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 T1 and T2 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 T2 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). T1 and T2 weighted images were acquired with turbo spin multi-echo sequences (15 echoes and echo time ranging from 20 to 170 ms) to generate T2 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 shows representative T2 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 T2 values are summarized in Figure 2. For normal dogs, upper limb muscles showed a slightly smaller T2 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 T2 values ranging from 35.3 to 39.2 ms. The treated cxmd dog showed T2 decrease for its treated TA and GA muscles by 8 and 10% of T2 reduction, respectively, comparing to T2 measured in untreated muscles of the contralateral right leg as shown in Fig. 2C.

Conclusions
MRI is a useful imaging technique that enables noninvasive assessments to evaluate therapeutic treatment responses. The T2 quantification would be a good MR marker to evaluate muscle involvement and treatment efficacy.

References