How to quantity ASL values in a perfusion phantom

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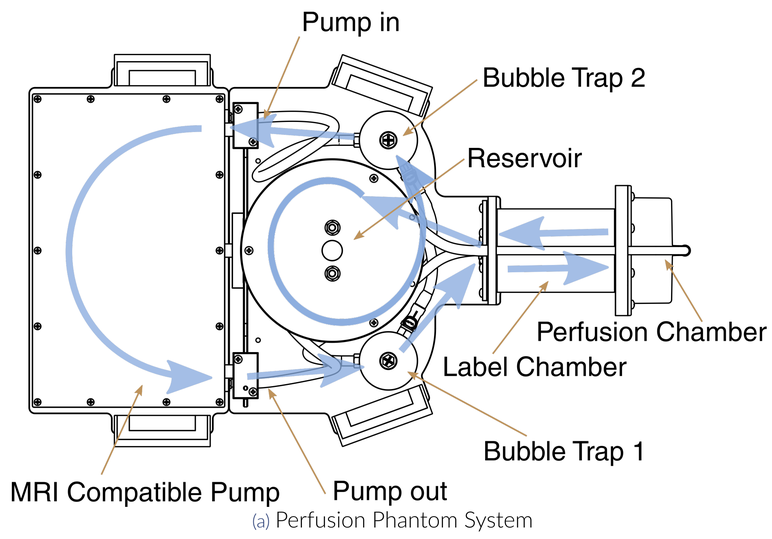
1. Introduction

Over the last four years, we have been developing an Arterial Spin Labelling (ASL) perfusion phantom aiming at providing reference values for quality assurance (QA) of ASL data in the clinics[1]. Preliminary data acquired during a round robin experiment[2] were quantified using the "White Paper" ASL equations[3], while realising that some of the assumptions behind these equations were not valid for the phantom. Here we show that the original equations from the General Kinetic Model (GKM)[4] can be used to quantify the ASL signal in the QASPER phantom[1].

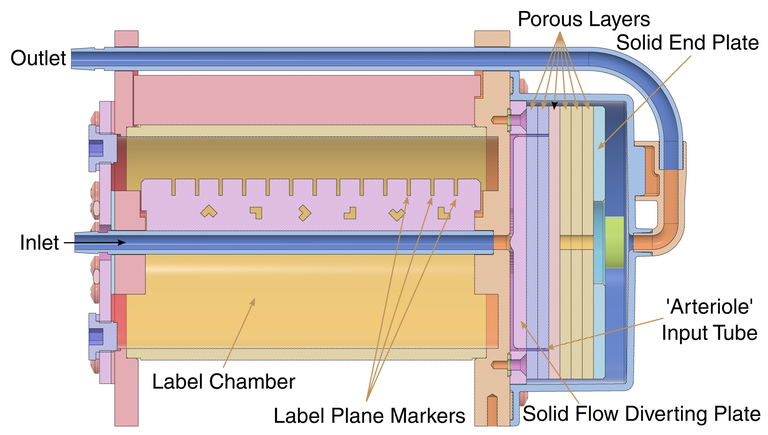
2. Perfusion Phantom

- MRI compatible pump delivers perfusate at a controlled, known flow rate to the perfusion chamber.
- Phantom has macroscopic coherent, and microscopic incoherent flow domains.
- Water based perfusate with additives for T_1 (Nickel Chloride, ~1900ms at 3T), improved wetting (surfactant), viscosity (water soluble polymer, ~1.65mPa.s @ 20°C), and preservative (isothiazolinone CMIT/MIT 1:3 ratio based).
- Porous substrate to simulate the capillary bed, mean pore size 7um, porosity 32%: six 4.75mm thick, 116mm diameter discs of sintered UHMW Polyethylene.
- Automatic flow control with integrated calibrated flow meter.
- Wireless communications for control and real-time telemetry of measured perfusate flow rate and temperature.

Figure 1. ASL Perfusion Phantom



(a) Perfusion Phantom System



(b) Cross section through the Perfusion Unit

3. Theory

The general hypotheses behind the GKM are that the signal can be described as:

$$\Delta M(t) = 2 \cdot M_{0b} \cdot f \cdot \{c(t) * [r(t) \cdot m(t)]\}$$

Where:

$*$ = convolution operator
$r(t)$ = residue function = $e^{-\frac{ft}{\lambda}}$
$m(t) = e^{-\frac{t}{T_1}}$
α = labelling efficiency
τ = label duration
Δt = initial transit delay

$c(t)$ = delivery function, defined as plug flow =
$$\begin{cases} 0 & 0 < t < \Delta t \\ \alpha e^{-\frac{t}{T_{1,b}}} \text{(PASL)} & \Delta t < t < \Delta t + \tau \\ \alpha e^{-\frac{\Delta t}{T_{1,b}}} \text{(CASL/pCASL)} & \\ 0 & t > \Delta t + \tau \end{cases}$$

- The GKM solution for pCASL/CASL is:

$$\Delta M(t) = \begin{cases} 0 & 0 < t < \Delta t \\ 2M_{0,b} f T_1' \alpha e^{-\frac{\Delta t}{T_{1,b}}} q_c(t) & \Delta t < t < \Delta t + \tau \\ 2M_{0,b} f T_1' \alpha e^{-\frac{\Delta t}{T_{1,b}}} e^{-\frac{t-\tau-\Delta t}{T_1'}} q_c(t) & t > \Delta t + \tau \end{cases} \text{ Where } q_c(t) = \begin{cases} 1 - e^{-\frac{t-\Delta t}{T_1'}} & \Delta t < t < \Delta t + \tau \\ 1 - e^{-\frac{\tau}{T_1'}} & t > \Delta t + \tau \end{cases}$$

- $r(t)$ definition based that the outflow of any labelled magnetisation out of a voxel is mixed, which is the case here as no exchange is modelled.
- In human physiology, the outlfow of magnetisation is going through the venous system.
- In the QASPER phantom, the magnetisation is flowing to an adjacent voxel, as no direct venous system is modelled.
- However, the assumption stands, with $\lambda = 0.32$ (equivalent to the porosity of the porous plastic).

5. Results

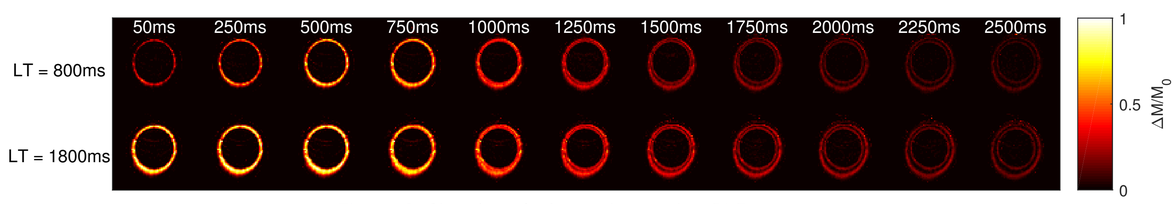


Figure 2. Signal evolution at increasing PLDs

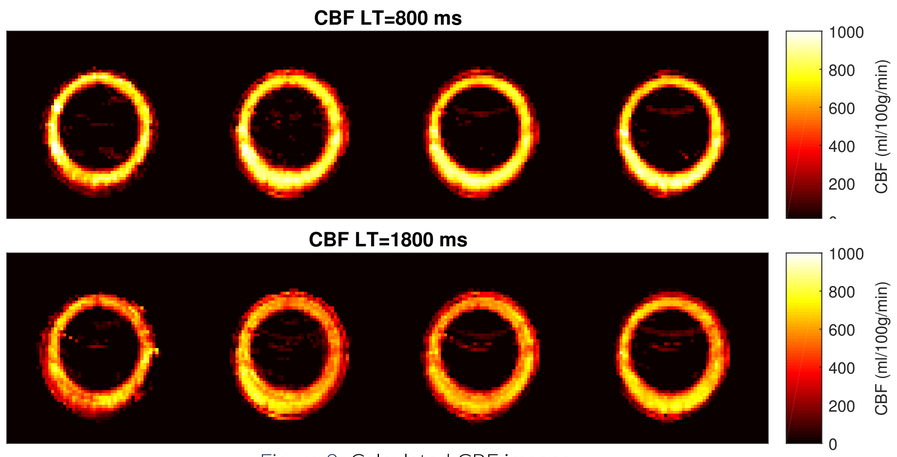


Figure 3. Calculated CBF images

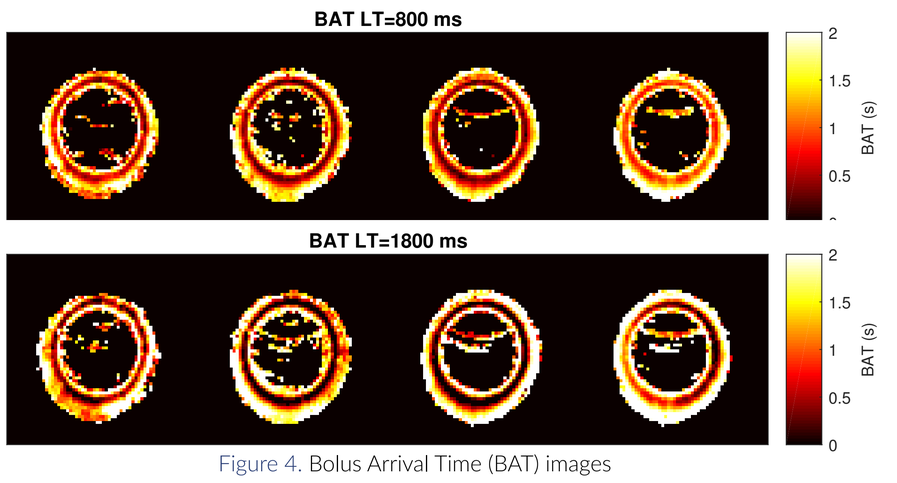


Figure 4. Bolus Arrival Time (BAT) images

The values associated with a set pump flow rate of 350ml/min are of the 500-600ml/min/100g on average for all voxels with LT = 800 and 1800ms respectively. Excluding the signals from the 'arteries' for the PLD = 800ms case leads to an equivalent perfusion distribution for both PLDs.

4. Image Acquisition and Analysis

- Data were acquired on the Philips 3T scanner (Achieva, R5.3). Two pCASL sequences with labelling time (LT) = 800/1800ms, and post-labelling delay (PLD) = 50, 250, 500, 750, 1000, 1250, 1500, 1750, 2000, 2250, 2500ms was designed.
- Other parameters were
  - Multi-slice EPI
  - Acquisition matrix = 64x64
  - FOV = 192mm
  - 20x 3mm slices
  - 4 averages per PLD.
  - Pump flow rate set to 350ml/min.
- Data were analysed using BASIL (www.fmrib.ox.ac.uk/fsl/BASIL), using a Variational Bayesian algorithm[5], with $T_1 = T_{1b} = 1900ms$ and a prior on bolus arrival time (BAT) of 1000ms (100ms variance).

6. Discussion

The general kinetics given by the perfusion phantom can be seen in Figure 5.

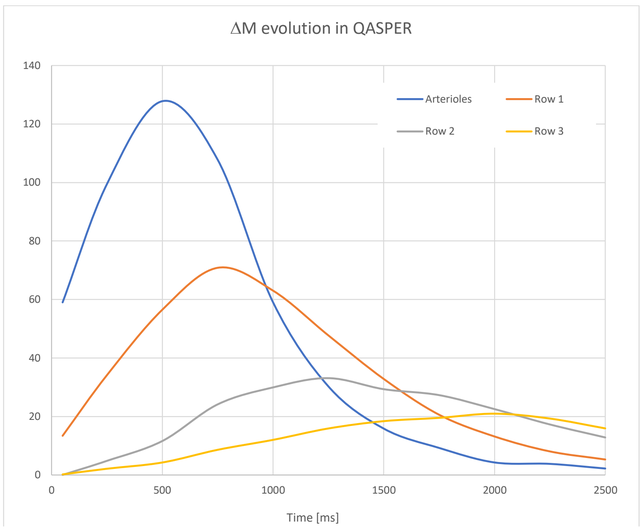


Figure 5. Signal time-curves for four ROIs from the centre of the 'arterioles' to the outer 'tissue' part.

- In this figure, four ROIs taken at different distances from the phantom's 'arterioles' show a behaviour in-line with that predicted by the GKM.
- While the direction that perfusate/blood generally flows is different in the phantom in comparison with in-vivo, the principles based on conservation of mass and diffusion tracer theory remain applicable.
- The General Kinetic Model is therefore usable without any adaptation.
- The solutions of the GKM are the same as the original ones, albeit with different numerical values.
- However: The larger flow values ($f_{phantom} \sim 10 \times f_{brain}$) and lower partition coefficient ($\lambda = 0.32$) means that the residue function will decay far faster than in humans, and therefore the assumptions at the basis of the reduced solution used in the White Paper[3] are **no longer valid**.

7. Conclusions

Here we have presented an analysis of multi-PLD pCASL data acquired at label durations of 800ms and 1800ms using the GKM. While the actual CBF values calculated differ to those found in the brain, the tracer kinetics match with normal neurovascular behaviour, and as such this treatment using the GKM is correct.

References

[1] Aaron Oliver-Taylor et al. "A Calibrated Perfusion Phantom for Quality Assurance of Quantitative Arterial Spin Labelling". In: *Proceedings of ISMRM 2017*. 0681. 2017.

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[4] Richard B. Buxton et al. "A general kinetic model for quantitative perfusion imaging with arterial spin labeling". In: *Magnetic Resonance in Medicine* 40.3 (Sept. 1998), pp. 383–396.

[5] M.A. Chappell et al. "Variational Bayesian Inference for a Nonlinear Forward Model". In: *IEEE Transactions on Signal Processing* 57.1 (Jan. 2009), pp. 223–236.

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