Compartmental Relaxation Measurements in a Graded Muscle Edema Model

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Introduction

Muscle inflammation is a common condition that may result from trauma or pathology. MRI provides an excellent way of visualizing inflammation; however, there are few techniques that serve to quantitatively assess edematous muscle. It is known that relaxation parameters change with inflammation, with some presenting multiexponential decay [1,2]. How much the relaxation times change may depend on the severity of the edema and swelling of the intracellular and extracellular tissue compartments. A graded edema model in rats can be produced by subcutaneous injections of a λ-carrageenan solution at varied concentrations. Integrated T_1-T_2 measurements, derived from a saturation recovery prepared multiple spin-echo acquisition, can be made to reveal whether the edematous tissue presents with multiexponential T_1 and/or multiexponential T_2. It can then be investigated how these relaxation times change with an increase or decrease in both extracellular and intracellular volume fractions.

Methods

Female Sprague-Dawley rats (n=9, weight_{avg} = 223g) were used for all experiments. To create edema in the hindlimb, each animal was given a 0.1 ml subcutaneous injection of a specific concentration of λ-carrageenan solution (1.0% w/v, 0.5% w/v, 0.25% w/v, or 0.125%w/v). A period of at least 6 hours was allowed for the edema to reach a plateau. The animals were then imaged at 9.4T. A multi-slice fast spin echo sequence was used to locate the edema in the hindlimb. An example FSE image of both healthy and edematous muscle can be seen in Fig. 1. With the edema located, a saturation recovery prepared multiple spin-echo (SR-ME) pulse sequence was run to make integrated T_1-T_2 measurements. The SR-ME pulse sequence included the collection of 36 spin echoes (30 at te = 10 ms and 6 at te_{late} = 50 ms). The saturation time, τ_{SR}, varied pseudo-logarithmically with 13 time points between 0.250s and 12s. The SR-ME data were then fitted in a non-negative least squares (NNLS) sense to Eq. 1 [3].

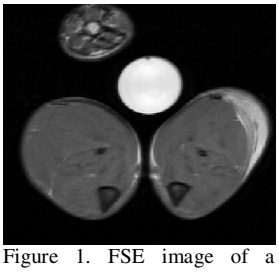

Figure 1. FSE image of a healthy rat hindlimb (left) and edematous hindlimb (right). Image parameters: 256x256, 40x40mm^2, TR=2s, TE=20ms.

$$M(\tau_{SR}, te) = \sum_{k=1}^{N_2} \sum_{l=1}^{N_1} S_{kl}(1 - \alpha \cdot \exp(-\tau_{SR} / T_{1k})) \exp(-te / T_{2l}) \qquad \text{(Eq. 1)}$$

To account for imperfect saturation, α, was estimated by fitting the first echo magnitude at each τ_{SR} to a monoexponential recovery. Three rats were imaged at an injection concentration of 1.0% w/v, while two rats each were imaged at 0.5%, 0.25%, and 0.125% w/v.

Results

It was found that the creation of edema in the muscle by means of an injection of λ-carrageenan solution resulted in two relaxation resolved components each with its own distinct T_1 and T_2 time constants. A typical T_1-T_2 spectrum can be seen in Fig. 2. The parameters in Table 1 reveal that the size of the long-lived compartment (Edema_B) decreases, with a decrease in the concentration of λ-carrageenan, as does the T_1 of this signal component. For most measurements, the T_1 and T_2 of the short-lived compartment (Edema_A) were larger than that of normal muscle, likely due to intracellular swelling. The resolution of T_1 values for each T_2 component indicates that with edema the compartmental exchange rates are not fast compared to the R_1s, however, it is possible the system has not yet reached a state of slow exchange.

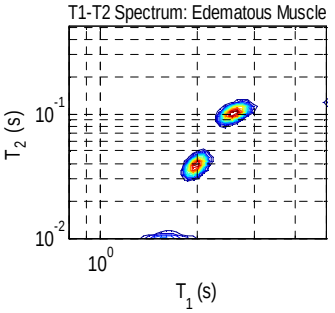

Figure 2. Example T_1-T_2 plot of edematous muscle.

Table 1. Calculated Parameters for Normal and Edematous Muscle from T_1-T_2 Measurements

	1.0% w/v injection (n=3)			0.5% w/v injection (n=2)		
	ρ	T2(ms)	T1(s)	ρ	T2(ms)	T1(s)
Normal	1.0	20.0±0.7	2.143±0.132	1.0	20.2±2.0	2.095±0.033
EdemaA	0.54±0.06	28.5±1.3	2.130±0.215	0.56±0.04	30.0±1.0	2.285±0.214
EdemaB	0.46±0.06	106.0±10.6	3.032±0.171	0.44±0.04	103.1±2.0	2.787±0.231
Phantom	1.0	78.4±1.6	1.358±0.099	1.0	81.0±2.4	1.341±0.082

	0.25% w/v injection (n=2)			0.125% w/v injection (n=2)		
	ρ	T2(ms)	T1(s)	ρ	T2(ms)	T1(s)
Normal	1.0	20.2±0.5	2.125±0.031	1.0	20.0±0.9	2.121±0.034
EdemaA	0.75±0.04	26.6±1.3	2.139±0.146	0.78±0.04	25.5±1.2	2.425±0.161
EdemaB	0.25±0.04	104.1±13.8	2.559±0.213	0.22±0.04	98.5±16.1	2.312±0.079
Phantom	1.0	83.4±1.0	1.283±0.050	1.0	79.1±3.3	1.282±0.040

Conclusion

This study shows how changes in relaxation times can be markers of muscle injury, specifically inflammation and edema. The observed change in T_1 with the extracellular volume fraction may be useful in developing an inversion recovery protocol for selectively nulling tissue compartments based on severity of muscle injury.

References

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