Magnetic Resonance and Optical Imaging as Biomarkers for Muscle Injury

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Introduction

Muscle damage and weakness remains a universal clinical outcome in a variety of disorders and following acute injuries due to eccentric muscle loading. The overall objective of this work is to evaluate high resolution Magnetic Resonance and tomographic Optical Imaging (OI) as new tools to longitudinally monitor muscle damage *in vivo*.

Experimental

A plantar flexed immobilization-reambulation casting model was utilized to induce acute muscle damage following eccentric loading of the mouse soleus during reambulation. After two weeks of casting, mice freely ambulated for up to a week.

Magnetic Resonance Imaging (MRI) and Spectroscopy (MRS) and OI data was collected throughout the week of reambulation. Muscle water T_2 times of the Soleus (Sol), Gastrocnemius (Gas), and Tibialis Anterior (TA) were all measured using a spin-echo sequence, controlled for diffusion. Variable Echo Time (TE) fixed diffusion weighting was used to create high-resolution T_2 maps, and regions of interest were drawn to measure T_2. Additionally, a ^{1}H localized NMR spectra from the Sol were acquired using STEAM localization with a 1x1x2 mm^3 voxel. All MR experiments were conducted on the 4.7 Tesla (200 MHz) 33 cm horizontal bore system within the Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) Facility.

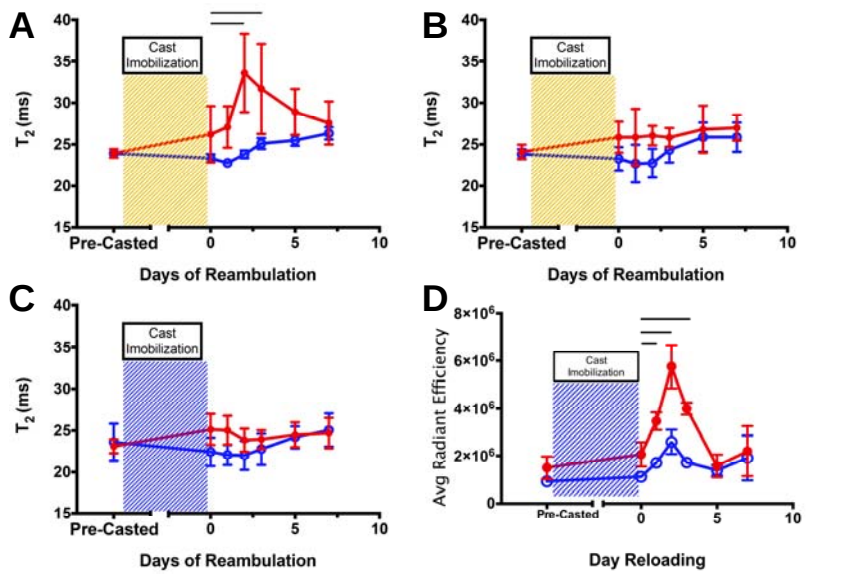

Fig 1: Preliminary data of MRI and OI results. Note that blue markers indicate non-casted limbs, and red marks indicate casted limbs. The T_2 values of the Sol (Fig. 1a), Gas (Fig. 1b), and TA (Fig. 1c) are shown. Optical Imaging Radiant Efficiency is shown in Fig. 1d. Note that horizontal significance bars indicate $p<0.05$ versus day 0.

Prior to OI experiments, mice were injected with Indocyanine Green (ICG). 2D images were acquired using an In Vivo Fluorescence Imager (Ex:745, Em:820) within the Cell and Tissue Analysis Core (CTAC) at UF and tomographic images using a custom built optical imaging device.

Results and Discussion

Both MRI and MRS demonstrated time dependent damage to the Sol of only the casted limb upon reambulation of the mice by changes in muscle water T_2 as shown in Figure 1a. Neither the Gas (Fig 1b) nor TA (Fig 1c) demonstrated any appreciable changes in muscle water T_2 from baseline values prior to casting. MRS = demonstrated a similar time dependent course of damage and recovery (not shown). OI of the posterior compartment of the lower leg demonstrated a similar trend of damage and recovery, as indicated by radiant efficiency (Fig 1d).

Conclusion

The immobilization-reambulation protocol induced acute muscle damage to the mouse soleus and regeneration, as confirmed by MRI, MRS. These results suggest that OI may provide a novel tool to assess muscle damage and recovery. Future work will be aimed at developing simultaneous MR and Optical measures.

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