Uptake and Retention Maps for Myocardial Perfusion Analysis: Application in Duchenne Muscular Dystrophy

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Introduction:

Myocardial perfusion studies using dynamic contrast-enhanced CMRI provide valuable, quantitative information regarding heart physiology in a variety of diseases. One potential application is the study of Duchenne muscular dystrophy (DMD), a progressive disease that commonly leads to heart failure [1]. A challenge in such applications is the difficulty in interpretation and communication of the quantitative perfusion parameters. The goal of this effort was to develop an intuitive, but physiologically meaningful method for quantifying myocardial perfusion by CMRI and to test the method on a dog model of DMD

Materials and Methods:

Our study involved 5 dogs with DMD aged 41 ± 38 months and 4 normal controls aged 19 ± 3 months. All were imaged with a protocol that included dynamic contrast enhanced CMRI on a 3T MRI system (Philips Achieva, Best, Netherlands). The dynamic perfusion sequence was a mid-ventricle, single-slice, single-shot saturation recovery TFE acquisition with TR/TE of 3.0/1.4 msec, 20 degree flip angle, 5 mm slice thickness and in-plane resolution of 1.99 mm x 1.96 mm. During the acquisition, 0.1 mmol/kg Gd-DTPA (Magnevist, Bayer Schering Health Care Limited, UK) was manually injected, followed by a saline flush.

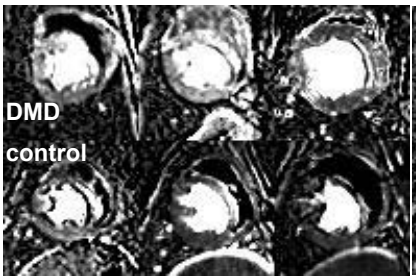

Figure 1. Uptake Maps

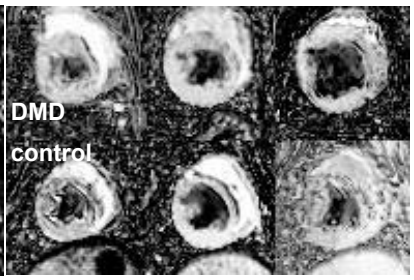

Figure 2. Retention Maps

Kinetic Analysis was performed using an automated program based on one previously proposed for vessel wall MRI [2] and applied to frames starting immediately before bolus arrival in the right ventricle and ending 30 seconds later. The program used an automatic registration algorithm to eliminate breathing motion within an 8.75cm x 8.75cm ROI centered on the left ventricle. Next, an automatic arterial input function (AIF) extraction algorithm was used to identify an enhancement versus time curve representing the blood within the left ventricle chamber. Finally, every pixel in the ROI was fitted using the discrete kinetic model [3] giving concentration in frame *n* as:

$$C_t[n] = UC_p[n] + RC_t[n-1]$$

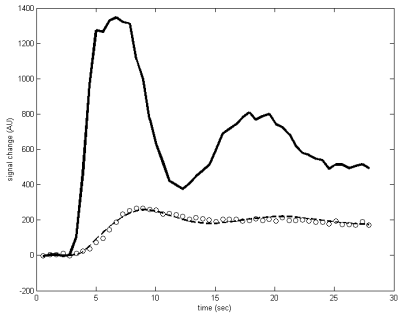

Figure 3. Model Fitting

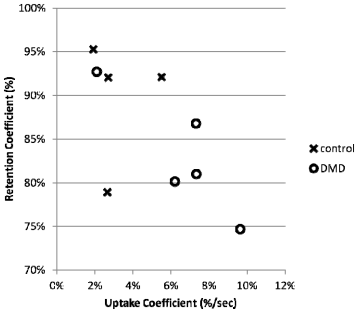

Figure 4. Average Parameters

where C_t and C_p are the concentrations in the tissue and blood, respectively, approximated as the change in intensity from the initial pre-contrast image. The model parameters *U* and *R*, are referred to as the "uptake" and "retention," respectively. For analysis and display, the parameters were normalized to a nominal 1 second time step between image frames.

Results:

The automated program successfully generated parametric maps of *U* and *R* in all cases, with examples from 3 dogs with DMD and 3 controls shown in figures 1 and 2. Overall, myocardial uptake appeared greater and retention appeared lower in dogs with DMD. Figure 3 shows the AIF (upper curve), tissue (circles), and model fit (dashed curve) for the average intensity change observed in the myocardium of one dog with DMD. Average values across all dogs showed a strong quantitative tendency for DMD dogs to exhibit higher average uptake and lower average retention (Figure 4).

Discussion and Conclusions:

This study illustrates the potential utility of an automated, discrete kinetic modeling approach for quantitative perfusion analysis by CMRI. Perfusion maps are presented in an intuitive representation of the rates of wash-in and wash-out. IN the model, $UC_p[n]$ is the total forward flux of contrast agent into the tissue over one time frame and $RC_t[n-1]$ is the amount of contrast agent still remaining in the tissue from the previous time frame (i.e. the amount not lost to efflux). Using this framework, the clinician can assess whether abnormal contrast enhancement is due to altered delivery of the agent, increased retention of the agent, or both. The application of this technique to a study of DMD in dogs demonstrated its ability to reliably and automatically extract quantitative representations of cardiac perfusion.

Regarding the discrete kinetic model implementation, insight can be gained by considering a hypothetical case in which the AIF rises to a concentration *C* for one time interval before returning to zero. In this case, the tissue concentration would rise to *UC* over the interval and then decay at a rate proportional to R^t. In actual situations, the contrast agent kinetics can be viewed as the superposition of such impulse responses due to the concentration in each interval. From this, we see that two aspects of contrast agent dynamics are neglected in the model. First, changes in the AIF over the interval are not modeled and second, the model does not account for any contrast agent that enters and leaves the tissue within the same interval. The impact of both of these assumptions is minimized by using short intervals, such as single heart beats. In this study, the interval was typically on the order of 0.5 sec.

References: 1. Finsterer *Cardiology* 2003; 99:1-19. 2. Kerwin *MRM* 2008; 55:659-68. 3. Kerwin *ISMRM* 2003; 704.