PATTERNS OF UPPER LIMB INVOVMENT IN DMD: CORRELATION WITH FUNCTIONAL ABILITIES

Brogna C[1], Cristiano L[1], Tartaglione T[2], Verdolotti T[2], Fanelli L[1], Ficociello L[2], Tasca G[3], Battini R[1,4], Coratti G[1], Forcina N[1], De Santis R[1], Norcia G[1], Carnicella S[1], Colosimo C[2], Carlier P[5], Pane M[1], Mercuri E[1]

[1]Pediatric Neurology and Nemo Clinical Centre, [2] Department of Radiology, [3]Institute of Neurology, Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario "A. Gemelli", Rome, Italy, [4] IRCSS Stella Maris, Pisa, Italy, [5] IM and CEA NMRoratory, Institute of Myology, Paris, France.

INTRODUCTION

In the last years there has been increasing attention on upper limb function in Duchenne muscular dystrophy (DMD) (1-3). New functional tools have been specifically developed for upper limb measurements following the gradient of progression observed in DMD. The Performance of Upper Limb (PUL) test, has been specifically designed to assess the progression of upper limb involvement in both ambulant and non-ambulant DMD patients. Early signs of proximal weakness at shoulder level muscle involvement can be detected also in ambulant boys with a predictable decline subsequently involving elbow and distal domains after loss of ambulation.

So far, only few studies have explored upper limb involvement using muscle Magnetic Resonance Imaging (MRI) and in some cases, also MR spectroscopy. These studies however have generally focused on one segment of upper limbs only (4-6).

The aim of the present study was to evaluate whether the functional involvement, detected on the PUL, is related to muscle involvement using a wider MRI protocol that includes shoulder, arm and forearm.

METHODS

- **Inclusion criteria**: DMD patients attending their routine follow up clinics between September 2016 and August 2017

- **Exclusion criteria**: impossibility to perform MRI without sedation, severe joint contractures, pace makers, respiratory or cardiac problems or other issues that would interfere with positioning or performing MRI

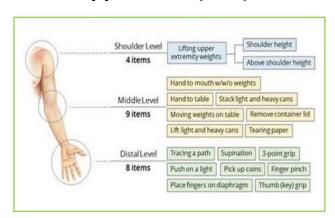They were all assessed using the **PUL 2.0** and **muscle MRI** of shoulder, arm and forearm

Muscle RM

- Unilateral upper-limb MRI performed at 1.5T (Philips Ingenia) using a flexible body coil
- Total examination time 20 to 30 minutes.
- Non contrast-enhanced images obtained from the dominant upper limb.
- TSE T1 -weighted spin-echo acquired on axial plane selected in respect to the long axis of the humerus for the shoulder and arm, and in respect of the long axis of the radius for the forearm.
- Descriptive analysis was used to identify the muscles that were more frequently affected in the different segments: muscles with normal or minimal changes (**score 0 and 1**), those with intermediate involvement (**grades 2 to 3**), and those with complete replacement (**grade 4**).

The Performance of Upper Limb (PUL)

Individual tasks represent real-world activites of daily living

RESULTS

Thirty-one patients were included in the study

Age ranged between 5 and 29 years (mean 12.7 SD: ±5.5).

17 were ambulant (age range 5-15) and 14 non-ambulant (age range 10-29). All the patients were on steroids.
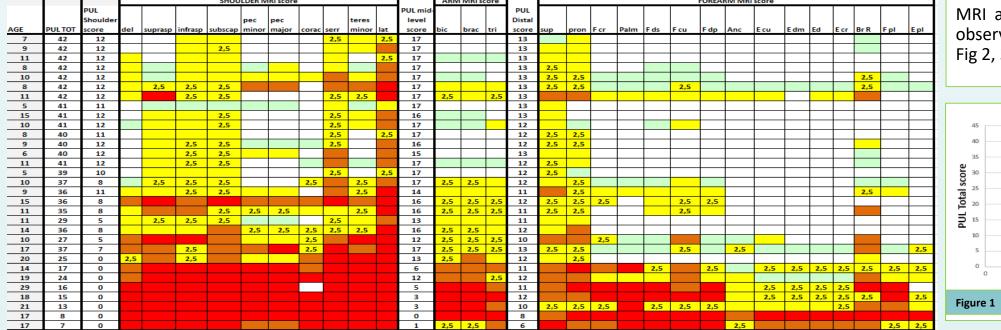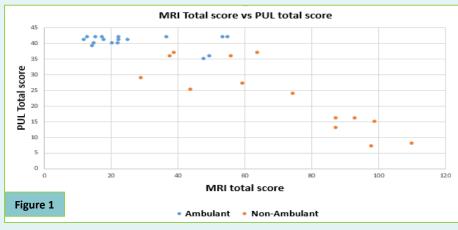
PUL 2.0

The total PUL scores ranged between 6 and 42 in the ambulant and between 7 and 37 in the non ambulant boys.

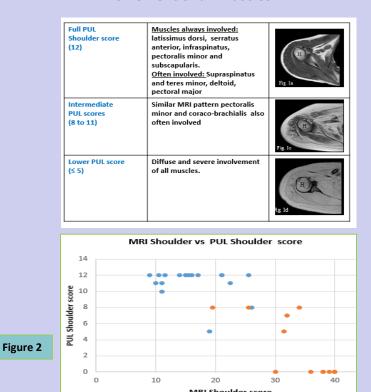**Table 1** provides individual details of the PUL global scores and of the subscores.

Muscle MRI

Table 1 provides individual details of the MRI scores at each level. Figure 1 shows the correlation between total MRI and total PUL scores. The Patterns of impairment observed in each level on both MRI and PUL are shown in Fig 2, 3 and 4.
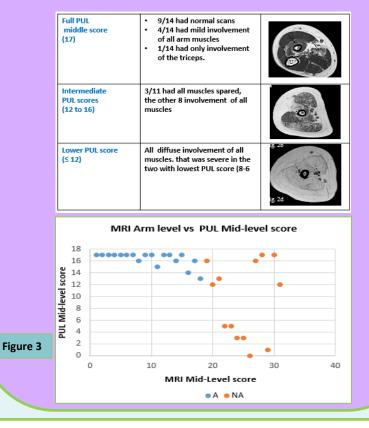

Figure 1

Table 1: Individual details of imaging and PUL findings at shoulder, arm and forearm level

Figure 2

At shoulder level very low scores (≤ 5) on the shoulder domain of the PUL were associated with diffuse and severe involvement of all muscles

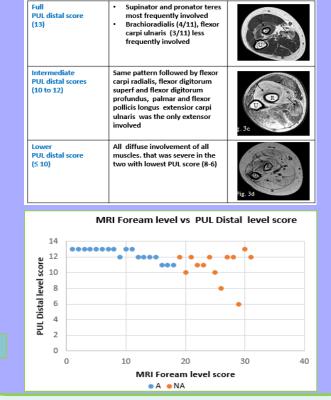|	
Full Shoulder score (12)	Muscles always involved: latissimus dorsi, serratus anterior, infraspinatus, pectoralis minor and subscapularis. Often involved: Supraspinatus and teres minor, deltoid, pectoral major
Intermediate PUL scores (8 to 11)	Similar MRI pattern pectoralis minor and coraco-brachialis also often involved
Lower PUL score (≤ 5)	Diffuse and severe involvement of all muscles.

Figure 2

Figure 3

At arm level, biceps, brachialis and triceps, were, with few exceptions, always concordantly involved. A PUL score <12 is associated with diffuse involvement and <6 with severe diffuse involvement

Full PUL middle score (17)	9/14 had normal scans, 4/14 had mild involvement of all arm muscles, 1/14 had only involvement of the triceps.
Intermediate PUL scores (12 to 16)	3/11 had all muscles spared, the other 8 involvement of all muscles
Lower PUL score (≤ 12)	All diffuse involvement of all muscles. that was severe in the two with lowest PUL score (8-6)

Figure 3

Figure 4

Full scores in the PUL distal domain were always associated with involvement of supinator (97%) and pronator (87%). Extensor muscles were often spared. Severe involvement was found with scores ≤ 10

Full PUL distal score (13)	Supinator and pronator teres most frequently involved, Brachioradialis (4/11), flexor carpi ulnaris (3/11) less frequently involved
Intermediate PUL distal scores (10 to 12)	Same pattern followed by flexor carpi radialis, flexor digitorum superf and flexor digitorum profundus, palmar and flexor pollicis longus extensor carpi ulnaris was the only extensor involved
Lower PUL distal score (≤ 10)	All diffuse involvement of all muscles. that was severe in the two with lowest PUL score (8-6)

Figure 4

CONCLUSIONS

✓ The integrated use of functional scales and imaging allowed to establish, at each level, the scores on the PUL more frequently associated with diffuse and severe involvement.

✓ Combined assessment of more segments of the upper limbs is often useful as there is often a concomitant involvement of muscles at different levels and that patterns of muscle involvement can be detected in both ambulant and non-ambulant patients.

✓ Some muscles are frequently involved even in younger stronger patients with normal PUL scores and that other muscles become progressively involved with increasing age and decreasing functional abilities.

REFERENCES

1. Pane M et al , Neuromuscul Disord. 2014;24(3):201-6.
2. Mayhew A et al Dev Med Child Neurol. 2013;55(11):1038-45.
3. Mazzone E et al Developmental Medicine Child Neurology. 2012
4. Ricotti V et al PLoS One. 2016;11(9):e0162542
5. Hogrel Jyet al Neurology. 2016;86(11):1022-30
6. Willcocks RJwt al J Neurol. 2017;264(1):64-71.