398P

Magnetic resonance imaging detects bone alterations in corticosteroid treated boys with DMD

*R. Kunnath Ravindranunni 1 , R . Grewal 2 , C. Cottrell 2 , A. Bernier 1 , I K. Vandenborne 1 ,G. Walter 1 ,C. Rajapakse 2 I.Tuna 1 , **R. Willcocks 1** 1 University of Florida, Gainesville, USA; 2 University of Pennsylvania, Philadelphia, USA*

Bone fragility is highly prevalent in individuals with DMD, and the scope of this problem is likely to increase as patients are treated with corticosteroids for increasing durations. A number of potential interventions may preserve bone 33 JID: NMD Abstracts ARTICLE IN PRESS in individuals with DMD, however biomarkers to measure the efficacy of these interventions are needed. The purpose of this study was to develop magnetic resonance imaging (MRI) biomarkers of bone quality in DMD. 32 individuals with DMD (12.9 ± 3.8 years old) and 18 unaffected control participants (11.9 ± 2.8 years old) provided informed consent to participate in the study. The DMD group was 100% corticosteroid treated (63% deflazacort, 15% prednisone, 22% prednisolone), with 23% of participants treated with bisphosphonates. 27% of unaffected control participants and 56% of participants with DMD reported a history of fracture. An MR examination including high resolution imaging and Dixon imaging was performed in the distal femur, and MR images were analyzed to extract trabecular and cortical bone parameters and bone marrow fat fraction. Boys with DMD had significantly worse bone quality than unaffected boys as measured by bone marrow fat fraction (0.85 ± 0.10 vs. 0.77 ± 0.08, p = 0.03), cortical thickness (1.6 ± 0.7 vs 2.3 ± 0.3 mm, p = 0.0 0 06), trabecular bone volume fraction (0.08 ± 0.03 vs 0.14 ± 0.03, p < 0.0 0 01), and finite element analysis-estimated bone stiffness (1.5 ± 0.5 vs 2.4 ± 0.4, p < 0.001). Additionally, these variables were significantly correlated with both age and duration of corticosteroid use in individuals with DMD. MRI can noninvasively measure trabecular and cortical bone alterations in DMD at the distal femur, a common fracture site in boys with DMD. These measurements may offer a way to track the effects of bone-targeted interventions for DMD and other neuromuscular disorders.

399P

MRI assessment of microdystrophin gene therapy in DMD: a five year longitudinal study

R. Willcocks *,D. Lott, S. Forbes, K. Vandenborne, G. Walter University of Florida, Gainesville, USA*

Microdystrophin gene therapy (GT) shows promise for treating Duchenne muscular dystrophy (DMD), but the results of clinical trials have had mixed results. Magnetic resonance imaging (MRI) data collected 6-24 months after delandistrogene moxeparvovec administration showed preservation of muscle quality in 3 boys with DMD, however the persistence and generalizability of this effect is unknown. The objective of this ongoing longitudinal study is to evaluate MRI-determined muscle fat infiltration in microdystrophin GT-treated boys with DMD relative to an untreated natural history cohort. Muscle fat fraction (FF) was measured using chemical shift-based imaging acquired using a 3T MRI scanner in 6 muscles of the upper and lower legs of 3 microdystrophin GT treated boys with DMD and group age-matched steroid-treated boys with DMD. The longitudinal study included 3 delandistrogene moxeparvovec treated boys with DMD (10.0, 10.6, and 12.1 years) and 71 corticosteroid-treated boys with DMD (11.0 ± 0.9 years). For each GT treated subject, an individual comparator cohort was generated comprising all untreated subjects whose age was ± 0.5 years. 5- or 6-years post-GT administration (range 4.8-6.0 years), muscle FF remained low in GT treated boys, with FF less than 0.20 across all muscles

measured including the proximal vastus lateralis (VL) and biceps femoris long head (BFLH) muscles. By contrast, the age- matched comparator cohorts had group mean FF of 0.40 to 0.47 in the VL and 0.60 to 0.63 in the BFLH. Boys treated with delandistrogene moxeparvovec were initially reported to have low fat infiltration 6-24 months after GT administration. More than five years after GT administration, these boys continue to show markedly slowed muscle fat accumulation compared with age-matched non-GT treated boys with DMD.