source code. The source code then outputted certain parameters: theoretical signal intensity curve, actual signal intensity curve, and BAT.

Model 2: The FTB Model

A MATLAB code for the FTB model was created for this research by using the theory as the foundation. In order to improve accuracy in the results, the original time samples were interpolated into 64 time samples. With the brain image, time parameters, and ROI implemented into the program, a Fast Fourier Transform was performed on each pixel. The phase value is examined in radians with respect to the frequency. To avoid phase wrapping, 2π is added to the angles of negative value. The BAT is then determined at each frequency by taking the phase angle and dividing it with the frequency value at that moment. The BAT around the area of the highest time is taken to determine the average BAT of the pixel. The CBF is then calculated based on the BAT.

Simulating Average BAT

A new image with the dimensions of the original brain image is created with the average signal intensity in a ROI and processed in the same manner of a pixel analysis. This new image was generated by creating an array of zeros with the brain image dimensions. The average signal intensity at different time samples is determined from the specified ROI. These values are then integrated into the zero array to generate an image with every pixel equal to the intensity value at the respective time sample. This image is then inputted into the MATLAB programs and processed in the same manner as the original brain image.

Comparison between FPSCS and FTB Model

With the BAT and CBF values for both pixel and average ROI analysis, the values for each algorithm were compared to determine the similarities. The time it takes to process the code on MATLAB was taken into account as well to determine if the FTS algorithm is faster than the FPSCS model.

IV. RESULTS

The following tests will display the concentration curve for each algorithm. The solid curve represents the actual concentration curve, and the solid vertical line represents the BAT for the FTB model. The dashed curve represents the theoretical concentration curve generated by the FPSCS model, and the dashed vertical line represents the BAT for the FPSCS model. The results for the BAT (seconds), CBF (ml blood/min/100 ml tissue), and program processing time (seconds) are displayed on a table.

Test 1

For this test, the initial brain image had 13 time samples.

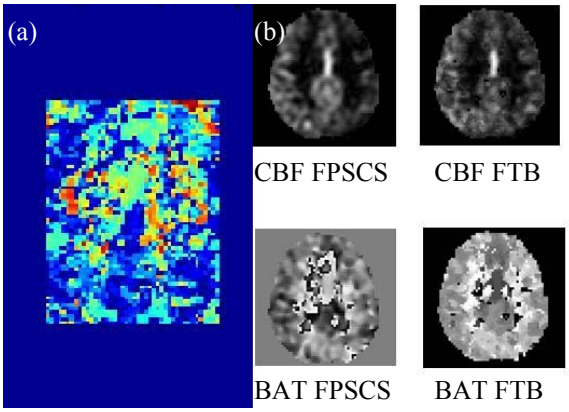

FIG. 1: (a): The mapping of the difference in BAT for each pixel between the FPSCS and FTB model in Test 1. (b): A visual comparison of the CBF and the BAT between the FPSCS and FTB model in Test 1.

Pixel Analysis

	BAT	CBF	Processing Time
FPSCS	0.4556	0.9487	87.2510
FTB	0.5878	1.0053	9.9840

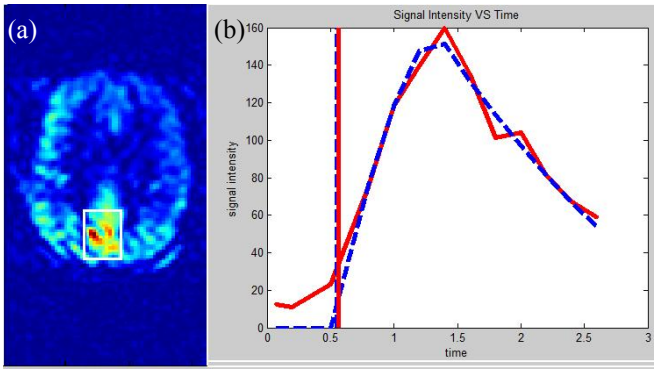

FIG. 2: (a): A map of the brain image in Test 1 with the ROI marked with white borders. (b): A curve analysis of the average ROI in Test 1.

Average ROI Analysis

	BAT	CBF	Processing Time
FPSCS	0.5482	0.5335	8.4550
FTB	0.5634	0.5354	9.9060

Test 2

For this test, the initial brain image had 6 time samples.

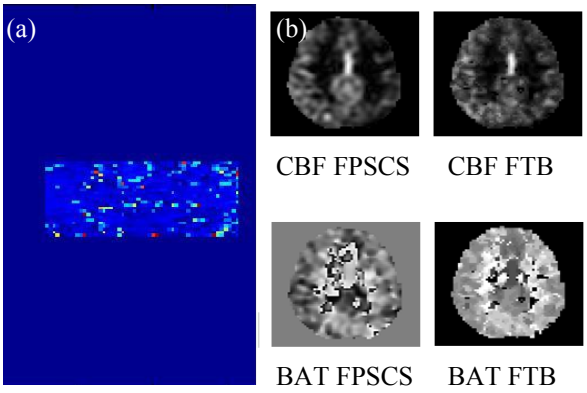

FIG. 3: (a): The mapping of the difference in BAT for each pixel between the FPSCS and FTB model in Test 2. (b): A visual comparison of the CBF and the BAT between the FPSCS and FTB model in Test 2.

Pixel Analysis

	BAT	CBF	Processing Time
FPSCS	0.36	0.0255	19.5780
FTB	0.4963	0.0241	10.5300

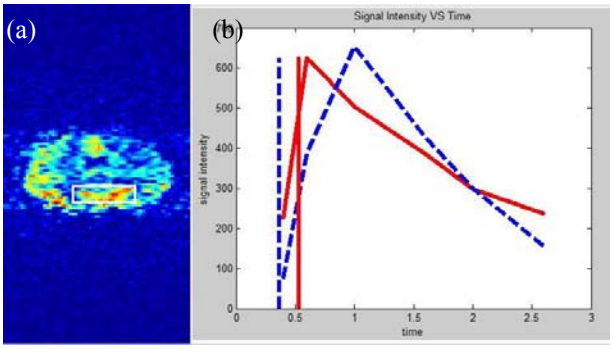

FIG. 4: (a): A map of the brain image in Test 2 with the ROI marked with white borders. (b): A curve analysis of the average ROI in Test 2.

Average ROI Analysis

	BAT	CBF	Processing Time
FPSCS	0.36	2.4763	1.7010
FTB	0.5319	2.4879	10.5300

V. DISCUSSION

The results in Test 1 show small differences for BAT and CBF. The BAT difference map shows many bright pixels. This could be due to the fact that some areas do not receive the tagged blood. The average ROI does not show as much difference in BAT or CBF. The difference in processing time is significantly different in pixel analysis compared to average ROI analysis, where the FTB algorithm is much faster. The results in Test 2 also show less difference in both pixel and average ROI analysis. This could possibly be due to the limited data points from the original brain image. The signal curve starts out rising in Test 2, which makes the BAT and CBF easier to calculate. It can be debated that finding the actual BAT in pulsed ASL is difficult to determine since the bolus duration only lasts for a few seconds. The general processing time does not show significant differences between the two algorithms in Test 2.

VI. CONCLUSION

In conclusion, the comparison between the FPSCS model and the FTB model does not show significant difference in calculating BAT or CBF for each pixel and average ROI. The processing speed of the two algorithms on MATLAB shows that the FTB model is generally faster. Future ASL analysis can utilize the FTB model to get similar results.

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REFERENCES

[1] C. Lanting. “Perfusion imaging using arterial spin labeling: a study of continuous and pulsed arterial spin labeling.” University of Groningen. 9th May 2005.

[2] K.L. Li, X. Zhu, N. Hylton, G.H. Jahng, M.W. Weiner, and N. Schuf “Four-Phase Single-Capillary Stepwise Model for Kinetics in Arterial Spin Labeling MRI.” *Magnetic Resonance in Medicine*. Vol. 53, 2005, pp. 511–18.

[3] R. B. Buxton, L. R. F., E.C. Wong., B. Siewert, S. Warach, and E. R.R. "A General Kinetic Model for Quantitative Perfusion Imaging with Arterial Spin Labeling." *Magnetic Resonance in Medicine.* Vol. 40, 1998, pp. 383-96.

[4] M. Guenther. "Analytical Parameter Estimation in Arterial Spin Labeling Time Series by Fourier Transformation." *Proceedings of the International Society Magnetic Resonance Medicine.* Vol.13. 2005, p. 1136.