# Assessment of muscle properties in neuromuscular disorders: The muscle toolbox

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Primary objective• To characterise natural disease progression rates of MRI- and/or US-assessed measures of muscle properties and muscle function and strength tests in children with neuromuscular disorders through standardized annual follow-up...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Muscle disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON57098

**Source**
ToetsingOnline

**Brief title**
The muscle toolbox

### Condition

- Muscle disorders

**Synonym**
muscle disease, neuromuscular disease

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Radboud Universitair Medisch Centrum
**Source(s) of monetary or material Support:** stichting Spieren voor Spieren

## Intervention

**Keyword:** functional tests, MRI, neuromuscular disease, US

## Outcome measures

### Primary outcome

The primary outcome measures are muscle fat fraction for MRI, mean muscle echogenicity for US, newtons for maximal isometric strength and motor function total score for functional tests.

### Secondary outcome

Other study parameters are muscle water characteristics (T2water) and muscle volume determined with MRI, muscle diameter and visual scoring with US, and additional muscle strength and function tests, like peak torque and muscle power, and disease-specific function scores.

# Study description

### Background summary

There are over 600 different neuromuscular disorders many affecting children, and virtually all are rare. Muscle weakness is the main characteristic of most neuromuscular disordres, but the causes, weakness patterns, and progression rates of the disorders are variable. Accurate assessment of disease progression in these disorders is very important for determining disease stage, as outcome measure in trials and to manage expectations, but is challenging in single centres due to the rarity of the disorders. Disease progression is determined with a wide variety of clinical measures, including imaging, muscle strength measurements, and motor function tests. Imaging has the advantage that it is very sensitive to small changes over time. However, clinical muscle imaging protocols are dominated by qualitative methods instead of quantitative methods, and each hospital makes different choices on what imaging techniques and parameters they use. Muscle strength and function assessment is more directly related to everyday function, but shows higher (inter-observer) variability and may be more subjective. Up to now, a combination of assessments is rarely used. Collaboration between centres to collect more uniform (and comparable) data

could increase insights on the natural disease progression of rare neuromuscular disorders by increasing sample sizes and thereby accelerating trial readiness. Therefore, we aim to implement a standardised muscle toolbox comprising qualitative and quantitative muscle ultrasound (US) and magnetic resonance imaging (MRI), and muscle function and strength tests in three paediatric neuromuscular disorder expert centres in the Netherlands: Radboud university medical center (Radboudumc), Leiden University Medical Center (LUMC), and Utrecht University Medical Center (UMCU).

## Study objective

Primary objective
• To characterise natural disease progression rates of MRI- and/or US-assessed measures of muscle properties and muscle function and strength tests in children with neuromuscular disorders through standardized annual follow-up examinations with our muscle toolbox over a four-year period.
Secondary objectives
• To determine the relationship between MRI- and/or US-assessed measures of muscle properties and muscle function and strength tests;
• To predict clinical milestones such as loss or gain of ambulation, and others - depending on the specific disease - using MRI- and US-assessed measures of muscle properties.

## Study design

This is an observational study that aims to include children with confirmed diagnosis of spinal muscular atrophy (SMA), Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD), limb-girdle muscular dystrophy (LGMD), facioscapulohumeral muscular dystrophy (FSHD), and myotonic dystrophy type 1 (DM1). All children will be invited to undergo MRI scans and/or US scans, muscle function, and strength tests. Functional and strength tests are part of current clinical care. Age will determine the examination approach as follows:
* Children < 5 years will be examined with US and muscle function and strength tests. These children will not undergo MRI examinations
* Children >= 5 years that do not have contraindications for MRI will be examined with an MRI scan and muscle function and strength tests. US is optional.
* Children >= 5 years that do have contraindications for MRI will be examined with US and muscle function and strength tests.

## Intervention

The imaging techniques (MRI and US), muscle- and function tests can be considered non-therapeutic interventions, as these are nog standard care for each child.

**Study burden and risks**

The maximum time burden will be 90 minutes. The participants will undergo an additional MRI scan and/or US assessment, each taking ~30 minutes each. Muscle function and strength tests are part of standard care, though some additional tests may be required depending on the centre and neuromuscular disease. This potential additional testing for muscle strength will not take more than 30 minutes.
Spieren voor Spieren*s youth panel has been consulted on the acceptability of additional imaging or strength tests, and their feedback has been incorporated into this protocol.
There will be no direct benefit for the child. In the future, however, this study will give more insight into disease progression at the group-level of specific neuromuscular disorders and at the individual patient level which the physician can use to give better, more-personalised advice. We think that the information will also add to our understanding of the natural history of muscle tissue quality and thereby help the design of future clinical trials. US and MRI are safe techniques. The MRI scan can trigger claustrophobia and can cause slight discomfort due to lying in supine position. To alleviate this potential burden, we will*amongst other things*use pads and cushions, permit children to listen to music or watch videos, and parents will be allowed to accompany children during the scan.

# Contacts

**Public**
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10
Nijmegen 6525 GA
NL
**Scientific**
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10
Nijmegen 6525 GA
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns

## Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Confirmed diagnosis of SMA, DMD, BMD, LGMD, FSHD, or DM1 by DNA analysis
• Younger than 18 years old at start of inclusion

## Exclusion criteria

Children can participate when they can undergo, at minimum, either the muscle MRI or muscle US examination.

MRI
Participants will be excluded from the MRI when they are not able to understand instructions and/or perform tasks related to MRI or when they have contra-indications to MRI scanning, these are:
• The impossibility to perform MRI without sedation, for example very young children (i.e. under 5 years of age) or those with severe cognitive or behavioural problems;
• Claustrophobia;
• Pacemakers and defibrillators;
• Nerve stimulators;
• Intracranial clips;
• Intraorbital or intraocular metallic fragments;
• Cochlear implants;
• Ferromagnetic implants (e.g. thoracic implant for scoliosis);
• Inability to lie supine for 60 minutes;
• Necessity of (continuous) daytime ventilation; and
• Inability to fit in the MRI scanner bore e.g. due to body size or contractures
If needed, a child can experience the feeling of being in the MRI via a *dummy*

MRI scanner, which is a replica of a clinical MRI scanner tunnel. This will help the child to determine whether they will feel comfortable in the bore during the real examination.

US
Participants will be excluded from the US when they are not able to understand instructions and/or perform tasks related to US.

Muscle function and strength
Participants will be excluded from some of the muscle function or muscle strength tests when they are not able to understand instructions and/or perform the relevant tasks, for example if they cannot exert maximal force. This may be the case for some tests in very young children (i.e. under age of 4 years of age) or those with severe cognitive or behavioural problems judged by evaluator or with recent history of surgery or illness.

# Study design

## Design

**Study type:** Interventional

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Other |

## Recruitment

NL

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| Recruitment status: | Recruiting |
| Start date (anticipated): | 07-01-2025 |
| Enrollment: | 143 |
| Type: | Actual |

# Ethics review

Approved WMO

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| Date: | 04-11-2024 |
| Application type: | First submission |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den |

Haag)

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
| --- | --- |
| CCMO | NL85997.000.24 |