Canine MRI for X-linked myotubular myopathy

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Target audience

Researchers who are interested in X-linked myotubular myopathy research and skeletal muscle MRI will benefit from this work.

Purpose

X-linked Myotubular Myopathy (XLMTM: MIM 310400) is a severe congenital myopathy affecting approximately 1 in 50,000 male births (1,2). XLMTM frequently presents in male infants with severe muscular hypotonia and weakness associated with ventilator insufficiency, and is diagnosed on biopsy by the presence of myofibers with centralized nuclei and mitochondrial aggregation. This study was to investigate the feasibility of MRI in noninvasively assessing the disease and treatment responses for XLMTM.

Methods

MRI was conducted to image dog hindlimb muscles *in vivo* using a two flexible element SENE surface coil (Philips Sense Flex M coil) on a 3T MR scanner (Philips Achieva, version 3.2.1 software). Quantitative T2 (multi-echo sequence: 15 echoes and echo times ranging from 20 to 170 ms) and ADC measurements were carried out along with 3 dimensional (D) T1 and T2 weighted imaging. Four XLMTM Dogs and one control dog were used for this study. Three XLMTM dogs were treated with adeno-associated viral (AAV) vector mediated gene therapy.

Results and Discussion

We performed MRI on live XLMTM dogs at approximately 7 weeks of age: one untreated dog and another dog treated by AAV gene therapy. Two sets of quantitative images are compared in Figure 1: one untreated dog and another treated dog. Quantitative T2 and ADC values were colorized for lower limb muscles for both legs. Slightly larger T_2 values were obtained in the untreated XLMTM dog muscles demonstrating potentially affected muscles with centralized nuclei in the untreated dog. Both T_2 and ADC maps were acquired by multi-echo imaging and echo planar imaging methods, respectively, both with fat suppression. Tibialis cranialis (TC) muscle volumes of left and right legs were measured from the 3D MRI: 5,299 and 5,154 mm^3 for the untreated dog while 6,756 and 6,747 mm^3 for the treated dog, respectively. We present our preliminary MRI results for XLMTM dogs to non-invasively assess the disease and monitor responses to an effective therapeutic treatment approach. To the best of our knowledge, this is the first MRI study using the canine model of XLMTM.

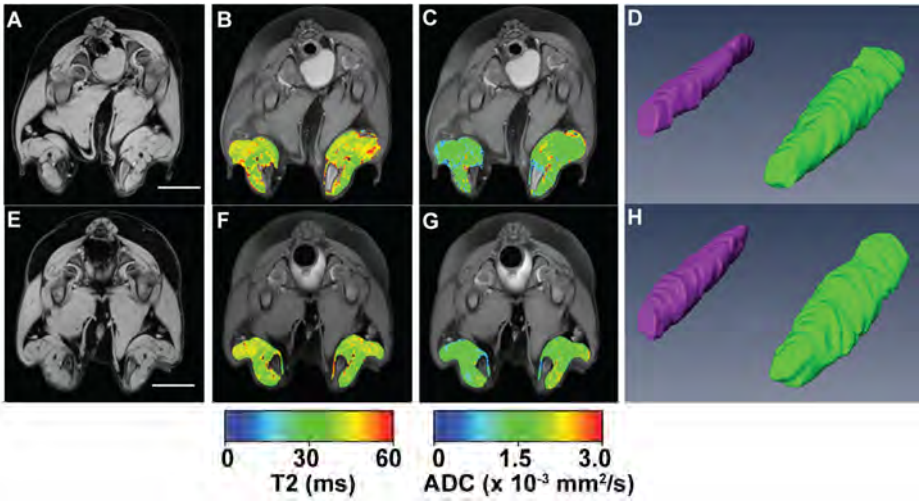

Figure 1. Multi-parametric MRI on both XLMTM dog: untreated (A – D) and treated (E – H) with AAV gene therapy. T_1 weighted gradient echo image with fat suppression (A and E), and colorized T_2 maps (B and F) and ADC maps (C and G) both overlaid on their corresponding T_2 weighted anatomic images. Three dimensional segmentation for TC muscle volumes for the untreated (D) and treated (H) XLMTM dogs. Scale bar = 2 cm.

Conclusions

Multi-parametric MRI utilizing T2, ADC and 3D volume measurements has feasibility in the identifying and monitoring the disease progression and treatment responses in the dog model of X-linked myotubular myopathy.

References

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2. Laporte J, Biancalana V, Tanner SM, et al. MTM1 mutations in X-linked myotubular myopathy. Human mutation 2000;15(5):393-409.