

# Model-Free Maximum Likelihood Deconvolution (MLD): A Novel Perfusion Analysis Method in MRI to Calculate Myocardial Blood Flow

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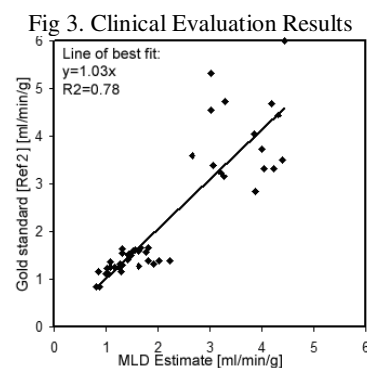
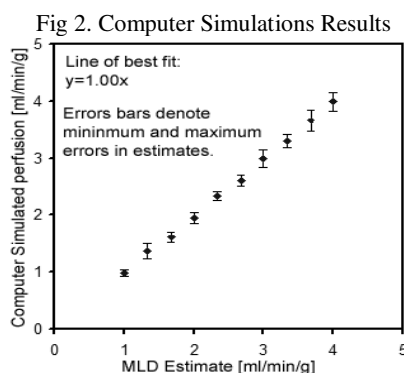
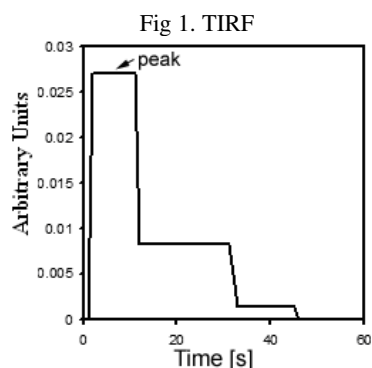
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**INTRODUCTION:** A promising technique for Cardiac perfusion analysis and ischemia detection is rapid MRI following a bolus injection of a contrast agent. This is followed by quantitative kinetic analysis of the contrast agent during first pass [1]. The perfusion analysis method proposed in this study is an implementation of the central volume principle to calculate myocardial blood flow using deconvolution to obtain a tissue impulse response function (TIRF). The maximum of the TIRF yields an estimate of the myocardial blood flow. Since deconvolution is numerically unstable and very susceptible to noise, current deconvolution techniques use constraints to improve numerical stability but this can compromise accuracy [2]. In this study we introduce a novel contrast enhanced perfusion analysis method – maximum likelihood deconvolution (MLD) – to estimate myocardial blood flow. MLD is designed to overcome difficulties that arise due to noise without compromising accuracy. MLD is evaluated using computer simulations and clinically in three volunteers.

**THEORY:** MLD estimates myocardial blood flow from a TIRF that is obtained by deconvolving the tissue curve (TIS) from the arterial curve (ART). The uniqueness of this method lies in that; (i) it explicitly considers the Rician noise distribution in MR data and (ii) the shape of the TIRF curve has only two constraints: a constraint based on physical considerations: TIRF must be  $\geq 0$  at its beginning and end; and a constraint based on physiologic considerations: TIRF has only a single local maximum.

**METHODS:** Computer simulations and a preliminary clinical evaluation were performed to test the ability of MLD to estimate perfusion. The simulations tested varying blood flows (1-4ml/min/g; perfusions observed clinically) with added noise (contrast:noise 20:1; typical clinical level). 100 noise realizations were produced for each flow rate. MLD estimated the TIRF for each noise realization and flow rate. The quality of the TIRF was evaluated as the standard error between the simulated TIS curve and the MLD reconstructed TIS. In the preliminary clinical evaluation, the deconvolution technique of [2] (gold standard), was compared to perfusion estimates from MLD using the following procedure. Three volunteers were injected with MRI contrast (Gd-DTPA, 0.04mmol/kg, 7ml/s power injected, 10ml saline flush), and T1-MRI (fast gradient echo sequence, 3 short-axis 8mm thick slices) acquired for 50 heartbeats to track contrast agent through first pass and recirculation. Scans were acquired at rest and, for two volunteers, scans were also acquired at adenosine-induced maximal vasodilation. Blood pool and tissue regions-of-interest were defined, from which ART and TIS curves were generated. For ART curves: a region was defined in the centre of the left ventricle. For TIS curves: Endo- and epicardial contours were traced manually, divided into 8 transmural equicircumferential sectors.

**RESULTS:** Figure 1 is graphical representation of the TIRF function. The results in figure 2 below demonstrate the correlation between simulated perfusion levels and MLD-calculated estimates. Figure 3 below demonstrates the general agreement between the gold standard and MLD.



**DISCUSSION:** The simulation test demonstrated that MLD is numerically stable and can accurately estimate perfusion at clinical contrast:noise levels for typical cardiac perfusion values. Theoretically, we expect MLD estimates of perfusion to be unbiased, and have minimum variance (achieving the Cramer-Rao bound). MLD estimates of perfusion when compared to estimates provided by an existing clinical perfusion package [2] correlate considerably well at lower blood flow rates (1-2ml/min/g). At increased flow rates there is variability. A reason for such variability is that existing deconvolution techniques either stabilize the deconvolved TIRF via smoothing penalty functions or constraining the TIRFs to smooth piece-wise functions (such as splines). MLD however, removes these constraints, and interestingly, MLD TIRFs appear step-like, which may indicate discrete capillary populations with differing transit times. MLD intrinsically models dispersion of the contrast agent between the arterial and tissue curves, which is not usually accounted for by standard deconvolution techniques. Future work could focus on validating MLD against microsphere measurements of perfusion in animal models of heart disease.

## REFERENCES:

1. NM Wilke, et al: **Magnetic resonance first-pass myocardial perfusion imaging: Clinical validation and future applications** *J Magn Reson Imaging* 1999, 10:676-685
2. Jerosch-Herold M et al: **Myocardial blood flow quantification with MRI by model-independent deconvolution.** *Med Phys* 2002, 29(5):886-897