T2 monitoring at 3T for canine model of Duchenne muscular dystrophy

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Introduction

Duchenne muscular dystrophy (DMD) is one of the most common forms of muscular dystrophy in humans with no cure. Clinical muscle MRI has been dependent on T_1 and T_2 weighted imaging to monitor inflammatory myopathies in patients with muscular dystrophy (1,2). Although these methods are useful because of their sensitivity to a wide range of mechanisms, they may not be able to identify specific cellular processes in the affected areas. Here we performed noninvasive MRI for both normal dogs and *cxmd* dogs to quantify T_2 values in dystrophic muscles comparing to those in normal muscles. The canine model of DMD, *cxmd,* has an X-linked muscular dystrophy (3). These *cxmd* dogs lack dystrophin and have clinical signs similar to humans. The goal of this quantitative MRI was to assess disease stages for dystrophic muscles and to evaluate treatment efficacy of adeno-associated virus (AAV) vector medicated gene therapy.

Methods

Eight *cxmd* dogs and five normal dogs were used for this study. MRI was conducted using a two flexible element SENSE surface coil (Philips Sense Flex M coil) on a Philips 3T Achieva (version 2.6 software). T_1 and T_2 weighted images were acquired with turbo spin multi-echo sequences (15 echoes and echo time ranging from 20 to 170 ms) to generate T_2 values and gradient echo sequences to obtain 3 dimensional images of muscle. One of the *cxmd* dogs were treated with the AAV mediated gene therapy by massively injecting into left lower limb muscles including tibialis anterior (TA) and gastrocnemius (GA) muscles. The contralateral right leg was uninjected and served as a control.

Results and Discussion

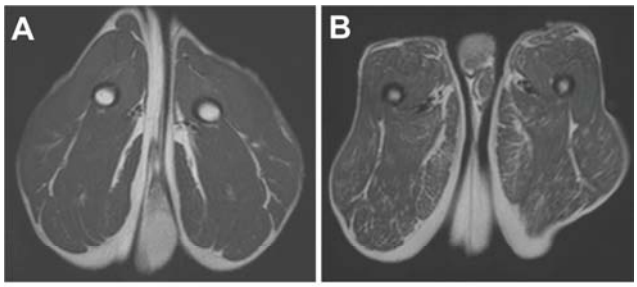

Figure 1. T2 weighted images (TR/TE = 3000/60 ms) comparison between a normal dog (A) and *cxmd* dog (B).

Figure 1 shows representative T_2 weighted images for upper limb muscles covering biceps, semitendinosus, semimembranosus and adductor muscles for both a normal dog and *cxmd* dog. Fatty infiltration was observed in dystrophic muscles (as shown in Fig. 1B) of *cxmd* dogs as opposed to homogeneous muscles with no fatty infiltration detected in normal dogs. Various measurements of quantitative T_2 values are summarized in Figure 2. For normal dogs, upper limb muscles showed a slightly smaller T_2 value (31.5 +/- 1.5 ms) than that of lower limb muscles (TA and GA muscles: 33.3 +/- 0.9). For *cxmd* dogs, there is no statistical difference between upper and lower limb muscles in their T_2 values ranging from 35.3 to 39.2 ms. The treated *cxmd* dog showed T_2 decrease for its treated TA and GA muscles by 8 and 10% of T_2 reduction, respectively, comparing to T_2 measured in untreated muscles of the contralateral right leg as shown in Fig. 2C.

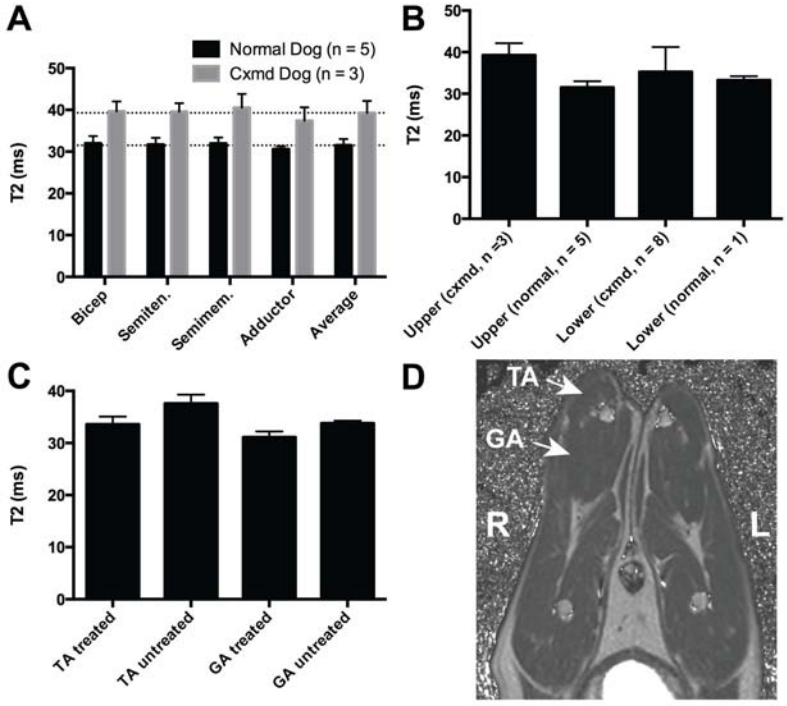

Figure 2. T2 quantification for normal and *cxmd* dogs. A. T2 values determined for upper limb muscles. B. T2 values compared between upper limb muscles and lower limb muscles (TA and GA muscles). C. T2 values measured between treated and untreated muscle (TA and GA) of lower limb. D. T2 maps generated for a cxmd dogs with a left leg treated with the gene therapy and its contralateral right leg untreated as a control.

Conclusions

MRI is a useful imaging technique that enables noninvasive assessments to evaluate therapeutic treatment responses. The T_2 quantification would be a good MR marker to evaluate muscle involvement and treatment efficacy.

References

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