# Iterative three compartment model for Look-Locker cardiac ASL acquisition

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**INTRODUCTION:** Arterial spin labelling (ASL) is an emerging technique for the non-invasive measurement of perfusion in preclinical cardiac disease research [1-3]. Typically, myocardial perfusion is quantified by comparing $T_1$ measurements following slice-selective and global inversion [4]: $P = \frac{\lambda}{T_{1,blood}}\left(\frac{T_{1,global}}{T_{1,slice-selective}} - 1\right)$

This method is based on a theoretical two compartment model developed by Bauer et al [5] (with P = perfusion and λ=blood/tissue water partition coefficient). In the mouse heart, $T_1$ is measured using Look-Locker acquisitions, which are characterized by a train of RF pulses. In the brain, there have been efforts to incorporate the RF saturation from the Look-Locker acquisition into the ASL kinetic models [6,7].

In this study, we have taken the preliminary steps toward developing a 3-compartment iterative ASL model for the heart, based on Francis et al [6], which includes the effects of the Look-Locker acquisition.

**METHODS:** Theory: In the myocardium, each voxel is composed of capillary space and tissue. We neglect vessels larger than capillaries, as their contribution to the myocardium is <3% [5]. Our model iteratively assesses, in intervals the length of one cardiac cycle, the magnetization in each of three compartments (Fig 1).

**Compartment 1:** Arterial blood, unaffected by RF excitation pulses, which arrives at slice of interest: $M_{in}(T) = M_a(0)\cdot e^{(-T/T_{1b})} + M_{b,0}\cdot\left[1 - e^{(-T/T_{1b})}\right]$

For global inversion: $M_a(0) = -M_{b,0}$

For slice-selective inversion: $M_a(0) = -M_{b,0}$ if $T < t_a$ and $M_a(0) = +M_{b,0}$ if $T > t_a$

**Compartment 2:** Blood passing through the slice of interest before entering the capillary bed (eg. vessels, right ventricle and left ventricle blood pools) exposed to RF excitation pulses throughout the Look-Locker acquisition. Inflowing blood from Compartment 1 is affected by RF pulses as follows: $M_2 = M_1\cdot\cos(\alpha)^{\#RF\,pulses}$. Using a segmented Look-Locker acquisition with 4 k-space lines acquired per heart beat, total magnetization ($M_{out}$) of blood entering the capillary bed is then taken to be a weighted average of blood affected by combinations of 0 to 4 RF pulses per interval, having 0 to 3 intervals of recovery, depending on the assumed circulation time.

**Compartment 3:** Tissue in the myocardium in fast exchange with the capillary bed, experiencing Look-Locker RF excitation pulses. NB: it is this magnetization that we are interested in measuring.

$$\frac{dM_{tissue}(t)}{dt} = \frac{M_{tissue,0} - M_{tissue}(t)}{T_{1,tissue}} + \frac{f\cdot M_{out}(t)}{\lambda} - f\cdot M_{tissue}(t)$$

Parameters: t = interval length (1 cardiac cycle), T = total time since inversion, $M_a(0)$= initial magnetization of arterial blood, $M_{b,0}$= equilibrium magnetization of blood, $t_a$ = arrival time of fresh blood into imaging slice after slice-selective inversion, α = flip angle, $M_{tissue,0}$ = equilibrium magnetization of tissue, f = perfusion rate, λ= blood/tissue partition coefficient.

Proof of Concept: Single slice ASL data sets were acquired in the same mouse with 3 different isoflurane levels (1.25%, 1.5% and 2.25% in 1L/min $O_2$) to vary the perfusion rate [9]. Data were acquired on an Agilent 9.4T Scanner (Agilent Technologies, Santa Clara, USA) using a 35mm volume resonator coil (RAPID Biomed, Rimpar, Germany) with small animal physiological monitoring (SA Instruments Inc, Stony Brook NY). $T_1$ was measured with a segmented ECG-gated Look-Locker sequence with 4 lines of k-space acquired each heart beat (TE/TR(inv)/TR(RF)=1.18ms/13.5s/2ms, flip=5°, in-plane resolution=200μm, slice thickness=1.5mm, matrix = $128^2$, Slice selective inversion thickness= 4.5mm, global inversion thickness = 150mm) [10]. $M_{tissue}(t)$ was fit to slice selective and global inversion recovery curves from average signal intensity in an ROI in the myocardium, with data around null with SNR<Rician noise threshold excluded. Perfusion and arrival time were fit from the model; $T_{1,tissue}$, $T_{1b}$, $M_{0,blood}$, $M_{0,tissue}$ were calculated from Look-Locker curves; flip angle and iterative interval were fixed.

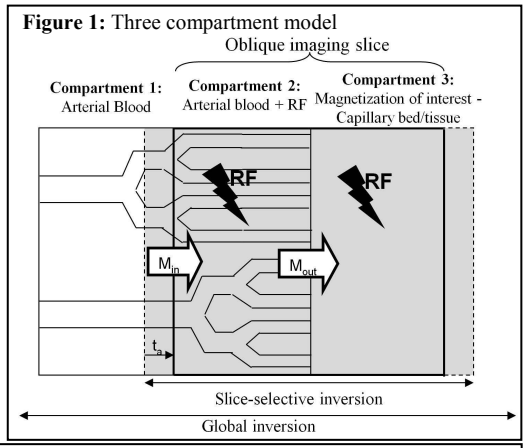


**Figure 1:** Three compartment model

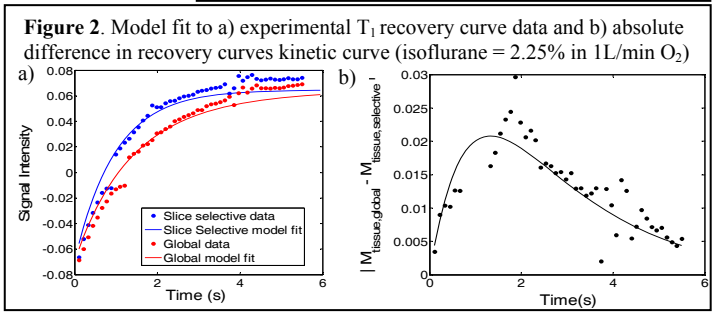


**Figure 2**. Model fit to a) experimental $T_1$ recovery curve data and b) absolute difference in recovery curves kinetic curve (isoflurane = 2.25% in 1L/min $O_2$)

**RESULTS:** Figure 2 demonstrates an example of the model fit to experimental data both for inversion recovery curves and kinetic curve. The perfusion values generated by the model were 6.3ml/g/min, 12.4ml/g/min, 17.3ml/g/min for isoflurane = 1.25%, 1.5% and 2.25%, which matches the expected range [9]. These values also reasonably agree with those generated by the standard model as given by: $P_{3comp} = 1.3P_{standard} - 2.5$ml/g/min.

**DISCUSSION:** In this abstract, the preliminary development of a new kinetic ASL model has been presented. We observe good fits and reasonable perfusion estimations. The model fit diverges from the experimental data at the end of the inversion recovery curve indicating that the model is predicting additional RF saturation. In order to correct this, more accurate estimation of the number of RF pulses experience by blood and circulation time in Compartment 2 is required.

For the single slice case, it is expected that this model would compare well with the standard model. For multi-slice data acquisition [10], slice-selective inversion slab thickness is increased, affecting the apparent $T_1$ and arrival times between slices; also additional RF pulses are added, meaning additional blood in the heart and surrounding vessels is saturated. Accurately modelling the multi-slice case will require the detailed model developed here, with further development.

In conclusion, we have shown a new, comprehensive kinetic model of Look-Locker ASL acquisition for the mouse heart. With further work, we believe that this model will provide additional insight into cardiac ASL data.

**REFERENCES:** [1] Kober et al, MRM **51**:62-67(2004) [2]Streif et al, MRM **53**:584-592(2005) [3] Vandsburger et al, MRM**63**:648-657(2010) [4] Belle et al, JMRI **8**:1240-1245 [5] Bauer et al, MRM **32**:43-55(1996) [6] Francis et al, MRM **59**:316-325 (2008) [7] Gunther et al, MRM **46**:974-984 (2001) [8] Campbell et al, ISMRM 19(2011): 4463 [9] Kober et al, MRM **53**:601-606 (2003) [10] Campbell et al, ISMRM 19(2011):21