Measurement of Skeletal Muscle Injury with Gadomer

A. Z. Faranesh[1,2], D. L. Kraitchman[3], E. R. McVeigh[2]

[1]Radiology, Stanford University, Stanford, California, United States, [2]Laboratory of Cardiac Energetics, NHLBI, National Institutes of Health, Bethesda, Maryland, United States, [3]Russel H. Morgan Department of Radiology and Radiological Sciences, The Johns Hopkins University, Baltimore, Maryland, United States

Introduction: Skeletal muscle infarction has been associated with pathologies such as diabetes and alcoholism, but in many cases is idiopathic (1, 2). In order to properly manage the condition, it is critical to be able to diagnose it early and differentiate it from tumor or infection. In this study, contrast enhanced MRI was used with a macromolecular contrast agent (Gadomer, Schering AG, Berlin, Germany) to characterize muscle necrosis in an animal model of skeletal muscle ischemia. Maximum contrast agent accumulation was measured in the tibialis anterior (TA) muscle at two different time points to evaluate functional changes in the tissue.

Methods: All animal procedures were conducted in accordance with the National Institutes of Health Animal Care and Use Committee guidelines. Unilateral hind limb ischemia was induced by femoral artery excision in New Zealand White rabbits (n=7). Imaging studies were conducted at day 14 and day 28 post surgery. Imaging was performed on a 1.5 T GE clinical scanner using 3-inch surface coils placed on the lateral side of each hind limb. The multi-echo TAPIR method (3) was used to acquire quantitative T_1 maps, with a four echo readout (TR/TE = 11.5 ms/2.6 ms) and voxel size of 1.25 mm x 1.25 mm x 4 mm. Gadomer was administered i.v. at a dose of 0.05 mmol/kg, and T_1 maps were acquired every 2-3 minutes for 60 minutes. The data was converted to ΔR_1 (post – pre contrast longitudinal relaxation rate) and analyzed using a two compartment kinetic model (4). For each pixel, the transfer constant (K^{trans}), fractional extravascular extracellular volume (v_e), and fractional plasma volume (v_p) were calculated. These model parameters were then used to calculate a theoretical fit to the tissue ΔR_1 time course, and the maximum value of the fitted ΔR_1 was stored for each pixel. A region of interest was drawn around the TA muscle in a central slice to calculate mean values for the maximum ΔR_1. These values were converted to contrast agent concentration by dividing by the nominal value for the r_1 relaxivity for Gadomer at 1.5 T (13 mM^{-1} sec^{-1}). Statistical comparisons between groups were performed using nonparametric Wilcoxon signed-rank tests. Statistical significance was indicated for $p<0.05$.

Results: The mean maximum ΔR_1 values for the ischemic and normal TA muscles on day 14 and day 28 are shown in Fig. 1. The right-hand axis converts the ΔR_1 values to Gadomer concentration (μm). The ΔR_1 values for the ischemic muscle were statistically significantly higher than the normal muscle on both days (day 14: 0.63 ± 0.18 vs. 0.27 ± 0.12; day 28: 0.47 ± 0.09 vs. 0.26 ± 0.07). Furthermore, the values for the ischemic muscle were statistically significantly higher on day 14 than on day 28 (0.63 ± 0.18 vs. 0.47 ± 0.09). An example parametric image of maximum ΔR_1 for the ischemic limb is shown in Fig. 2, along with delayed enhancement spin-echo images for reference. The delayed enhancement images were acquired approximately one hour after contrast administration, with TR/TE = 300ms/14 ms. Note the increased ΔR_1 values on day 14 compared to day 28, which correlate with increased enhancement on the spin-echo images.

Conclusion: Quantitative T_1 mapping was used to track the dynamics of Gadomer, a macromolecular contrast agent, in skeletal muscle. In regions of skeletal muscle injury, decreases in maximum ΔR_1, a measure of total tissue contrast concentration, were observed between day 14 and day 28 post surgery. These changes may reflect reduction of inflammation or transition from tissue necrosis to fibrosis.

Acknowledgements: This research was supported by the intramural research program of the NHLBI, NIH. The authors also thank Schering AG for generously supplying the contrast agent for this work.

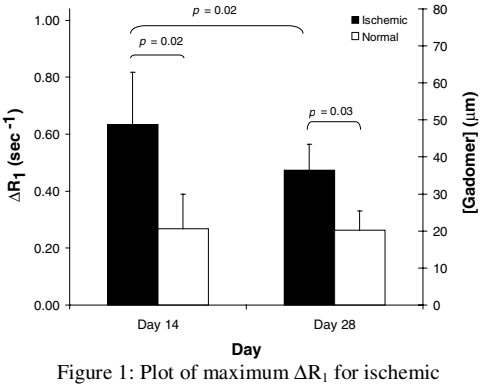

Figure 1: Plot of maximum ΔR_1 for ischemic (filled) and normal (unfilled) TA muscles on day 14 and day 28.

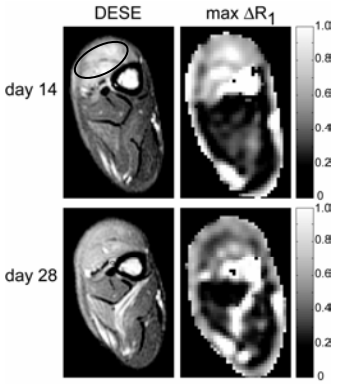

Figure 2: Delayed enhancement spin-echo (DESE) and maximum ΔR_1 axial images for ischemic limbs on day 14 and day 28. Scale is in sec^{-1}. The TA muscle is outlined by the black oval in the day 14 DESE image.

References

1. Kattapurm TM, Skeletal Radiol 34: 203-209 (2005).
2. Jelinek JS, Radiology, 211:241-247 (1999).
3. Steinhoff S, Magn Reson Med 46:131-140 (2001)
4. Tofts PS, J Magn Reson Imaging 10:223-232 (1999)