Examination of the Effects of Myocardial Hypertrophy On Myocardial Microvascular Volume and Blood Oxygenation

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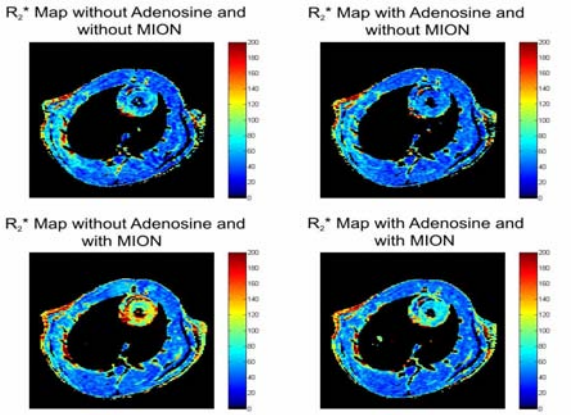
INTRODUCTION

The measurement of microvascular blood volume in the myocardium has potential for evaluating disorders of myocardial microvascular physiology. Newly proposed methods to measure myocardial oxygen extraction ratios using magnetic resonance imaging techniques assume no change in the microvascular blood volume after the administration of a vasoactive agent.[1,2] We have previously proposed a method of quantitatively measuring blood volume, drug-induced microvascular volume changes, as well as drug-induced changes in blood oxygenation. In this work, we have examined the effects of N omega-nitro-L-arginine methyl ester (L-NAME) induced myocardial hypertrophy on these parameters.

THEORY

We postulate that at high fields there is a contribution to transverse relaxation rates that reflects the presence of microvessels and depends on the oxygenation state of the blood. We therefore model the measured relaxation rate R_2^* as $R_2^* = R_2 + kV(\chi_b - \chi_t)$, where R_2 is the relaxation rate when the blood susceptibility matches that of tissue, and $kV(\chi_b - \chi_t)$ is the contribution from blood in the microcirculation (k is a proportionality constant that depends on field strength, V is the blood volume, and χ_b and χ_t are the susceptibilities of blood and tissue). χ_b depends on the blood oxygenation state. In the presence of an intravascular contrast agent such as iron oxide, the rate becomes $R^*_{2a} = R_2 + kV(\chi_b + \chi_a - \chi_t)$, where χ_a is the susceptibility of the agent. By measuring the R_2^* before and after administering the agent, and knowing the susceptibility of the agent, we can calculate kV. We thus obtain a map of relative blood volume in the tissue.



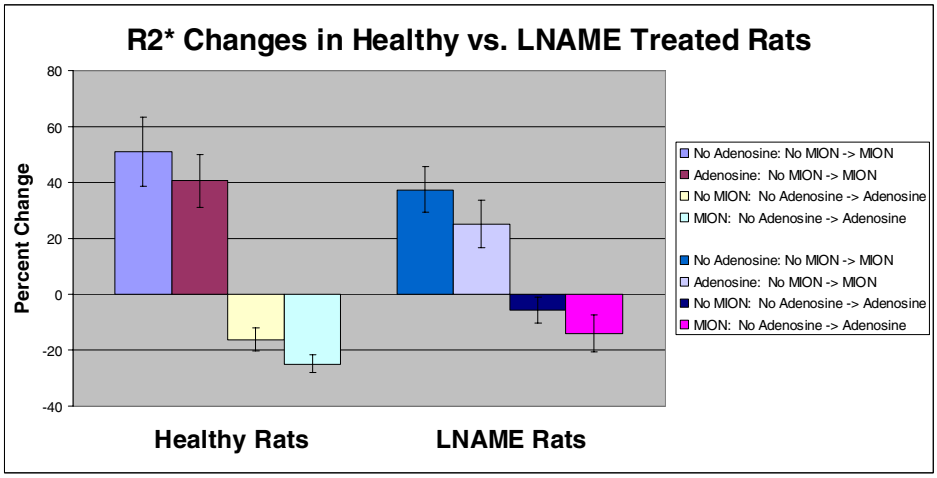
Administration of adenosine or dobutamine causes potential changes in both the blood volume and oxygenation. The relaxation rate may then be modeled as $R^*_{2aden} = R_2 + k(V+\Delta V)(\chi_{aden} - \chi_t)$, , where χ_{aden} is the blood susceptibility during the adenosine episode and is again a direct measure of the blood and tissue oxygenation change. For the same dose of adenosine in the presence of the intravascular monocrystalline iron oxide nanoparticle (MION) contrast agent, $R^*_{2(aden+a)} = R_2 + k(V + \Delta V)(\chi_a + \chi_{aden} - \chi_t)$, from which we can compute the relative volume change, $(\Delta V/ V)$. We thus obtain a map of the fractional change in blood volume due to the effect of adenosine or dobutamine, using the value of kV obtained above.

METHODS

Healthy rats were imaged using a 4.7T Varian imaging system. Scout images were obtained to find the optimal short axis view for imaging. Maps of R2* were obtained using a multi-echo, gradient-echo sequence with the following parameters: TR/TE= 300/(4.4*n, n=1-12), FOV=65mmX65mm, RO/PE=256/128. The images were acquired using cardiac triggering and respiratory gating, and the total imaging time for one $R2^*$ map was approximately six minutes. $R2^*$ maps were acquired with and without infusion of adenosine at a rate of 0.375 mg/kg·min, before and after an injection of MION (5 mg Fe/ kg rat). The same series of images were acquired in two rats that had been exposed to L-NAME (20 mg/rat per day) to induce myocardial hypertrophy.

RESULTS AND DISCUSSION

Myocardial maps of percent change in $R2^*$ due to adenosine were calculated in healthy rats, as well as rats with LNAME induced myocardial hypertrophy. The data in the figure below represent the $R2^*$ values measured in the healthy and diseased rat hearts. This data was used to calculate kV, as well as the percent change in the microvascular blood volume. The percent change in microvascular volume induced by adenosine was observed to decrease by 14% in the hypertrophied hearts when compared to healthy hearts. We propose that our methods have demonstrated that LNAME induced myocardial hypertrophy decreases the responsiveness of the myocardial vasculature to adenosine. In summary, we have developed a protocol based on gradient-echo relaxation theory that shows great potential for measuring microvascular blood volume changes, as well as blood and tissue oxygenation changes.



References

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2. Zheng J, Wang J, Nolte, M, Li D, Gropler RJ, Woodard PK. Mag Reson Med 2004;51:718-726.