longitudinal study to establish assay selection best practices and comparative natural history of DMD animal models (part of a broader multi-stakeholder research collaboration known as 'Of Mice and Measures'). A 2-day training and planning session involving all parties was hosted at Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA. Researchers became versed and competent in current EIM techniques. They also identified technique refinements to enable improved testing and application in DMD models of interest. Next steps will be additional data collection and analysis, including through the 'Of Mice and Measures' study. The goal for this collaboration is to help identify and advance opportunities for expanded EIM application in preclinical DMD drug studies, and ultimately connect to and inform human clinical application.

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Reliability and validity of trunk control measurement scale in Duchenne muscular dystrophy

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Trunk control is essential for many daily activities such as sitting and walking. Impaired trunk control causes difficulties in performing daily activities especially at later stage of Duchenne muscular dystrophy (DMD). This study was planned to demonstrate the reliability and validity of trunk control measurement scale (TCMS) in DMD. Twenty boys with DMD were included in the study. Two physiotherapists evaluated all boys with TCMS for inter-rater reliability. TCMS was applied with two weeks interval by the same physiotherapist to examine inter-rater reliability. Criterion-related validity was determined with the correlation between TCMS and motor function measure (MFM), and functional independence measure (FIM). The mean age of children was 9.4±3.3 years. The ICC value of inter-rater reliability was 0.953-0.994 and intra-rater reliability was 0.978-0.997. A positive, strong correlation was found between TCMS and MFM ($p<0.01$, $r=0.88$) and TCMS and FIM ($p<0.01$, $r=0.85$). TCMS is found to be a reliable and valid assessment to measure trunk control in boys with DMD. The scale can help to clinicians and researchers to observe and determine the trunk control in clinical trials as well as clinical practice.

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Patient perception of outcome measures for non-ambulant Duchenne muscular dystrophy patients

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Many therapeutic clinical trials are ongoing in ambulant Duchenne muscular dystrophy (DMD) patients. However, drugs proven effective in ambulant patients will have to be tested separately in non-ambulant patients. Several outcome measures for non-ambulant patients are under development. Natural history data of these measures is needed, while patients struggle to combine this type of extra visits with their daily life. We assessed patient's perception of several different outcome measures for non-ambulant DMD patients. Non-ambulant DMD patients underwent muscle MRI, peak muscle force tests using a Hand-held dynamometer and Myotools, Functional Workspace, Leap Motion and PUL 2.0 assessments of the right arm, and Active-Seated and PROM assessment of both arms. Using visual analogue scale (VAS) scores (range 0-10), all patients were asked directly after the respective assessment how much fun, annoying and tiresome they perceived it. Highest VAS scores on all three domains were correlated to PUL total score using Spearman correlation coefficients. 20 non-ambulant DMD patients (range 8.6-24.1 yrs) were included. Active-Seated scored highest on fun (median 8), followed by muscle force tests and PUL (median 7). MRI was the most annoying (median 5), while all other tests had a median score of 1 or 2. Active-Seated was the most tiresome (median 6), followed by muscle force tests (median 5), and Functional Workspace (median 4). No significant correlation with PUL total score was found for Active-Seated VAS fun and tiresome scores (ρ=-0.04, p=0.871 and ρ=-0.13, p=0.598), and MRI VAS annoying scores (ρ=-0.46, p=0.053). While Active-Seated and muscle force tests score highest on fun, they are also the most tiresome. MRI has the advantage of no motivation component, but scored highest on annoyment. To improve participation in both therapeutic and natural history studies, patient's perception of outcome measures for non-ambulant DMD patients and their respective burden need to be considered.

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E-POSTERS – NEXT GENERATION SEQUENCING

EP.96

"Double trouble" in a large cohort of patients with unexplained muscle weakness

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The MYO-SEQ project, stablished as a collaboration between Newcastle University, the Broad Institute of MIT and Harvard, industry and patient organizations, aims to genetically diagnose patients with unexplained limb-girdle weakness and/or elevated CK. We have so far collected over 1,500 patients from 54 European referring centres. Whole exome sequencing was carried out and data analysed by interrogating a panel of 429 genes known to be associated with neuromuscular disease (NMD). A likely disease-causing variant was identified in 52% of the cohort. Of these 816 cases, 30 (3.6%) carried pathogenic or likely pathogenic variants in two neuromuscular disease genes, usually known as 'double trouble' patients. Almost a third of these cases (n=12) carried heterozygous variants in the RYR1 gene in combination with another NMD gene. This reflects the high incidence of reported RYR1 variants in our cohort as dominant RYR1variants are associated with risk of malignant hyperthermia, and have therefore been reported even if their pathogenicity was not fully confirmed. Of the remaining cases, heterozygous variants in *TTN* or *MYH7* together with homozygous or compound heterozygous variants in a recessive NMD gene were the most frequent combinations (n=5), and in two affected individuals from a dominant pedigree heterozygous *TTN* and *MHY7* variants were found together. In addition, three patients from consanguineous families carried two pairs of homozygous variants, all in combination with one of the sarcoglycan subunits genes (ie *SGCG/PFKM*, *SGCG/COL6A3* and SGCA/POMT1). Interestingly, two patients had variants in two of the COL6 genes (*COL6A1/A2* and *COL6A2/A3*) both presenting with a complex Bethlem-like phenotype. In general, the clinical presentation of these 'double trouble' cases was somehow unusual, and not simply the combination of the phenotypes associated with each individual gene. Here we aim to describe in more detail some of these remarkable patients.

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