Funded by the European Union

European Reference Network for rare or low prevalence complex diseases

Network Neuromuscular Diseases (ERN EURO-NMD)

8th ERN EURO-NMD
Annual Meeting

A panorama of devices for the non-invasive assessment of the neuromuscular system

5th – 7th March 2025

Jean-Yves Hogrel

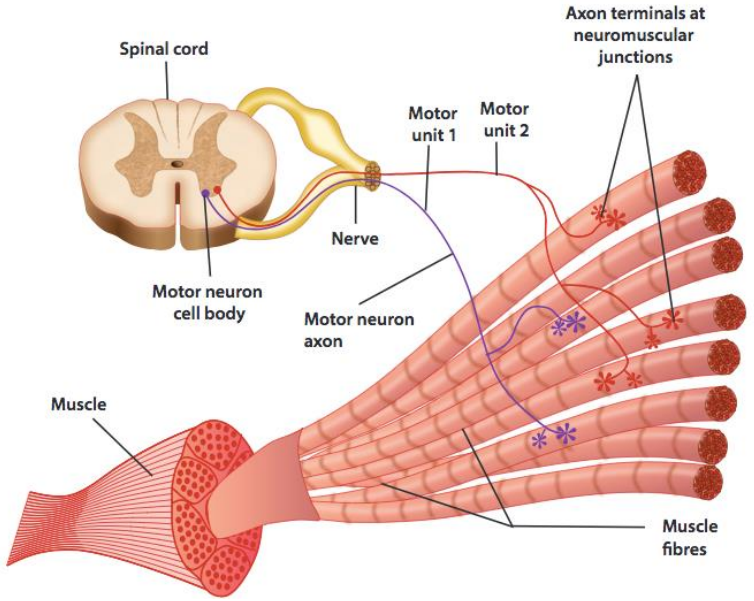
Institute of Myology

The ERN EURO-NMD is funded by the European Commission under the EU4Health programme (EURO-NMD 23-27 — 101156434 — EU4H-2023-ERN2-IBA)

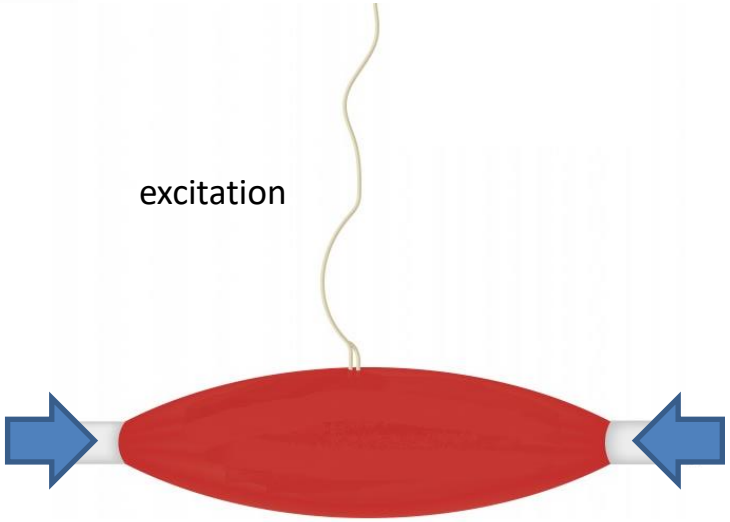
Preliminary remarks

- *I have taken the word "device" on a very broad sense*
- *This survey is not exhaustive*
- *I am far to be an expert in most of the various techniques*
- *I will not deliver a comparison between the devices to discuss what is the best*
- *I will go fast and will not enter into technical details*
- *I have to disclose a link of interest with some of the devices/methods because they have been developed in my lab*

Complementarity of measurements

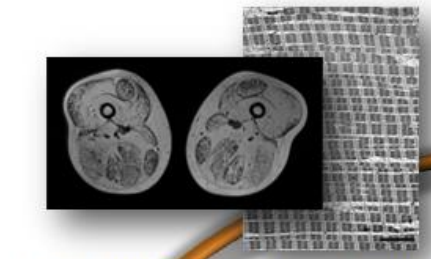


- *Muscle = organized and excitable tissue aiming to produce tension and generate force towards the bones to make them move, organize the movement to fulfill autonomy and quality of life*

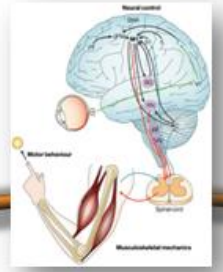


muscle tissue (volume and composition) → strength → mouvement → motor abilities → autonomy → quality of life

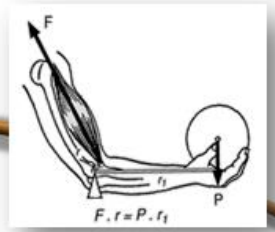
The various levels of investigation



muscle volume and composition



motor control



strength

movement and motor skills

histology morphology

biomarkers

psychology neuropsychology

autonomy

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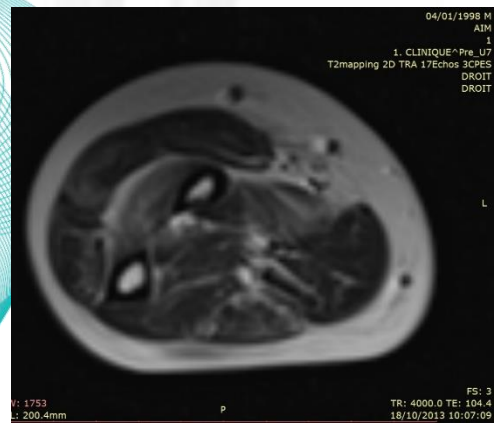
Exemple : distal measurements

- *Imaging*
- *EMG (CMAP)*
- *Strength*
- *Dexterity test (Purdue, 9 Hole Peg Test)*
- *Scales (AbilHand, Cochin)*

ABILHAND - Manual Ability Measure
English version

Patient _____ **Date** _____

	How **DIFFICULT** are the following activities?	**Impossible**	**Difficult**	**Easy**	**?**
1.	Pulling up the zipper of trousers		X		
2.	Peeling onions	X			
3.	Sharpening a pencil		X		
4.	Taking the cap off a bottle		X		
5.	Filing one's nails				X
6.	Peeling potatoes with a knife		X		
7.	Buttoning up trousers	X			
8.	Opening a screw-topped jar		X		
9.	Cutting one's nails				X
10.	Tearing open a pack of chips			X	
11.	Unwrapping a chocolate bar			X	
12.	Hammering a nail	X			
13.	Spreading butter on a slice of bread		X		
14.	Washing one's hands			X	
15.	Buttoning up a shirt		X		



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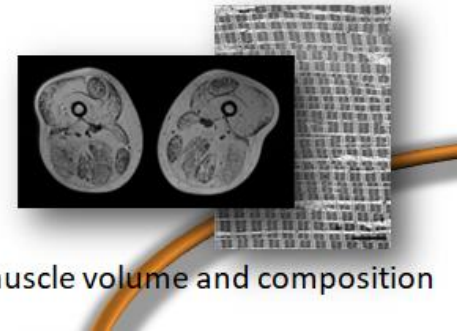
Imaging techniques


muscle volume and composition

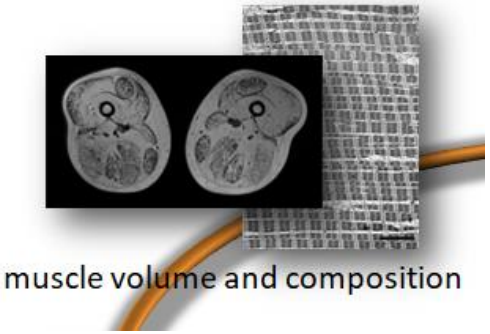
- *Magnetic resonance imaging (MRI)*

	Qualitatively		Quantitatively
• **Trophicity**	Normal, hypo-, Hyper *(T1w)*	→	CSA in cm^2 Volume in cm^3 *(Out of Phase of Dixon)*
• **Chronic degenerative changes**			
# fatty replacement muscle	Grading 1-4 *(T1w)*	→	% fatty infiltration *(Water-Fat « Dixon »)*
# fibrosis	-----		% interstial collagen *(?? UTE ?? DEMRI)*
• **« Disease activity »**	Fat Sat-T2w *(STIR)*	→	T2 in ms *(MultiTE SE no Fat Sat; B1 mapping)*

Fig. 1. Skeletal muscle tissue characterization by NMR imaging. Comparison of qualitative and quantitative approaches. CSA: cross-sectional area; UTE: ultra-short echo time; DEMRI: delayed enhancement MRI; Fat Sat: fat saturation.

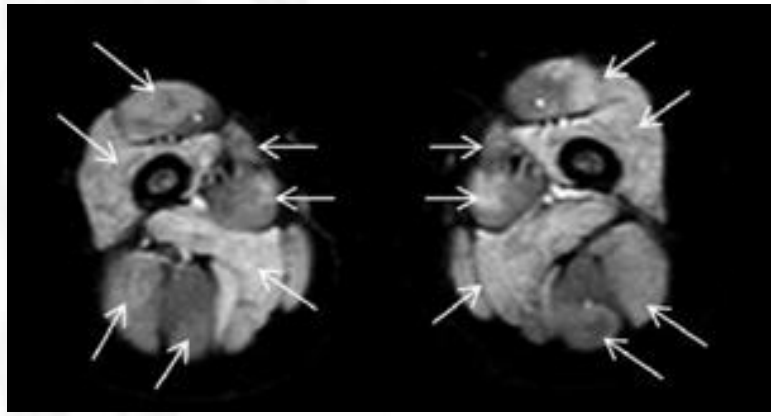
from Carlier et al (2016)

Imaging techniques

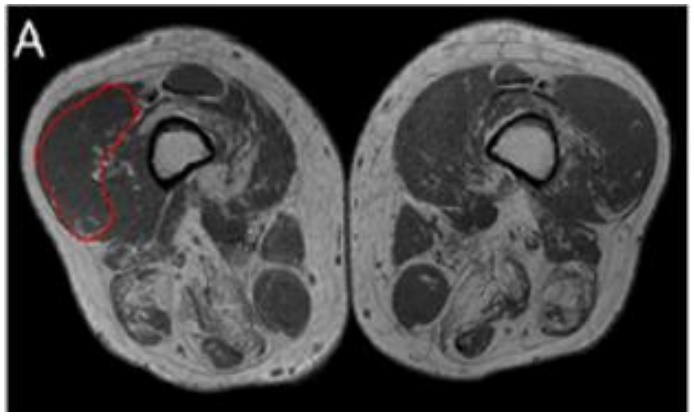


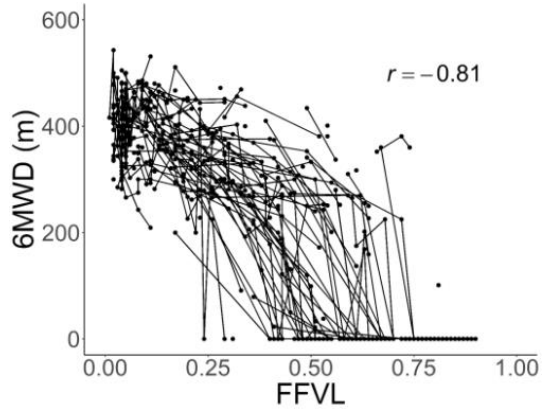
- *Magnetic resonance imaging (MRI)*

T2-weighted



T1-weighted





Early signs of active muscle damage → Muscle fatty replacement → Clinical signs (loss of function)

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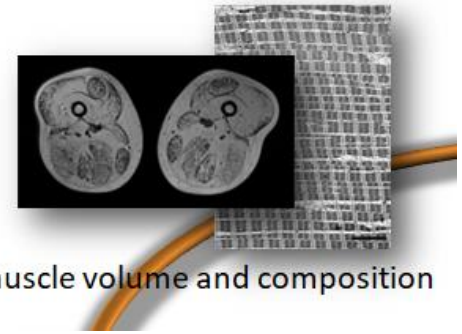
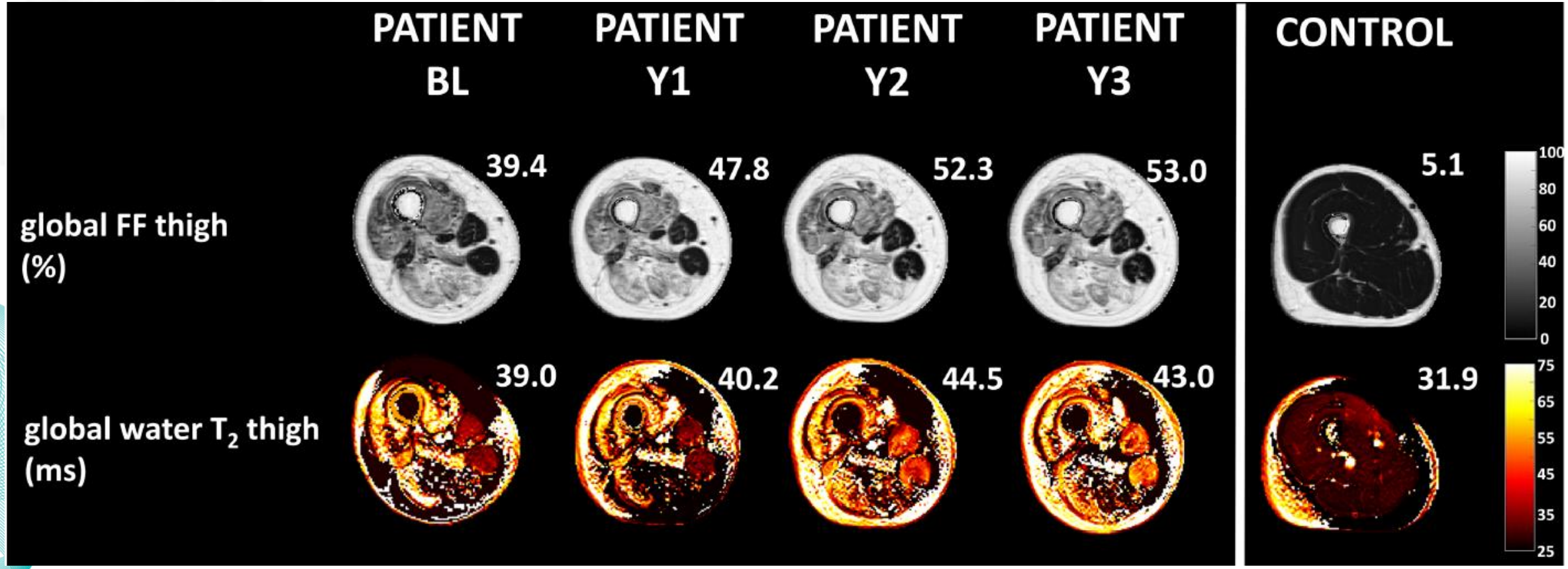
Imaging techniques



- *Magnetic resonance imaging (MRI)*

patient with LGMD2B



from Reyngoudt et al (2022)

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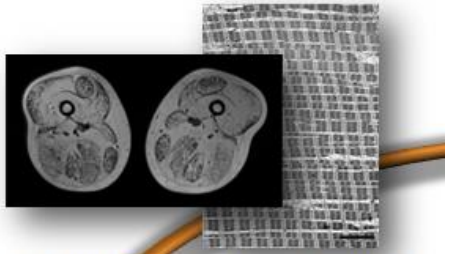
Imaging techniques



- *Magnetic resonance spectroscopy (MRS, ^{1}H, ^{31}P, ^{23}Na)*

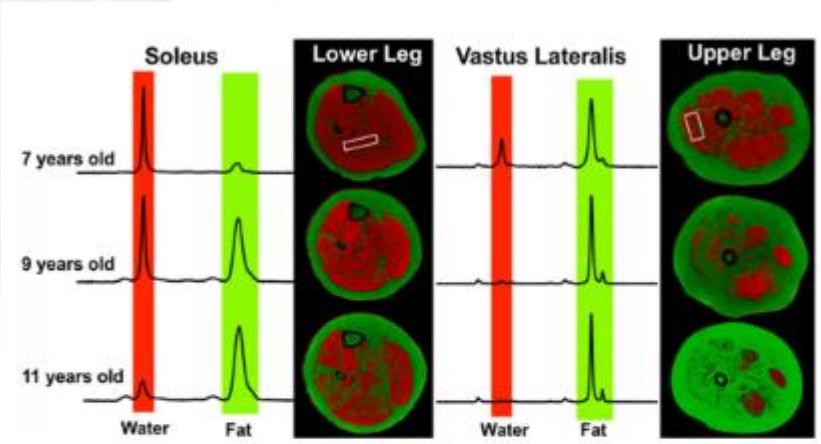
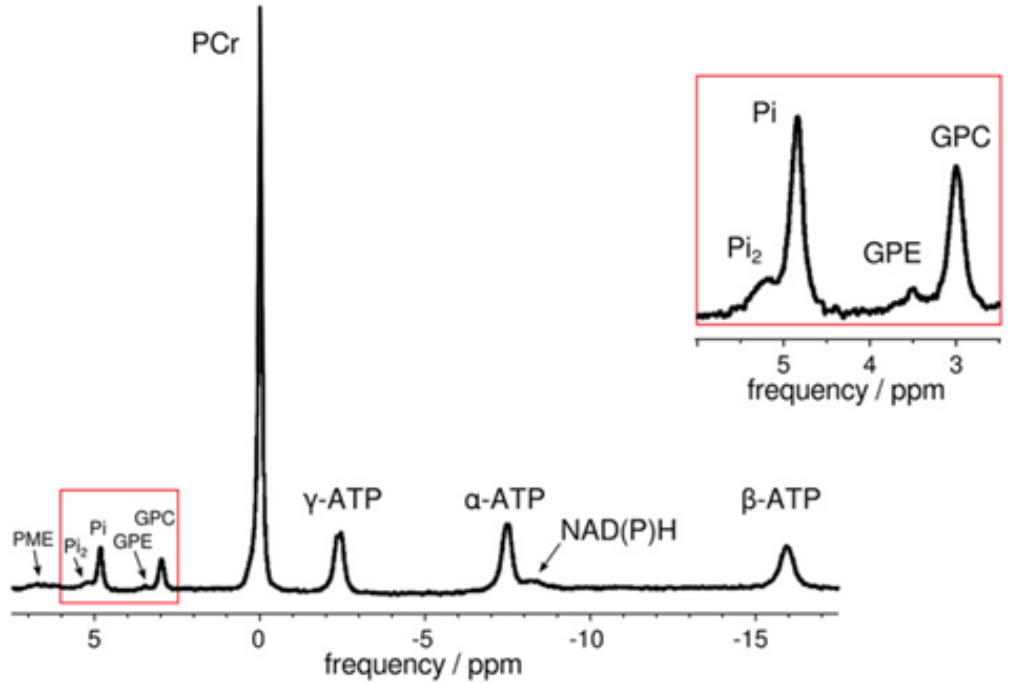


FIGURE 1 Magnetic resonance (MR) spectra and images from a single subject capturing 4 years of disease progression. In these transaxial images and spectra, red indicates muscle water, and green indicates fat. MR spectroscopy fat fraction is measured from a single voxel, shown as the white rectangles in top images, and quantifies the ratio of the peak areas of fat (green) to the sum of peak areas of fat (green) and water (red).

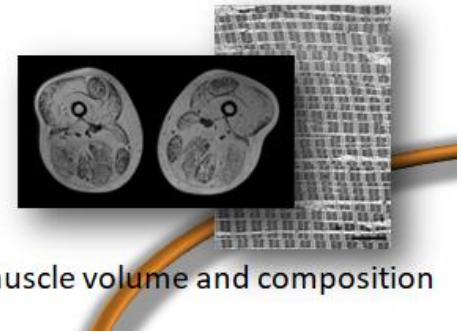
from Kim et al (2023)



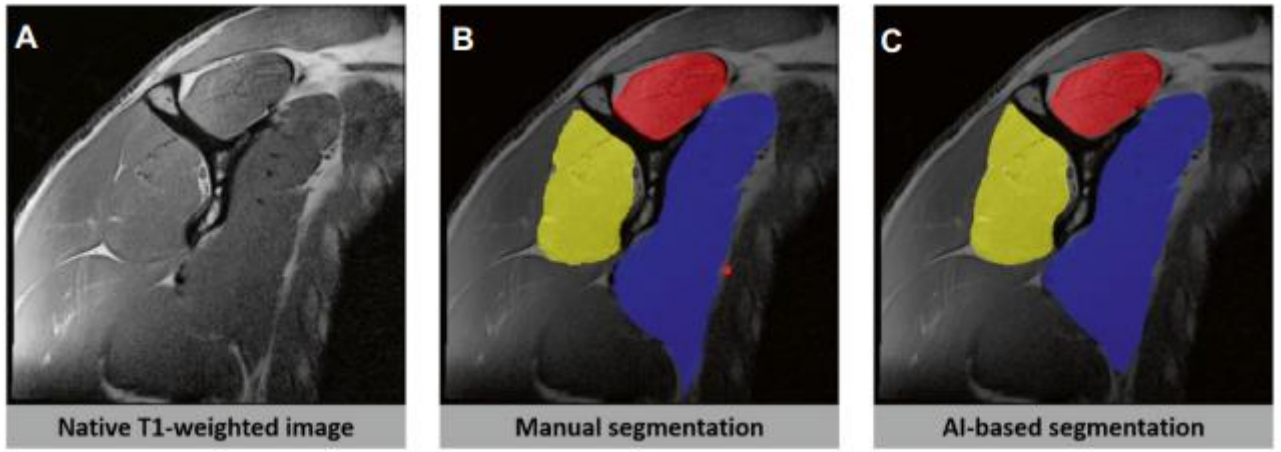
A typical ^{31}P MR spectrum of the resting soleus muscle of a healthy volunteer acquired at 7 T, with the region between 2.5 and 6 ppm enlarged (right). Signals of an extra Pi pool and phosphodiesters (PDE) and phosphomonoesters (PME) are visible. Peak assignments: two signals for inorganic phosphate (Pi and Pi_2), glycero-3-phosphocholine (GPC), glycero-3-phosphoethanolamine (GPE), phosphocreatine (PCr), three signals for ATP and pyridine nucleotides (NADPH/NADH). Data were acquired using a pulse-acquire sequence with a block pulse of 200 µs with a 5-cm surface-coil (*TR* = 5 s, bandwidth = 5 kHz, 2048 data points; 128 averages).

from Meyerspeer et al (2021)

Imaging techniques


muscle volume and composition

- *MRI and AI*
- *Accuracy of a machine learning muscle MRI-based tool for the diagnosis of muscular dystrophies (Verdu-Diaz et al, 2020)*
- *Texture analysis of muscle MRI: machine learning-based classifications in idiopathic inflammatory myopathies (Nagawa et al, 2021)*
- *A Deep Learning Algorithm for Automatic 3D Segmentation of Rotator Cuff Muscle and Fat from Clinical MRI Scans (Riem et al, 2023)*



from Fritz and Fritz (2022)

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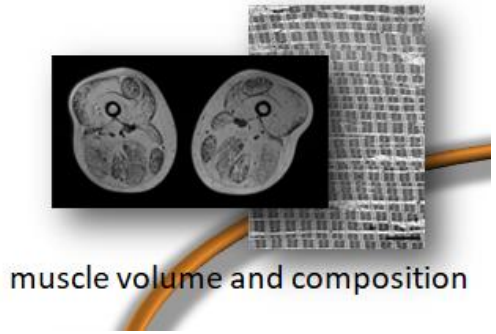
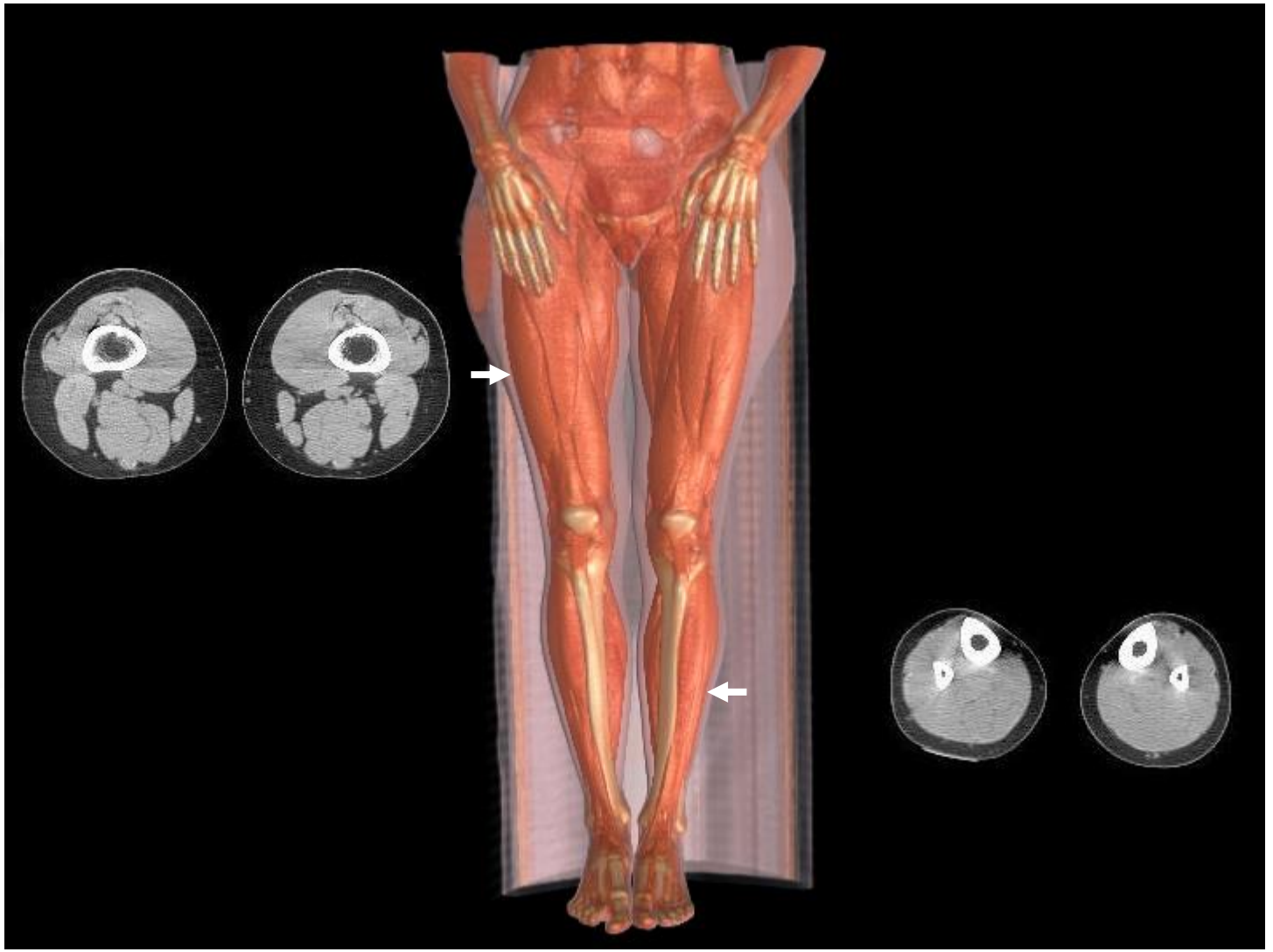
Imaging techniques



- *CT-scan*



healthy woman
24 y

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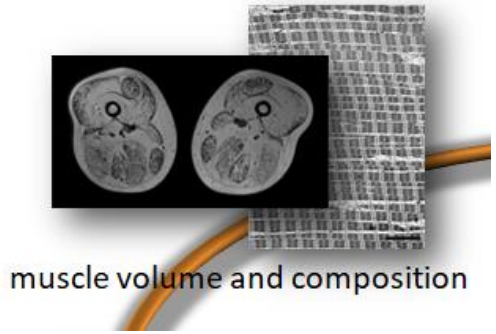
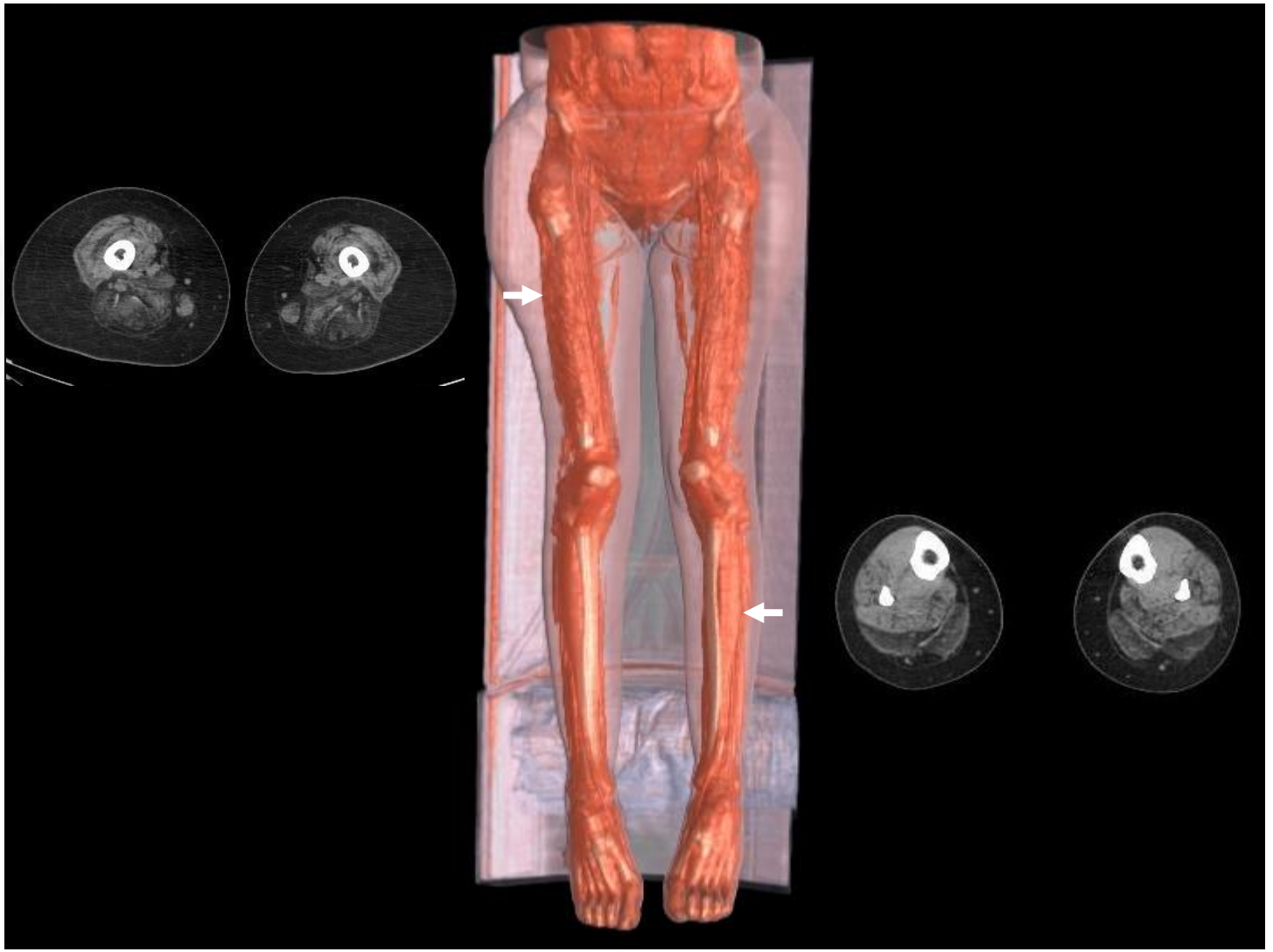
Imaging techniques



- *CT-scan*



woman with LGMD2A
24 y

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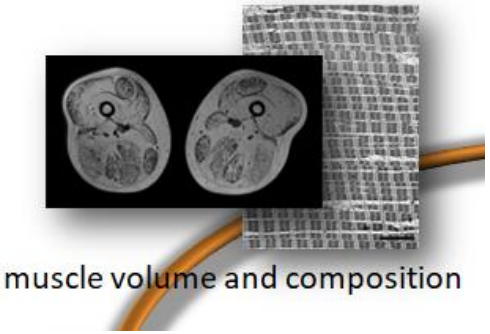
Imaging techniques



- *CT-scan*

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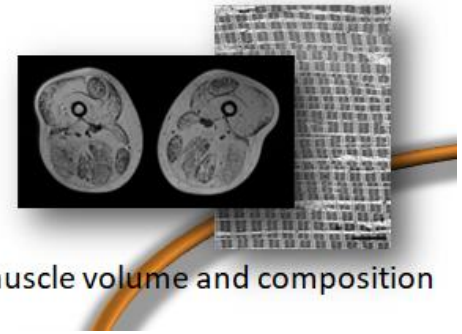
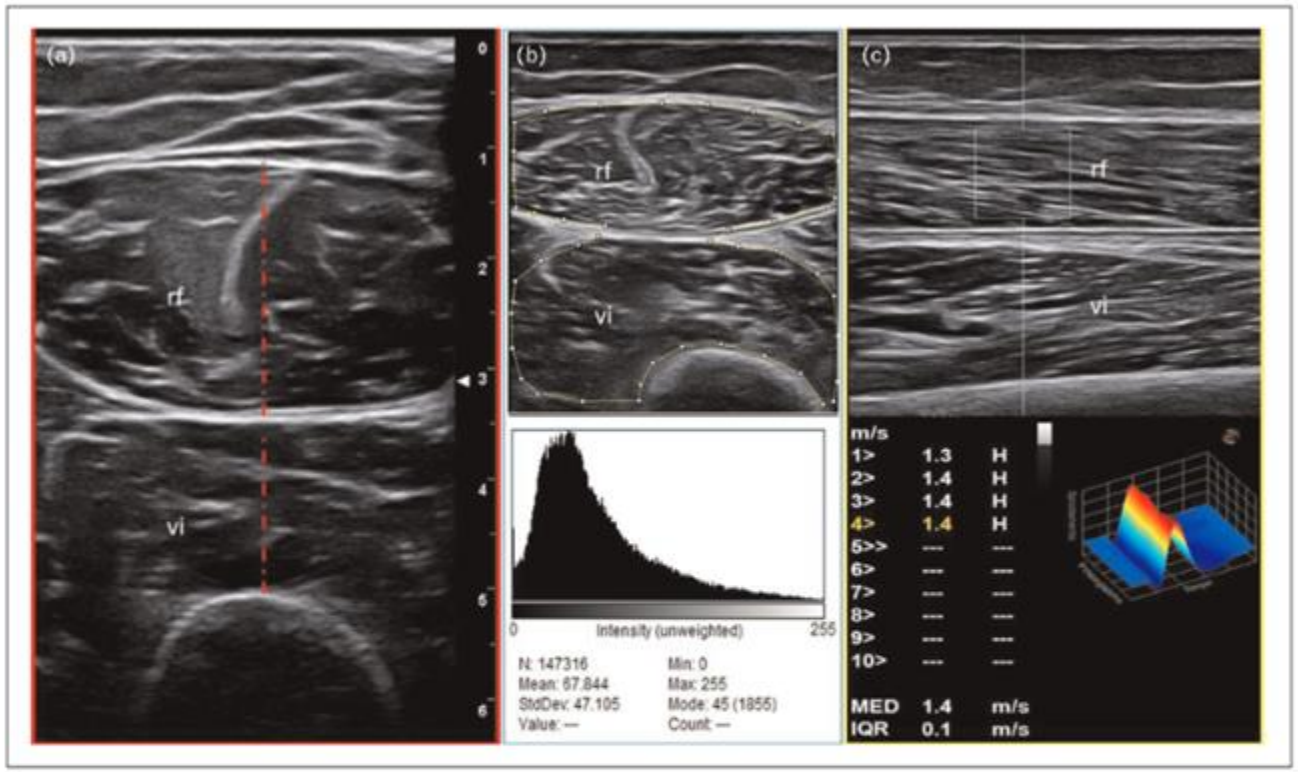
Imaging techniques



- *Ultrasound*



from Tan et al (2023)

FIGURE 2. 'Multimodal' assessment of quadriceps muscle mass (a), muscle quality (b, muscle echogenicity assessment using ImageJ analysis) and muscle stiffness (c, point shear wave elastography) in two healthy individuals. In figure a, the typical 'starry night' appearance of a normal muscle (28–year-old man) can be observed. A transverse approach is preferred for the measurement of muscle thickening (red dashed lines) of the rectus femoris (rf) and vastus intermedius (vi) muscles. Figure b shows a moderate increase in muscle echogenicity in a 55-year-old woman. Muscle echogenicity can be measured using a dedicated image analysis program, which measures the gray scale intensity in a region of interest (ROI) utilizing histogram function (i.e. ImageJ). In the same person, muscle stiffness of the rectus femoris is measured using point shear wave elastography (longitudinal approach) and it is expressed by m/s.

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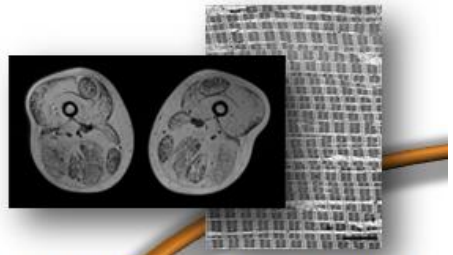
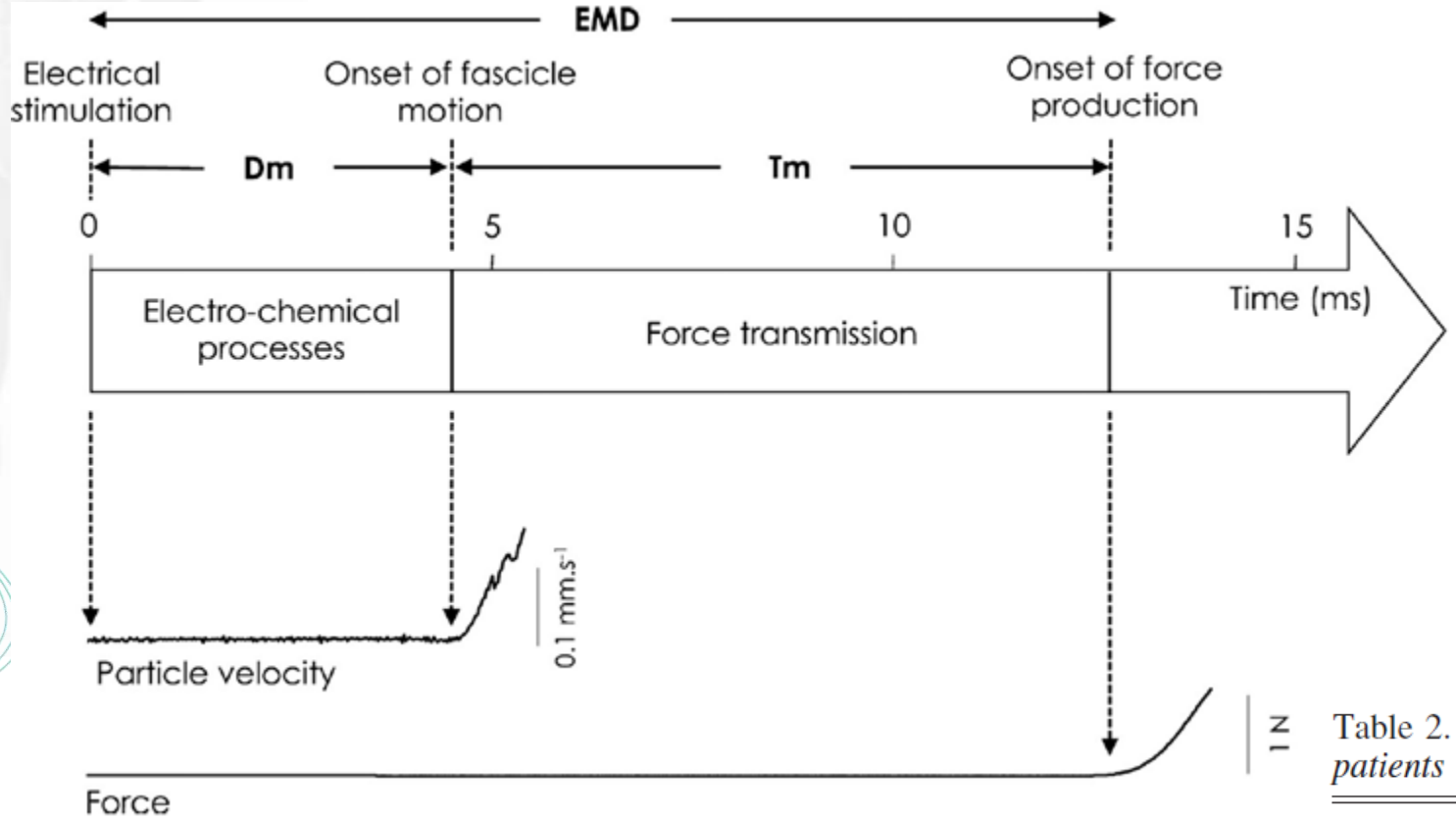
Imaging techniques


muscle volume and composition

- *Ultrasound (ultrafast imaging)*



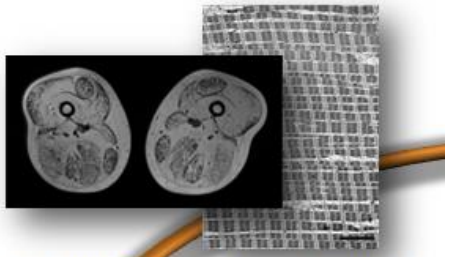
from Lacourpaille et al (2014)

Fig. 1. Representation of the electro-mechanical delay (EMD) and its components. The delay between muscle electrical stimulation and the onset of muscle fascicle motion (particle velocity) is mainly attributed to electrochemical processes [referred to as time delay for muscle contraction (Dm)]. The delay between the onset of fascicle motion and the onset of force production is attributed to the force transmission [referred to as time delay for force transmission (Tm)].

Table 2. *Averaged data for healthy controls and DMD patients*

	n	Evoked Maximal Torque, N·m	EMD, ms	Dm, ms	Tm, ms
Controls	13	2.8 ± 1.7	12.5 ± 1.4	4.6 ± 0.7	7.9 ± 2.0
DMD	13	0.3 ± 0.2*	18.5 ± 3.9*	4.9 ± 1.7	13.6 ± 3.1*

Imaging techniques



muscle volume and composition

- *Ultrasound (anisotropy)*

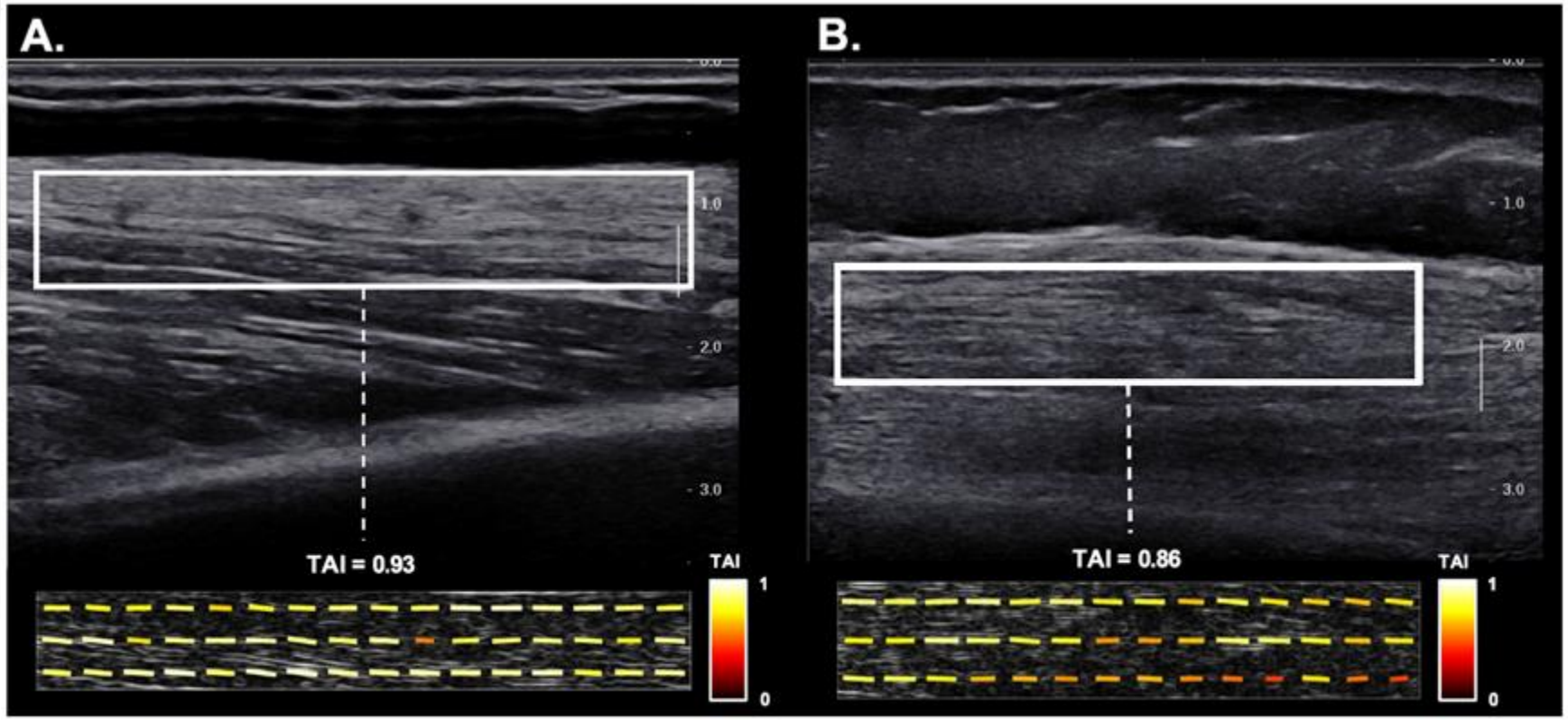


Fig. 2. Texture anisotropy index (TAI) values in moderate (A) and severe (B) muscle impairments in two patients with inclusion body myositis. Patients in (A) and (B) had maximal isometric elbow flexor strength corresponding to 69% and 42% of predicted values, respectively. Gray-scale index was 0.62 and 0.75, respectively.

from Dubois et al (2018)

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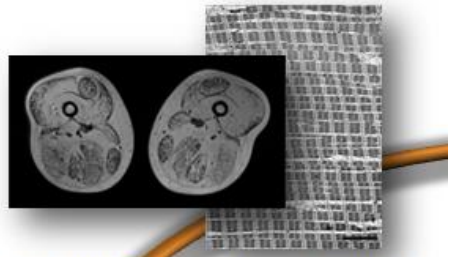
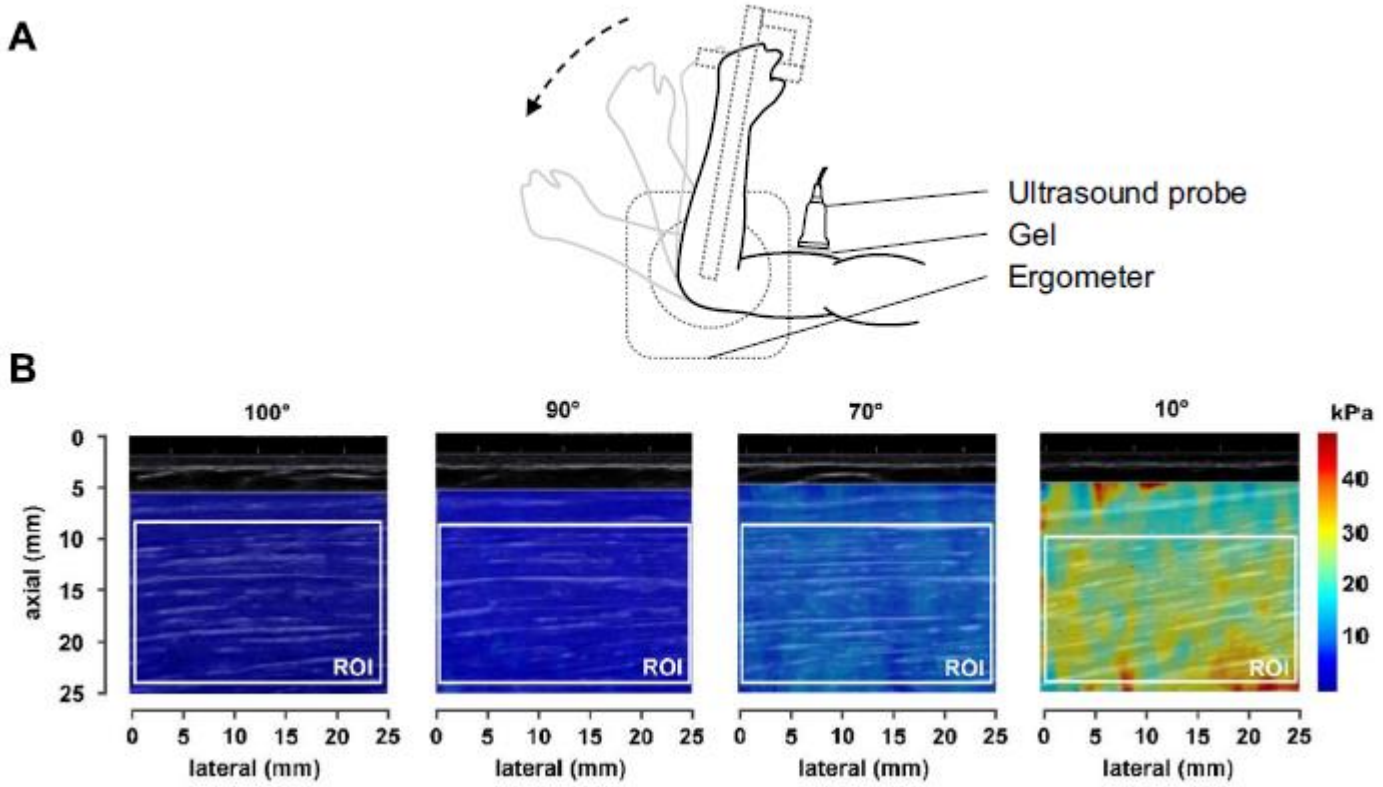
Imaging techniques


muscle volume and composition

- *Shear wave elastography (shear modulus)*



from Bachasson et al (2018)

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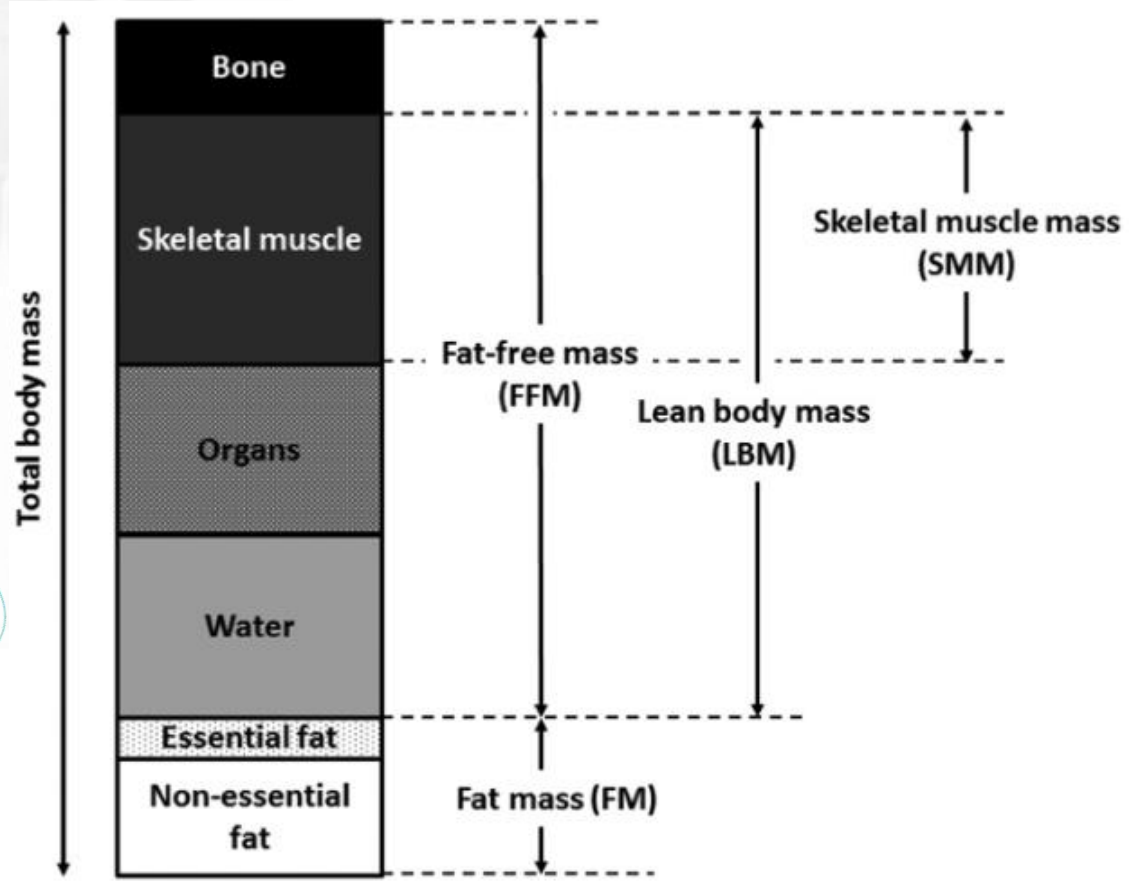
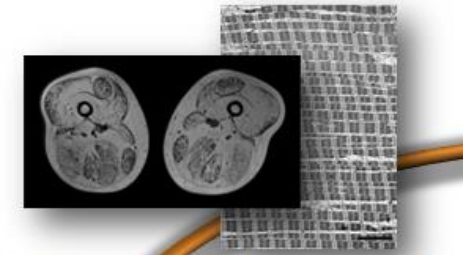
Imaging techniques

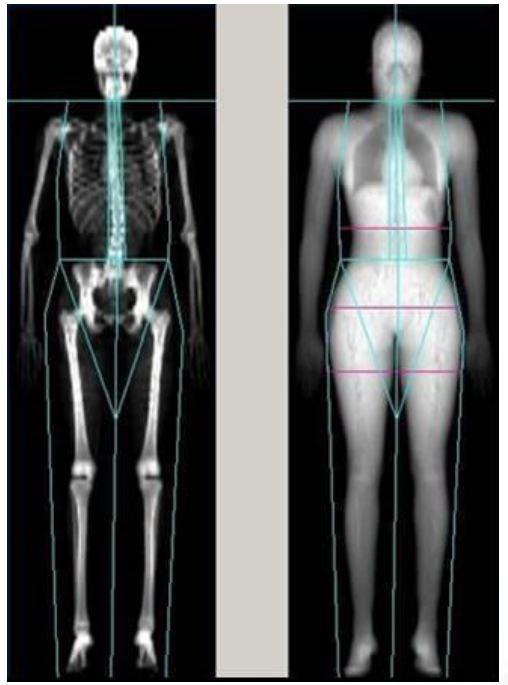
- *DEXA (dual-energy X-ray absorptiometry)*



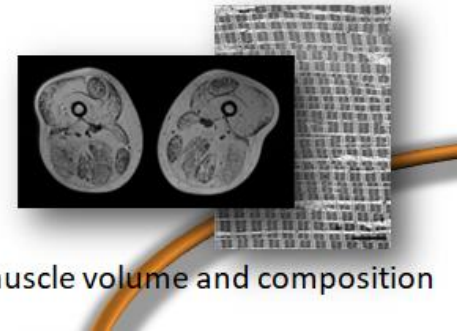
from Nuijten et al (2021)



muscle volume and composition



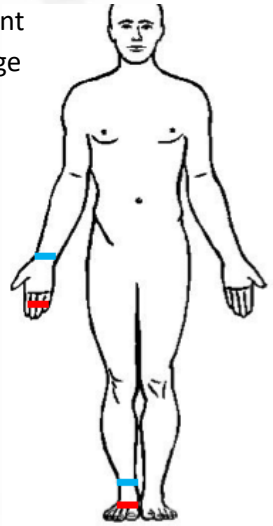
Imaging techniques



- *Bioelectrical impedance analysis (BIA)*

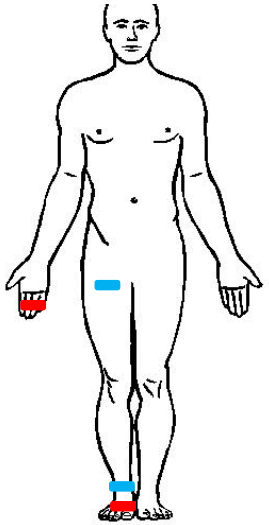
Whole-Body

current
voltage



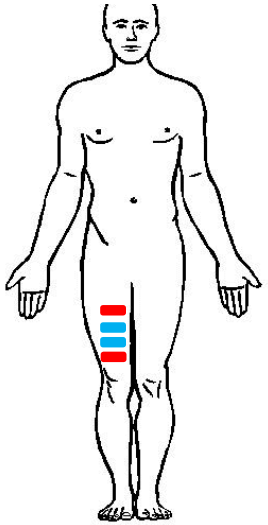
InBody

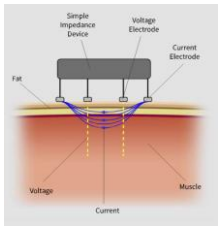
Segmental



BIOPARHOM

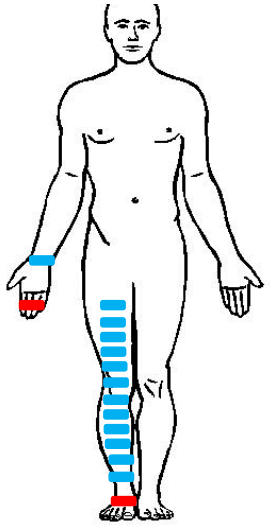
Local
(misleadingly named EIM)

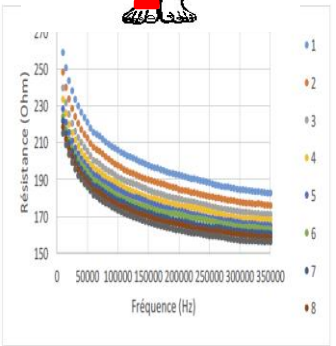




SKULPT

Differential





Seward Rutkove Laboratory

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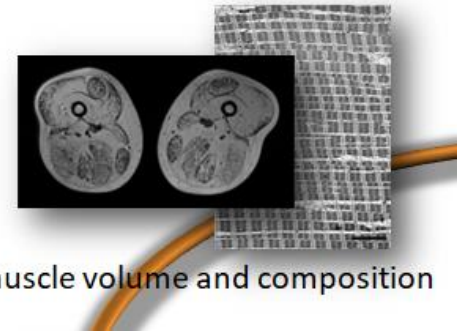
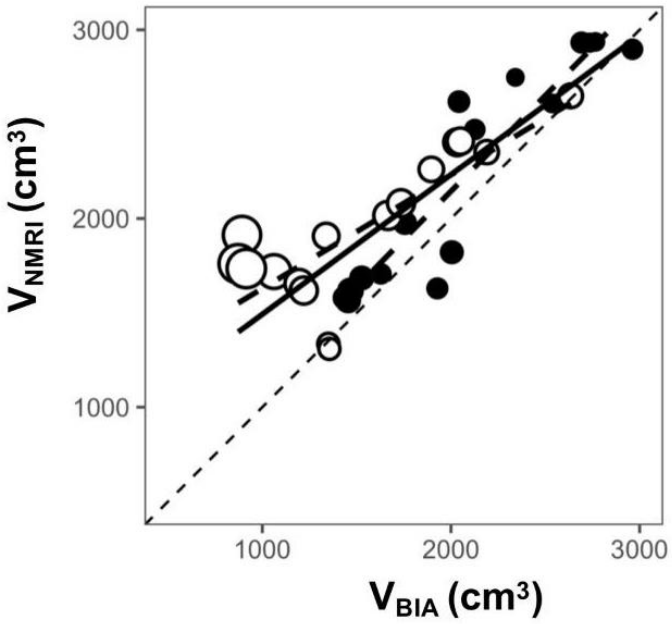
Imaging techniques

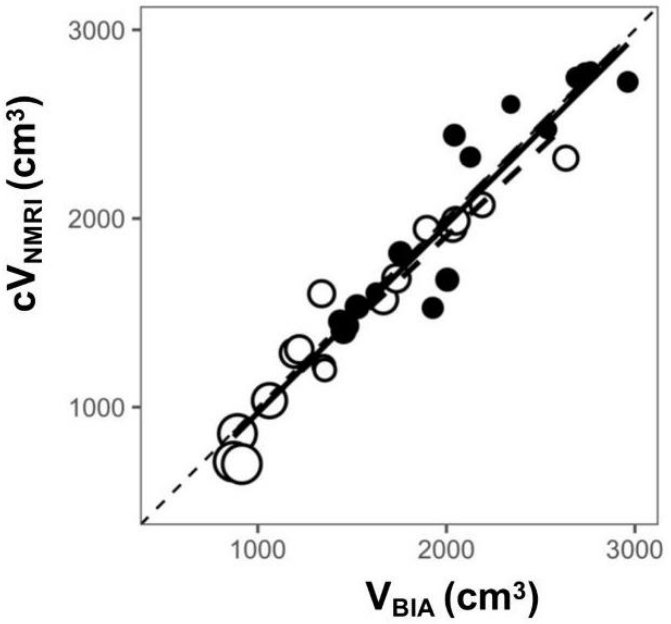


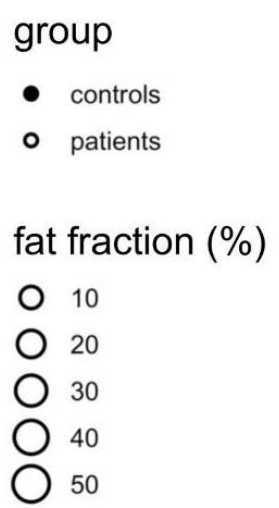
- *Bioelectrical impedance analysis (BIA)*

A. cross-sectional area

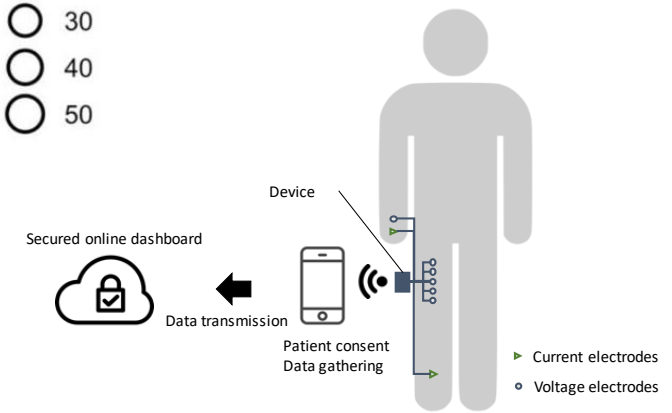


B. lean cross-sectional area (fat removed)

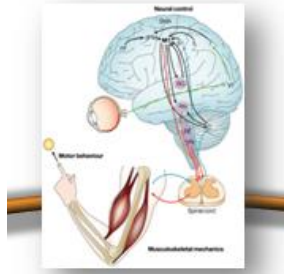




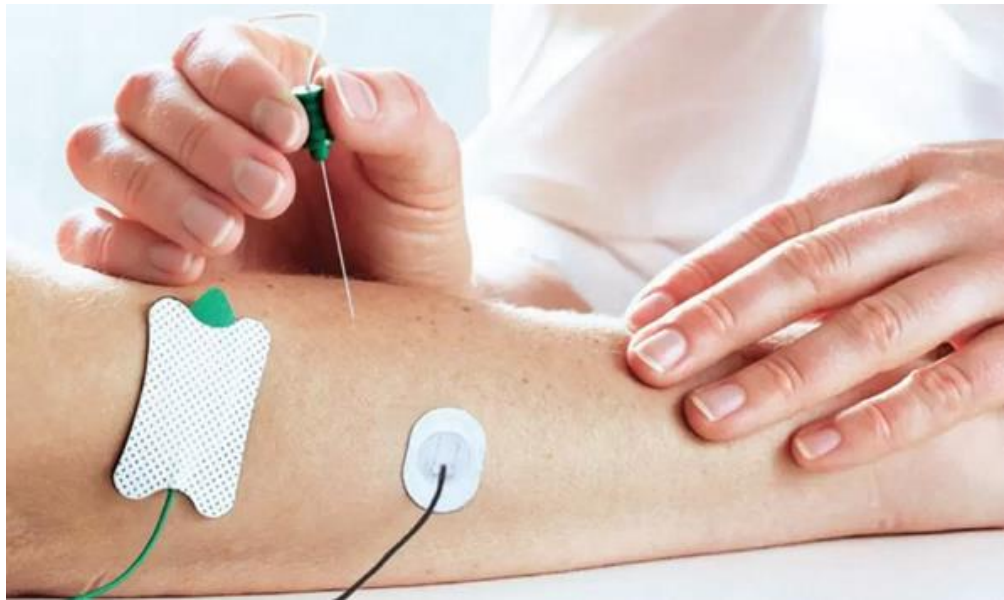
from Bachasson et al (2021)



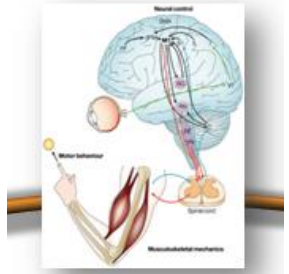
Electrophysiological techniques


motor control

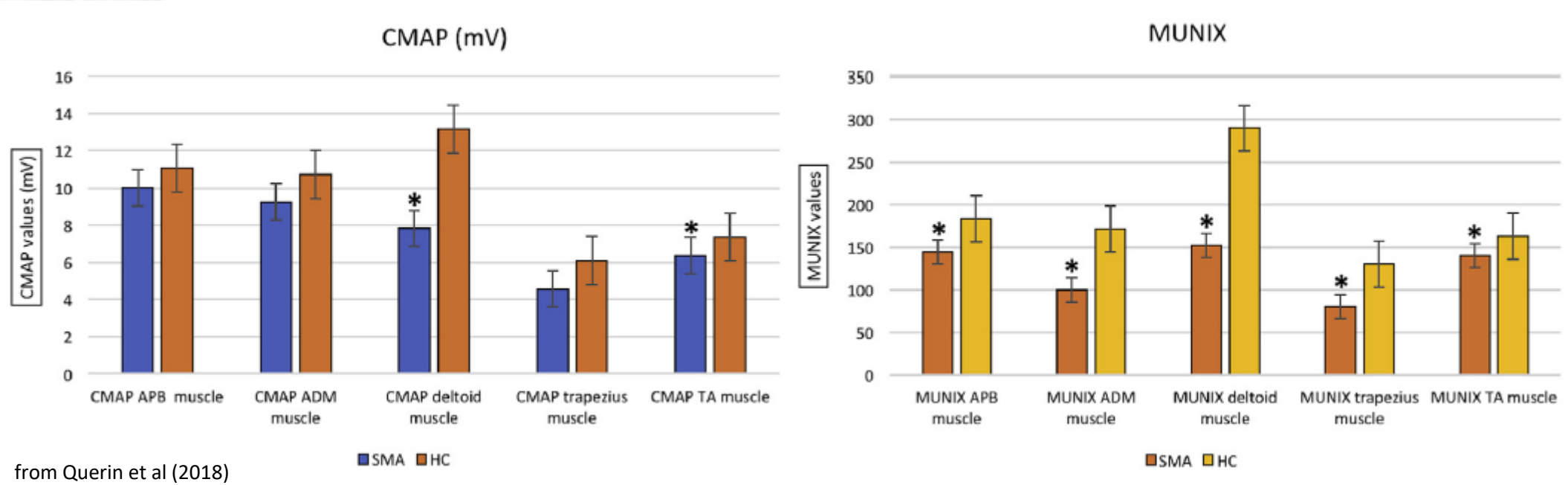
- *Conventional ENMG*
  - ✓ Detection (needle or surface electrodes)
  - ✓ Nerve conduction velocity (motor and sensitive nerves)
  - ✓ Evoked potentials (motor, somatosensory, visual, auditory…)
  - ✓ Rest, voluntary contraction, electrical or magnetic stimulation, superimposed stimulation, reflexes…
- *Numerous signal detection and processing methods*
- *Hardly used in multicenter studies*



Electrophysiological techniques


motor control

- *Motor unit number estimation (MUNE)*
  - ✓ CMAP
  - ✓ Incremental stimulation
  - ✓ Multiple point stimulation
  - ✓ Spike triggered averaging and decomposition
  - ✓ Statistical MUNE
  - ✓ MUNIX…



from Querin et al (2018)

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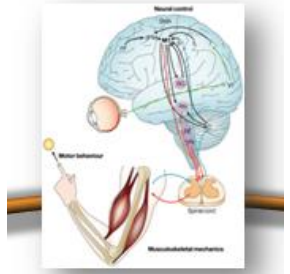
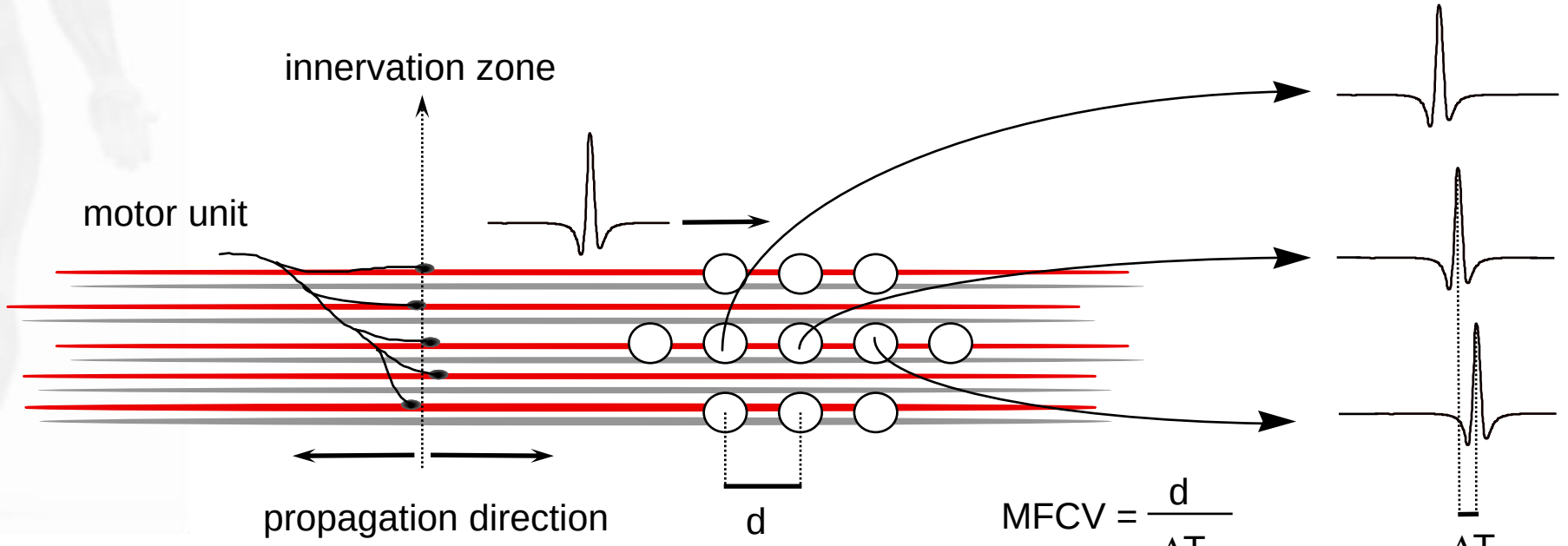
Electrophysiological techniques


motor control

- *Muscle fibre conduction velocity (high spatial resolution EMG)*



from Hogrel (2005)

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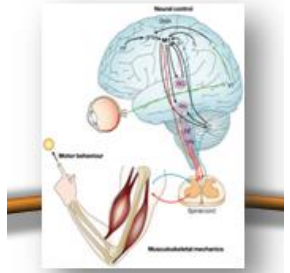
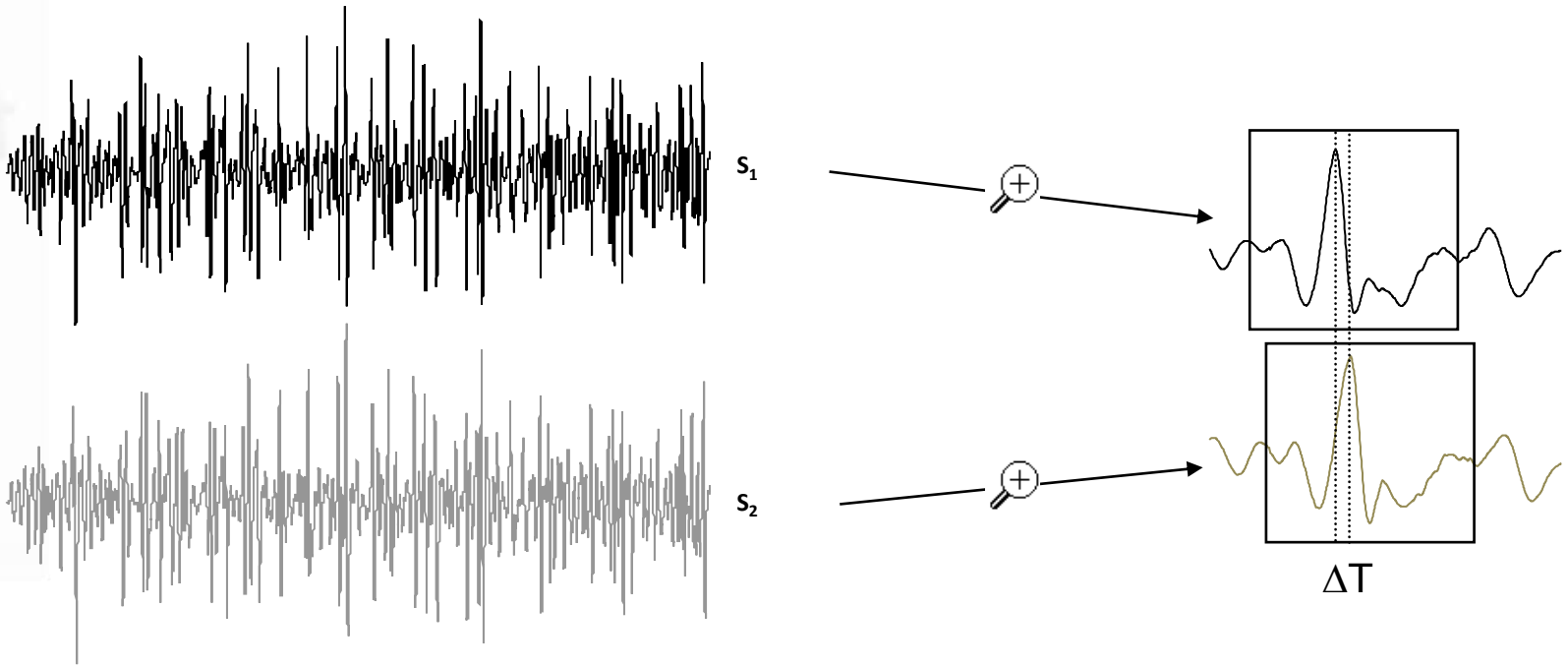
Electrophysiological techniques



- *Muscle fibre conduction velocity*



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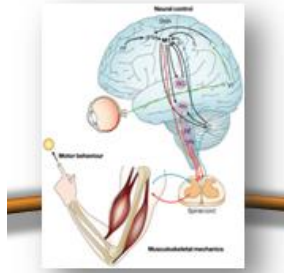
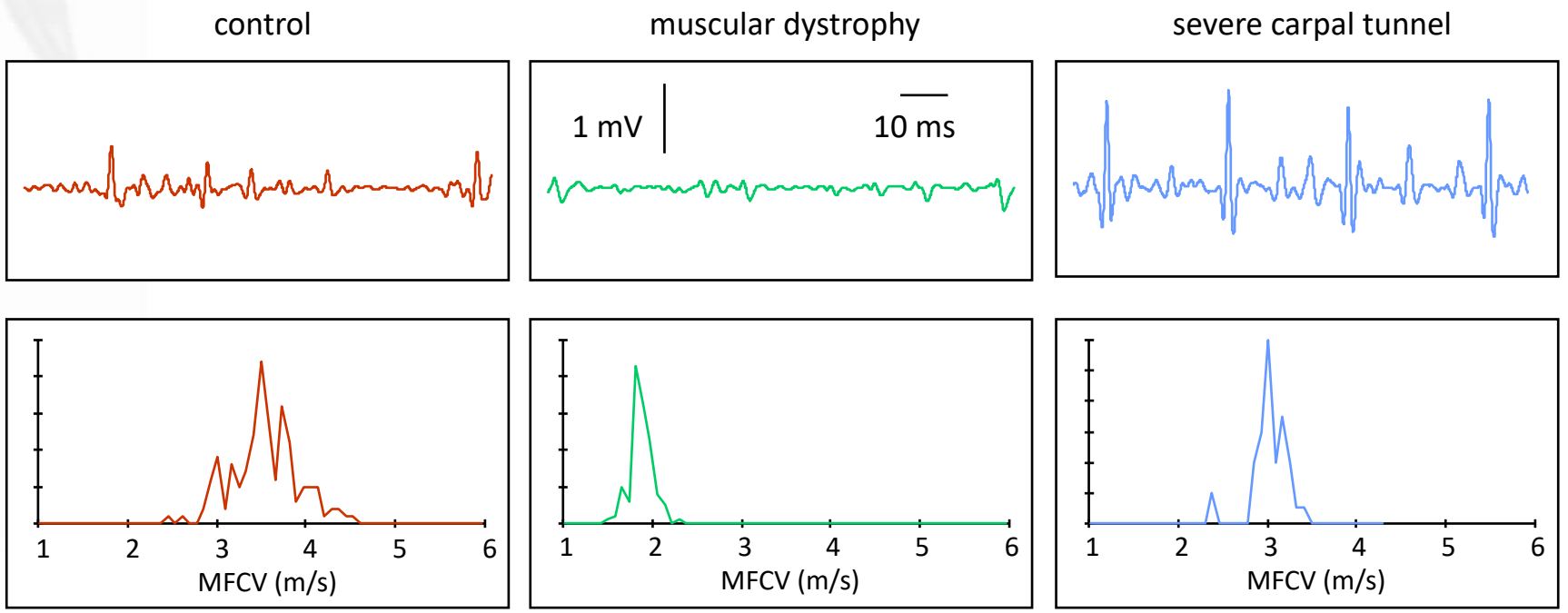
Electrophysiological techniques


motor control

- *Muscle fibre conduction velocity*

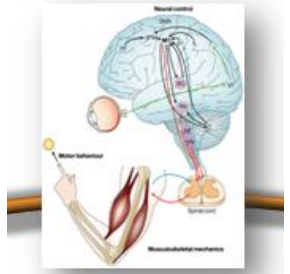


MFCV=3.54 ±0.37 $m.s^{-1}$

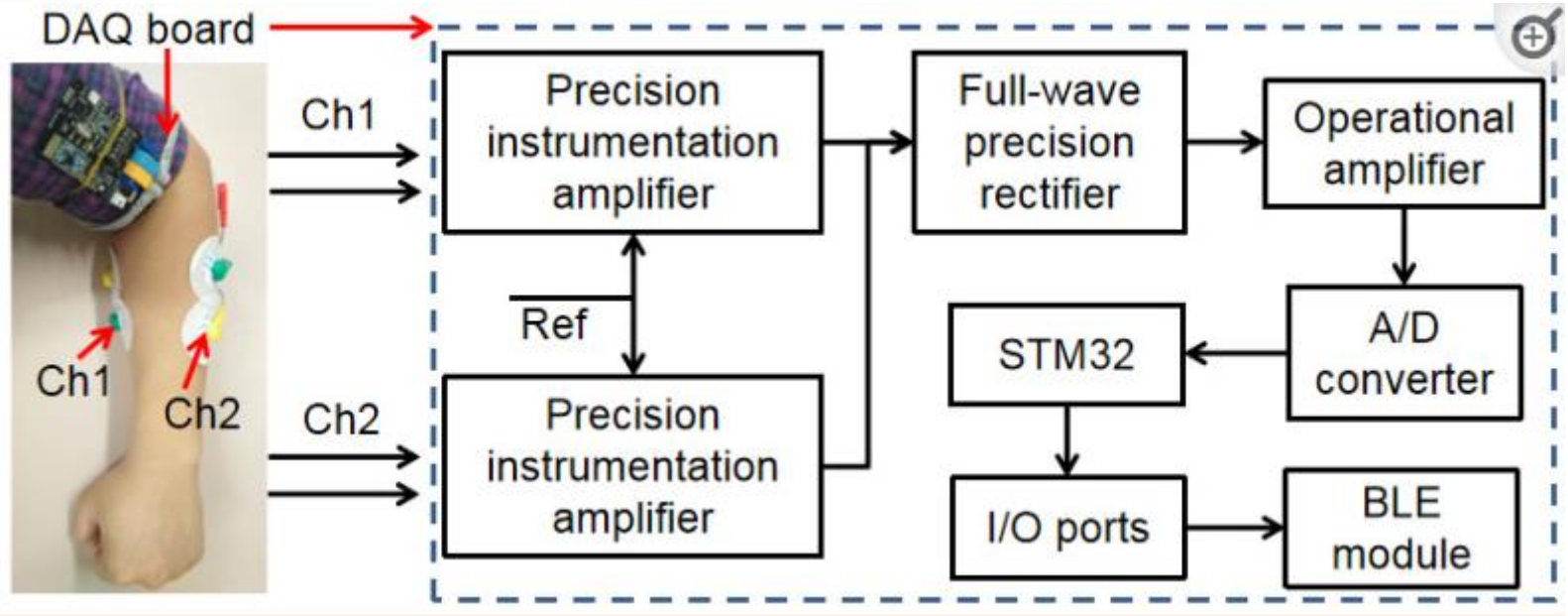
MFCV=2.17 ±0.13 $m.s^{-1}$

MFCV=3.01 ±0.20 $m.s^{-1}$

Electrophysiological techniques

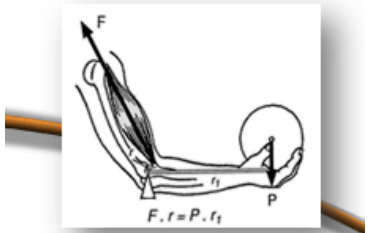

motor control

- *Several wearables to monitor muscle activity*
  - ✓ *for muscle fatigue monitoring (using muscle fibre conduction velocity)*
  - ✓ *for controlling robotic arms*
  - ✓ *for rehabilitation*
  - ✓ *for biofeedback*



from Zhao et al (2020)

Strength assessment



strength

- Manuel muscle testing (MMT)
- Hand-held dynamometry (HHD)
- Fixed dynamometry (FXD - also know as QMT)
- Isokinetic dynamometry (IKD)
- Specific dynamometry





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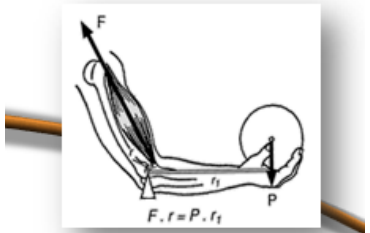
Strength assessment



strength

- New dynamometers every year

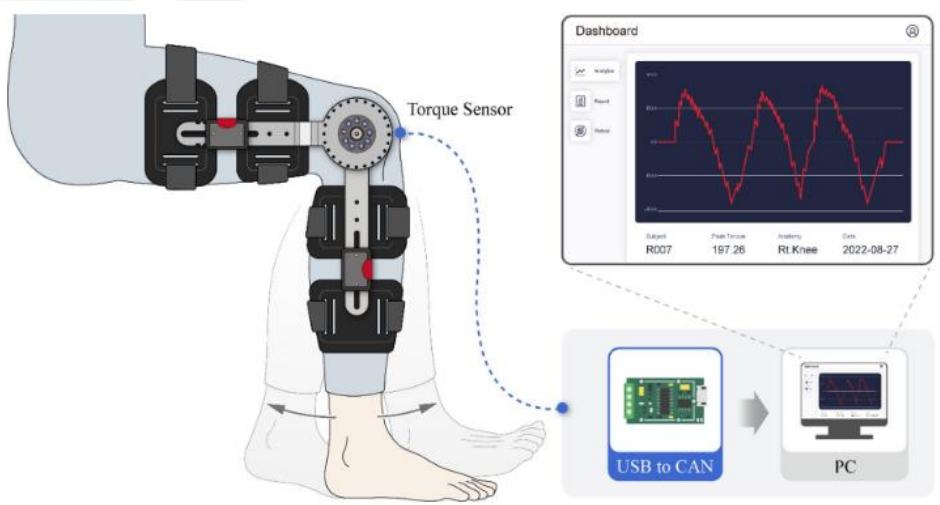


Figure 5. Conceptual diagram and visual representation of measurement using the device.

from Park et al (2024)

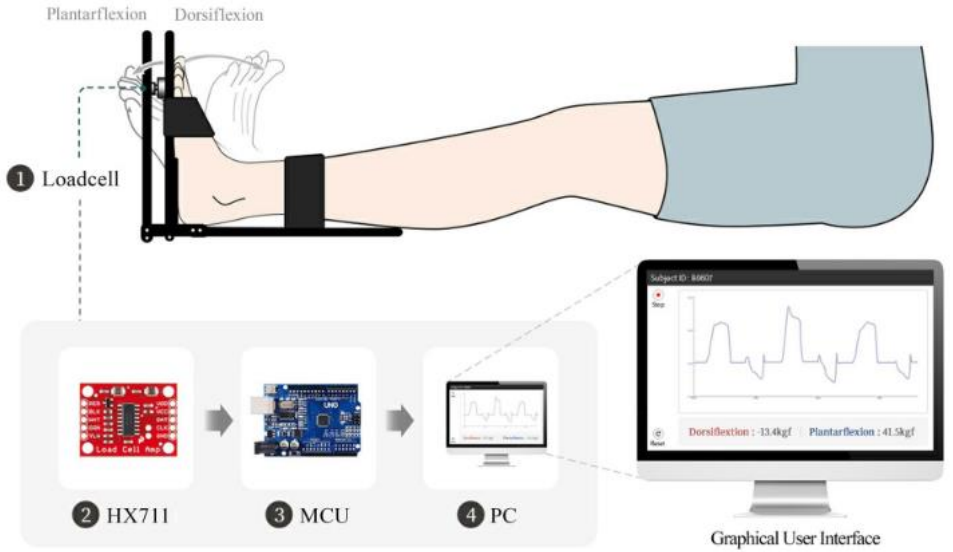
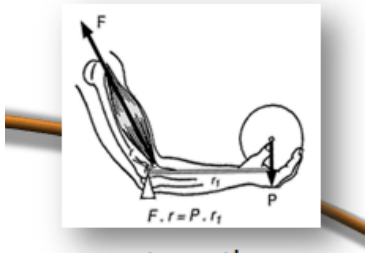


Figure 5. Graphical diagram of the overall flow of the dynamometry system.

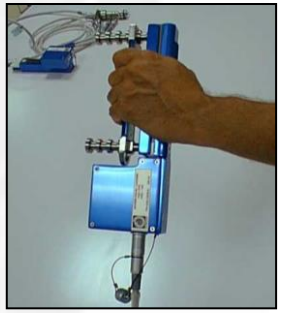
from Cho et al (2023)

Strength assessment

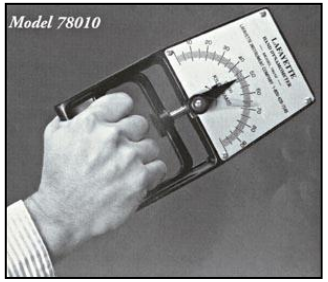
- The particular case of grip strength assessment



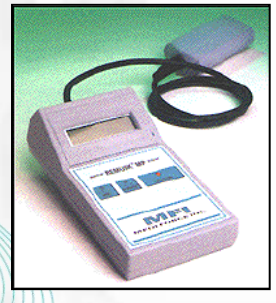
strength



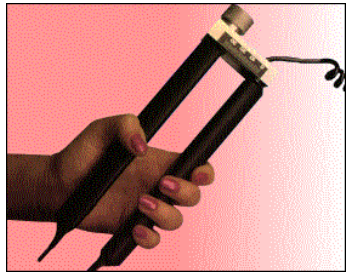


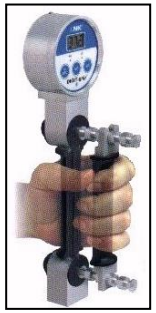



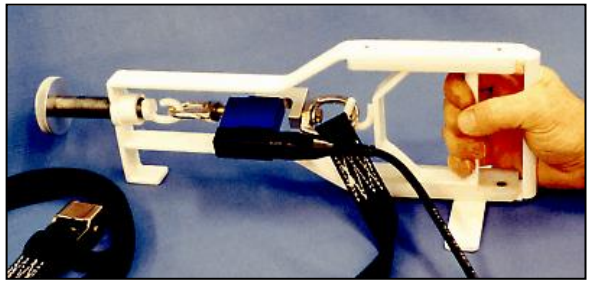




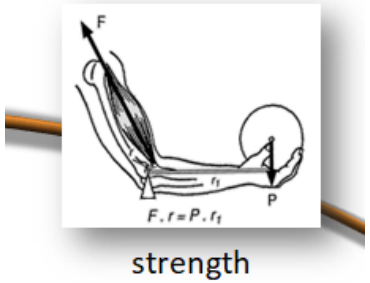


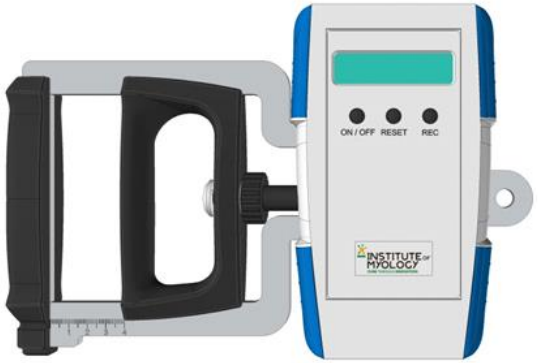
Strength assessment



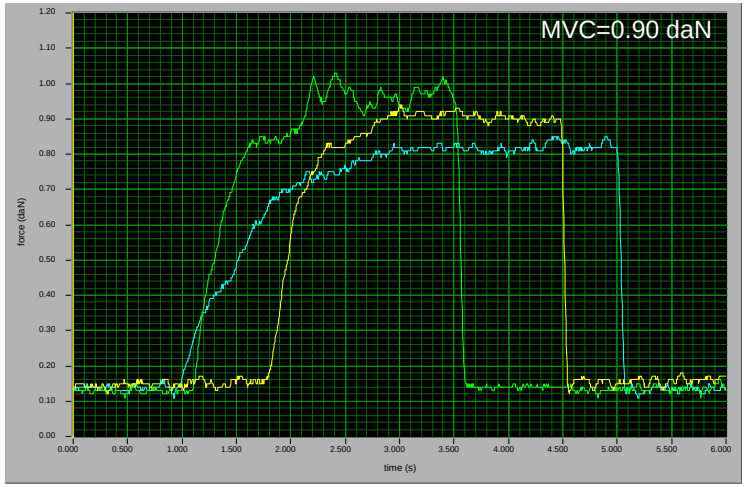
strength

- Specific dynamometry (exemple of the MyoTools)

A



B



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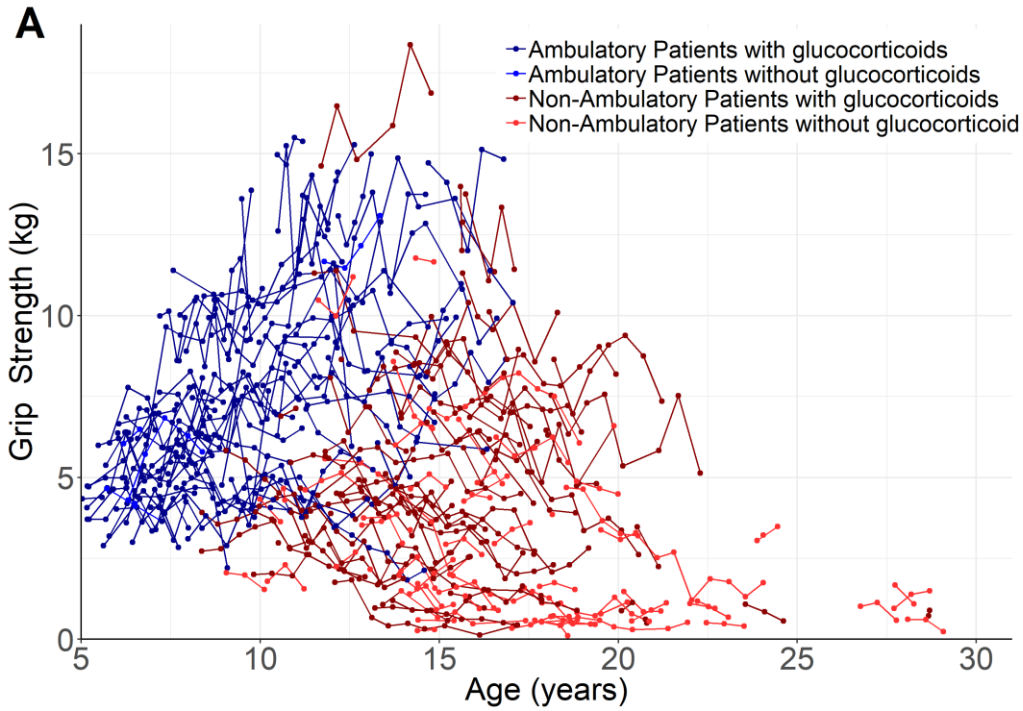
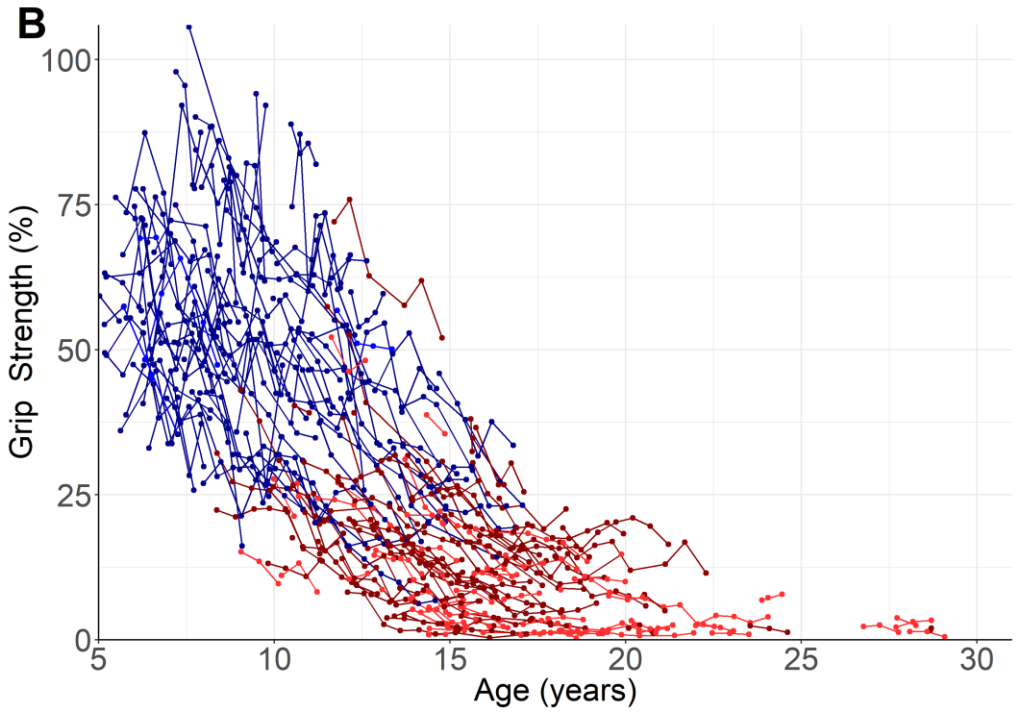
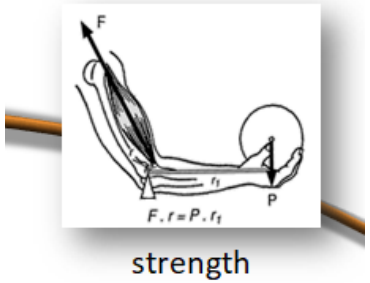
Strength assessment

- Grip strength in DMD
- Using proper dynamometers make the measurements on the weakest patients still feasible and reliable







strength

from Hogrel et al (2020)

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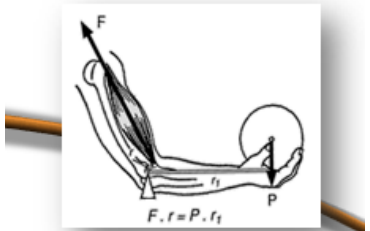
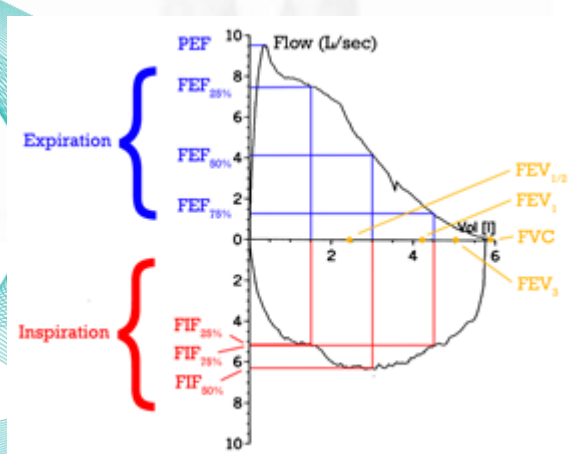
Respiratory muscles

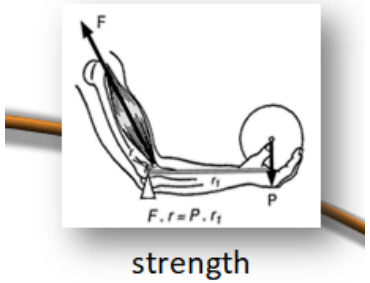


strength

- Respiratory assessements
  - ✓ FVC, FEV1
  - ✓ SNIFF test
  - ✓ Cough test
  - ✓ MIP, MEP
- Indirect measures of force (pressure), muscle length (volume) and contraction velocity (flow rate)

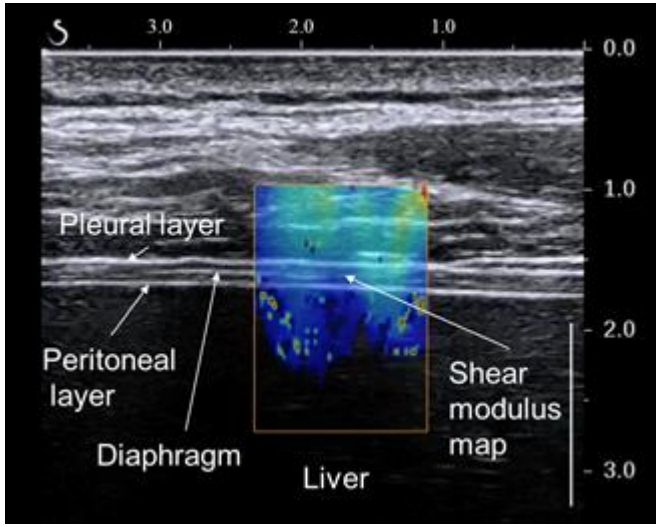


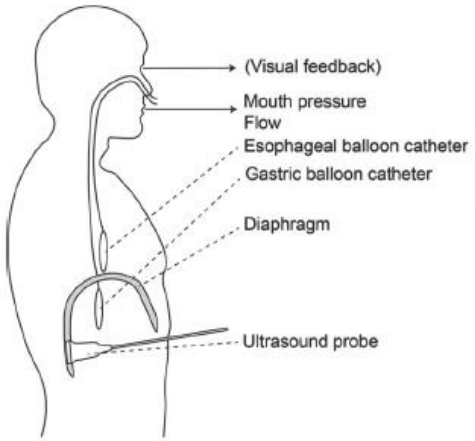
Respiratory muscles

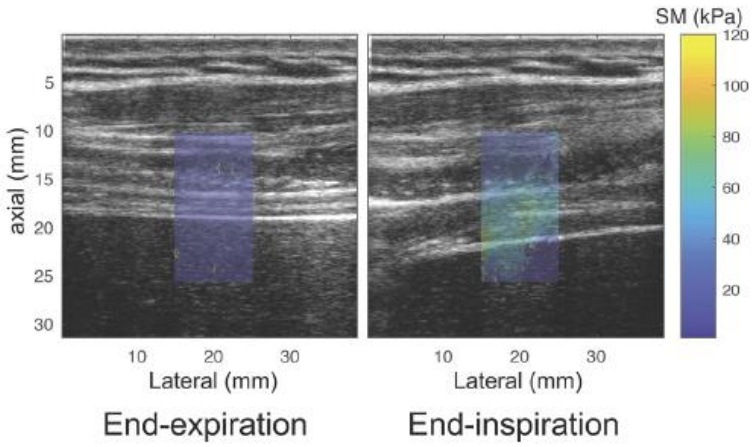


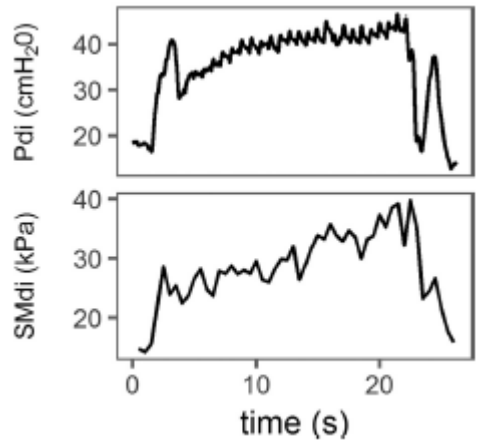
strength

- *Ultrasound : diaphragm*



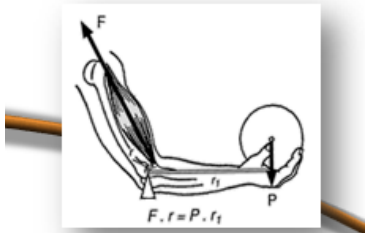






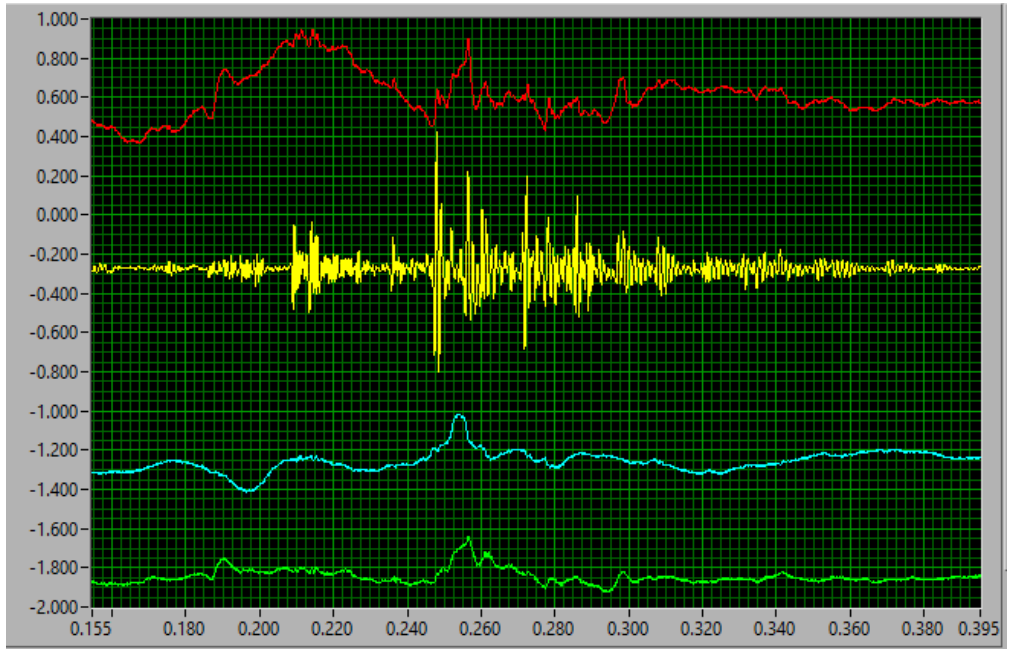
from Bachasson et al (2019)

Muscles of the face and the neck



strength

- *Orofacial, laryngeal, pharyngeal, swallowing muscles, speech muscles…*
- *Example of dysphagia*



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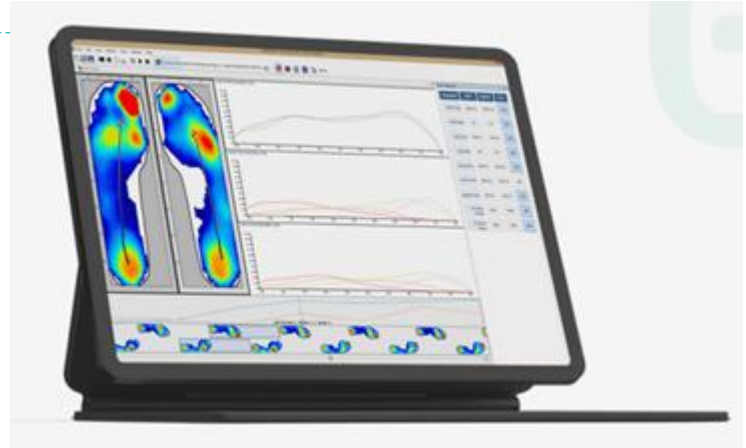
Gait analysis

- *Gait analysis systems (markers)*
- *Sensitive walkways*
- *Insoles*
- *Accelerometers or inertial measurement units (IMUs)*
- *Video*

movement and motor skills

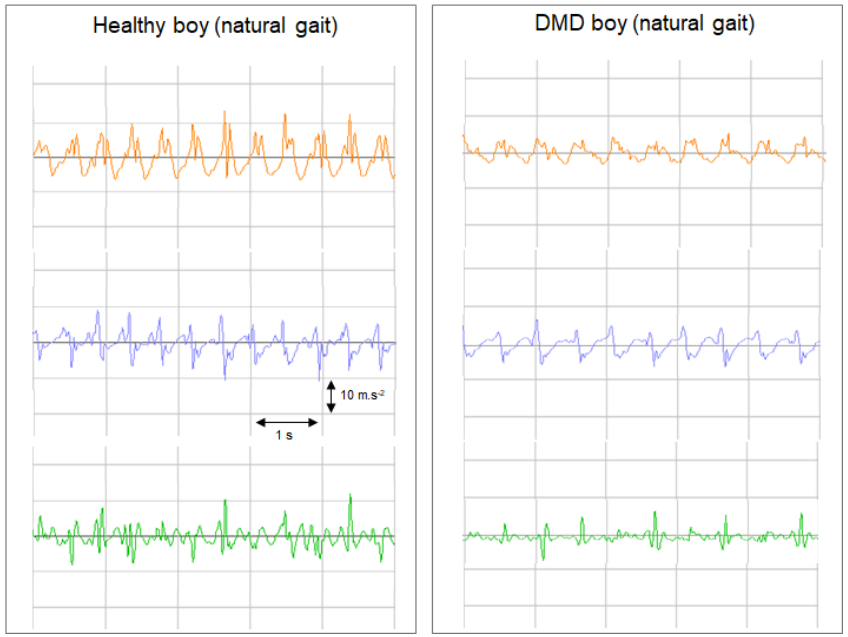


Optical motion capture using reflective markers

from Kindzinski et al (2020)

Single-camera recording

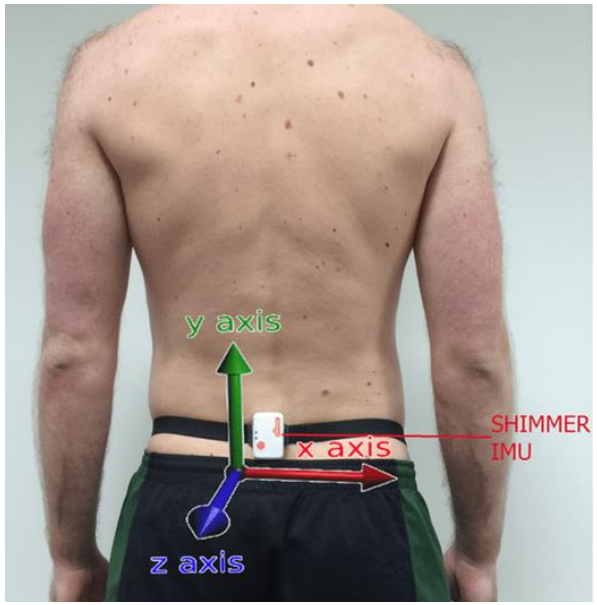
Video keypoint detection algorithm (e.g. OpenPose)

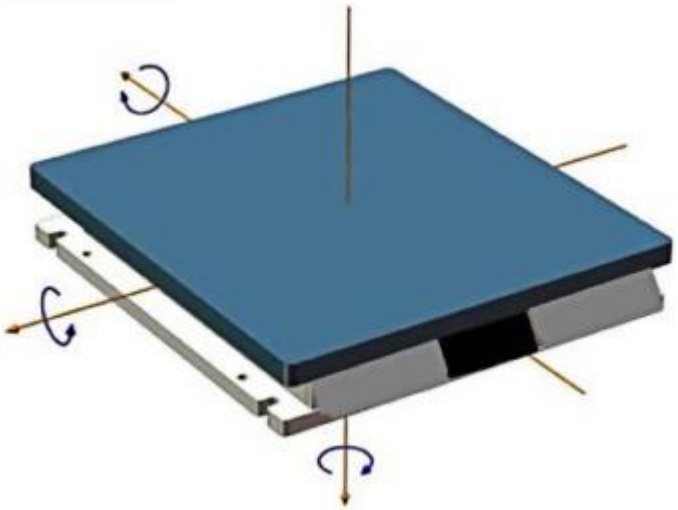


Posture analysis

- *Force plate*
- *Inertial measurement units (IMUs)*
- *Insoles*

movement and motor skills

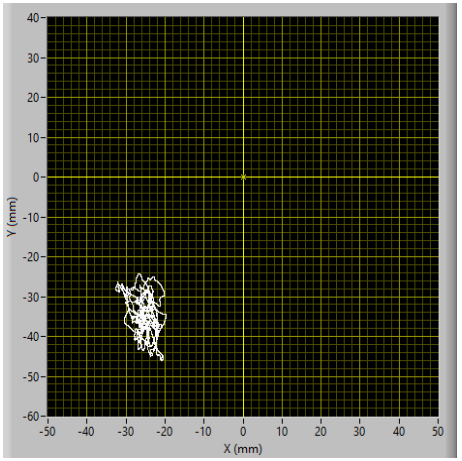
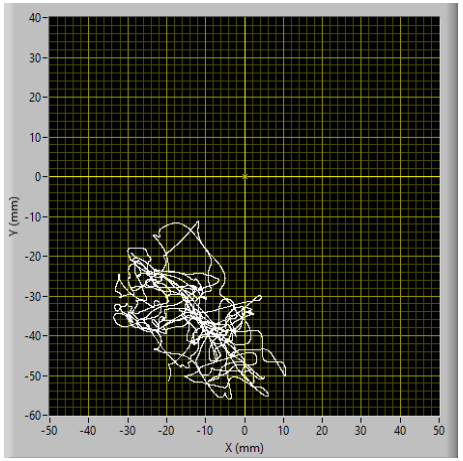
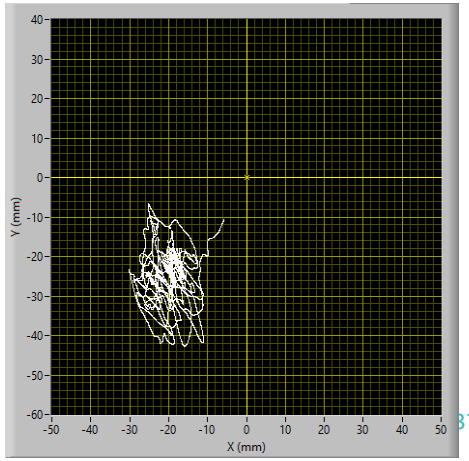
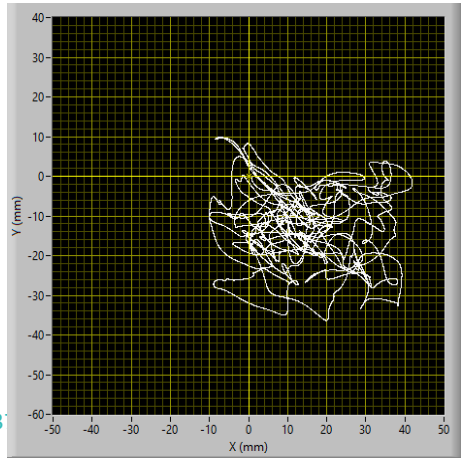




BBalance

Posture analysis

- *Length and velocity of the center of pressure trajectory on a force plate*

	eyes open	*eyes closed*
feet apart		
feet together		

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Metabolic costs of motor tasks

- *O2 consumption*
- *CO2 production*
- *Heart rate*
- *surface EMG, IMUs*
- *Treadmill, bicycle, rowing machine*

movement and motor skills

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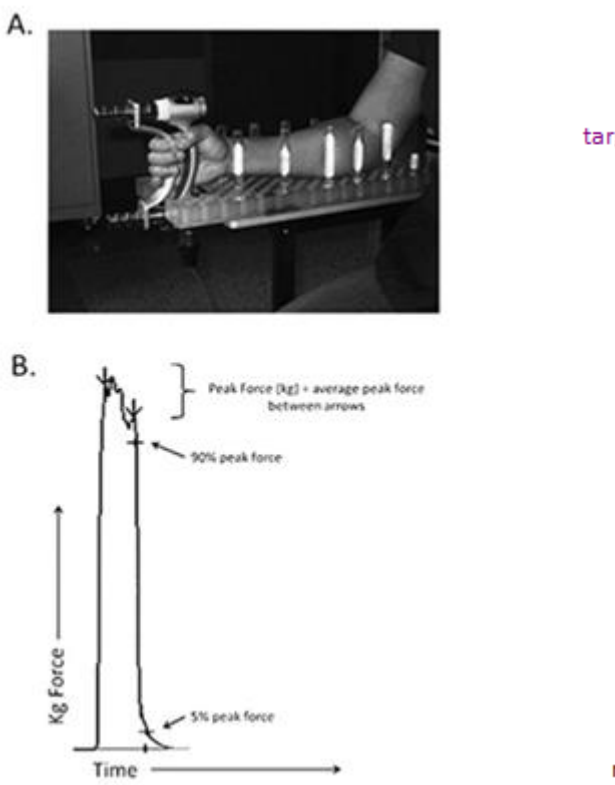
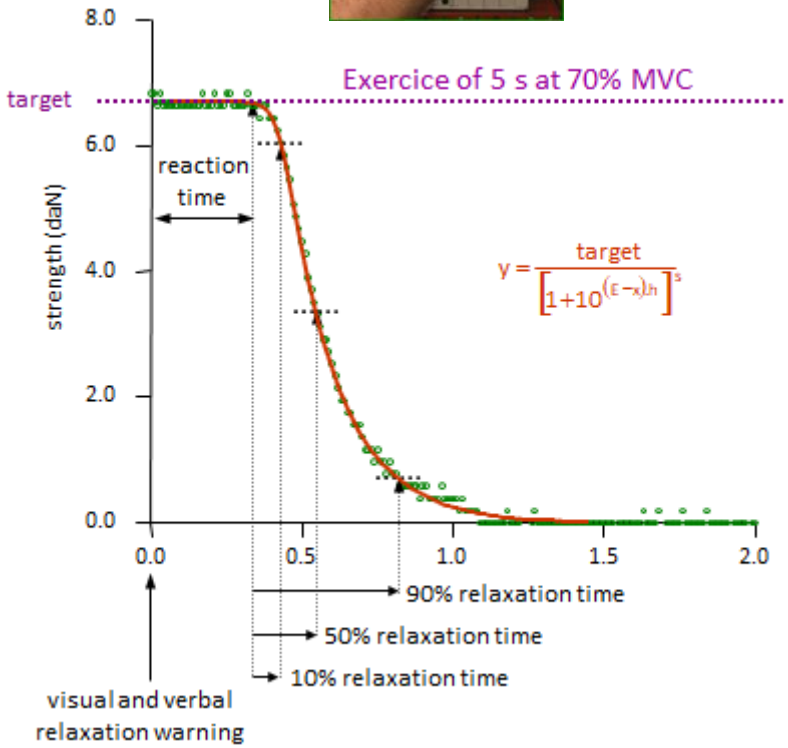
Myotonia

- *QMA-based method*
- *MyoTone test*
- *HandClench Relaxometer*
- *Video hand opening test (vHOT)*

from Bulea et al (2022)



from Statland et al (2012)



from Hogrel (2009)

from Hughes et al (2014)

Spasticity

- *Isokinetic method during passive movements*

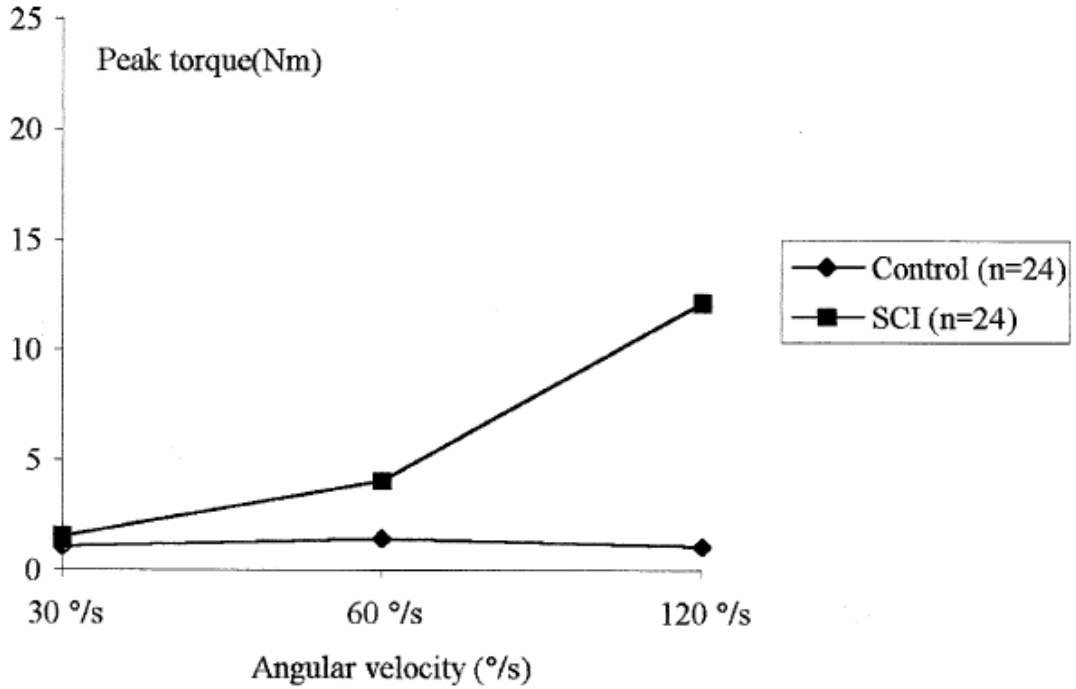
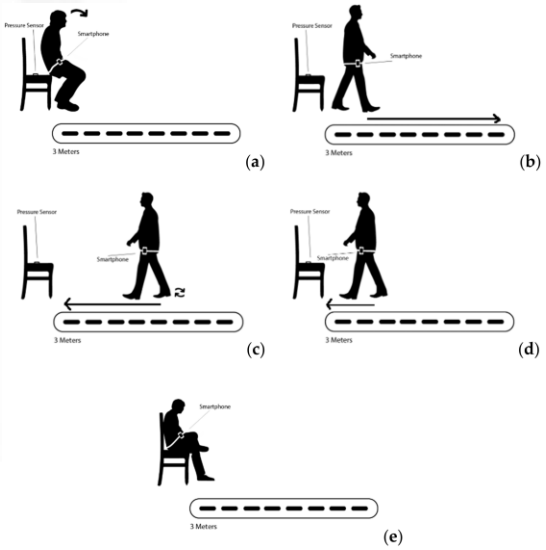


Figure 2 Average peak torque in flexion movement of control ($n = 24$) and SCI ($n = 24$) groups as studied velocities (30, 60, 120° per second)

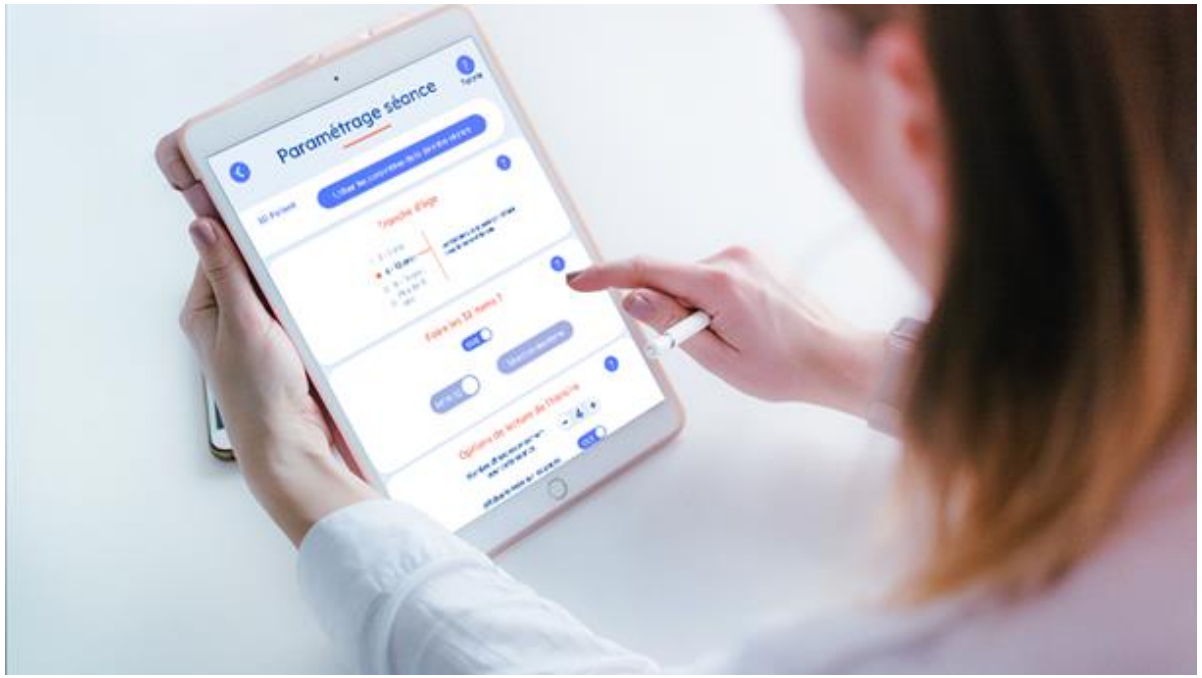
from Franzoi et al (1999)

Digitalization of timed tests and scales

- *Example of the time-up-and-go (TUG) using a smartphone*
- *Example of MFM-play*



from Ponciano et al (2020)



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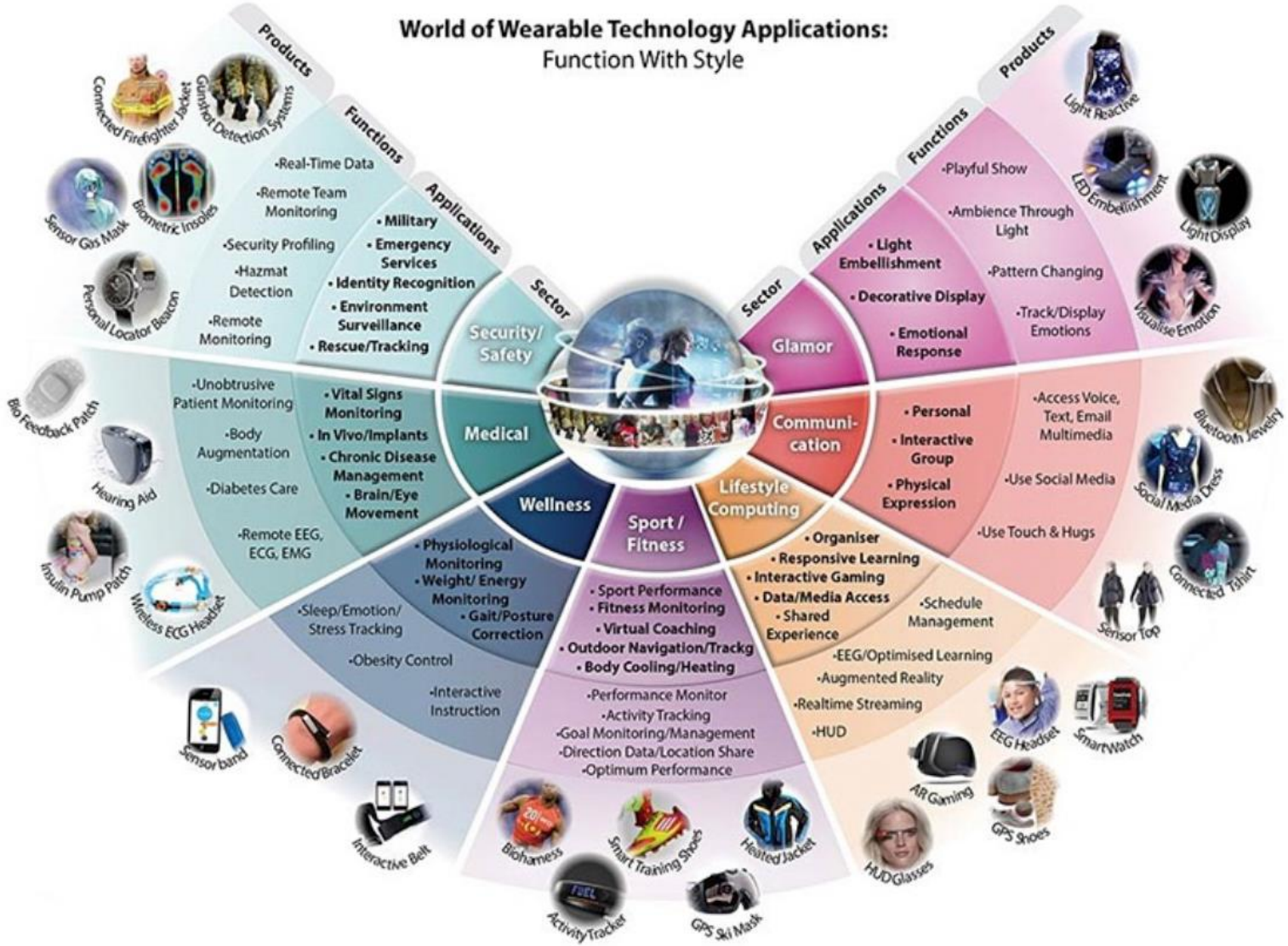
CURE THROUGH INNOVATION

Connected objects, IOT, wearables, apps…

autonomy



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Daily life physical activity analysis

- *Gait assessement and continuous monitoring of physical activity*

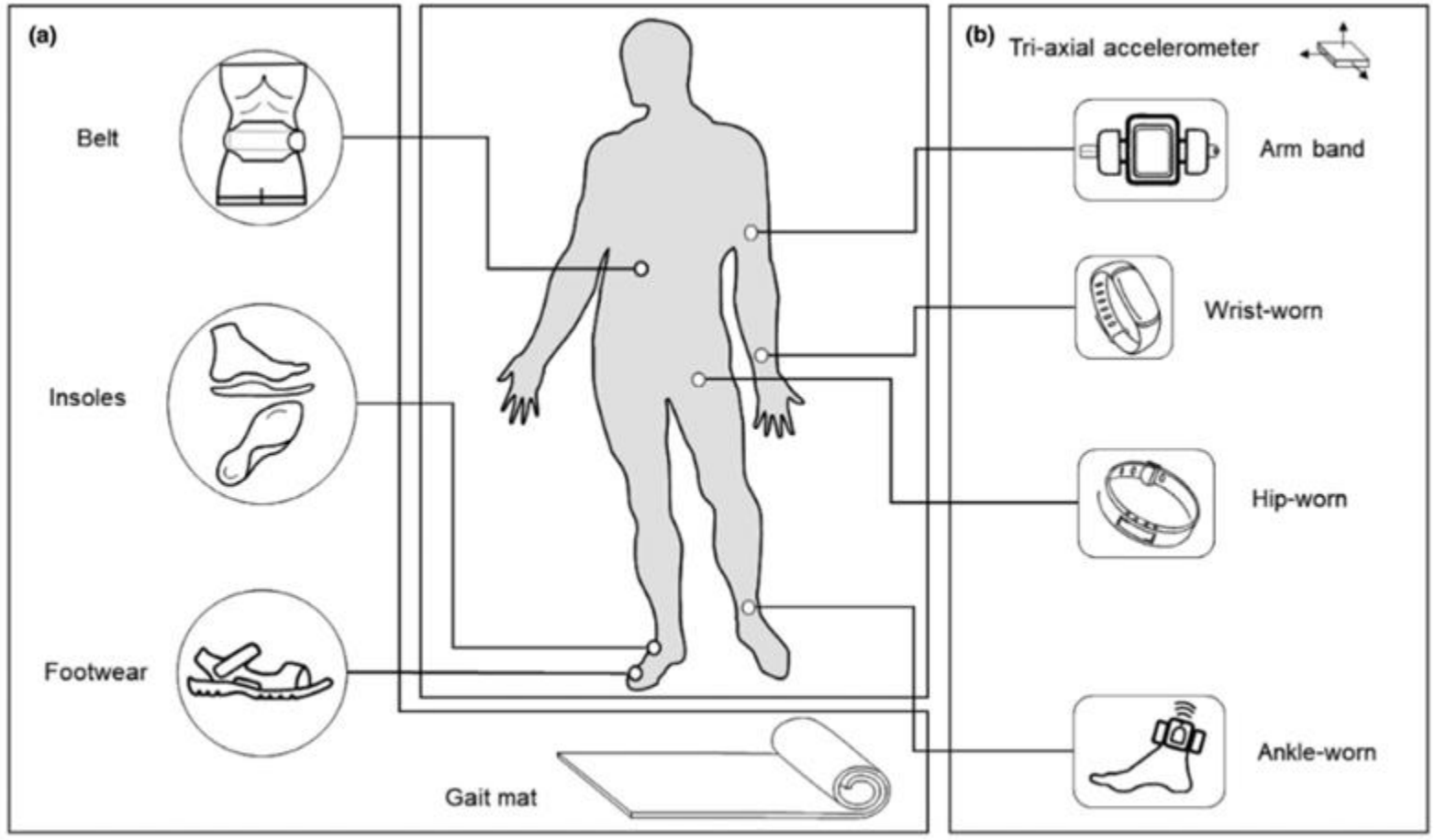

FIGURE 2 Technological devices for portable and wearable gait analysis and continuous monitoring of physical activity. Examples of portable and wearable devices used for gait assessment (a) and continuous monitoring of physical activity (b)

from Bortolani et al (2022)

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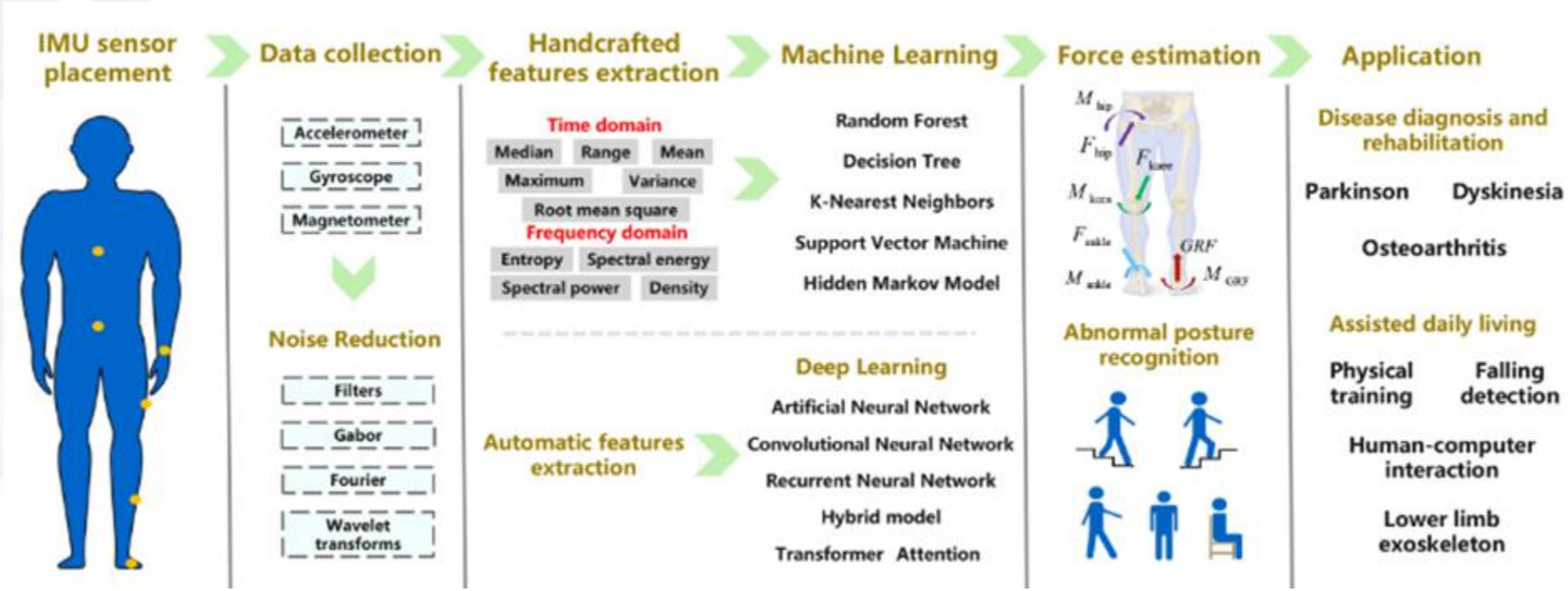
Daily life physical activity analysis

- Inertial measurement units (IMU)



from Lian et al (2023)

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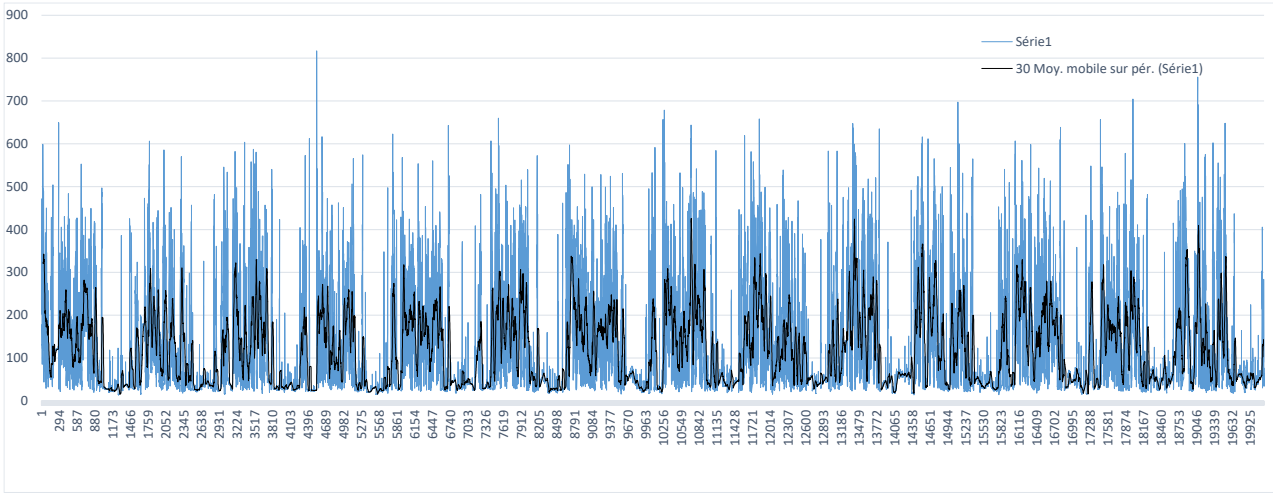
Daily life physical activity analysis

- *Activity trackers*

Table 4
Summary of all tools used with ambulatory and non-ambulatory participants in DMD

Ambulatory	
Direct Tools	Indirect Patient Reported Tools
Actigraph GT3X	self made questionnaire
Motionlogger Watch	modified activity diary
Actiwatch 2	PA questionnaire
StepWatch	activity log
GENEActive	
ASUR	
MOX Accelerometry	
ActiLife 5	
Non-Ambulatory	
Direct Tools	Indirect Patient Reported Tools
Actigraph GT3X	self made questionnaire
Silmee Bar-type Light	modified activity diary
Motionlogger Watch	PA questionnaire
Actiwatch 2	
GENEActive	
MOX Accelerometry	
Actimyo	

from Uher et al (2023)



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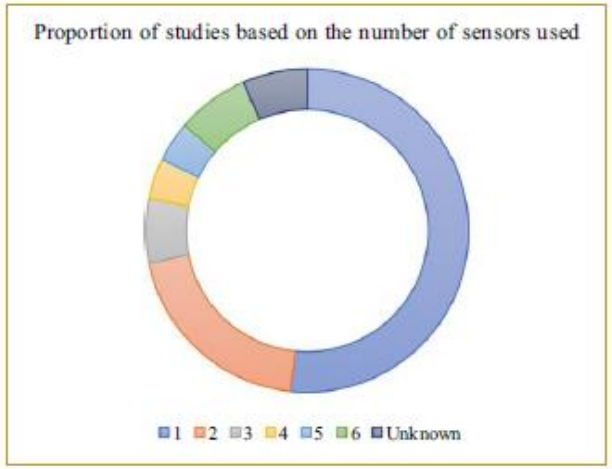
Daily life physical activity analysis

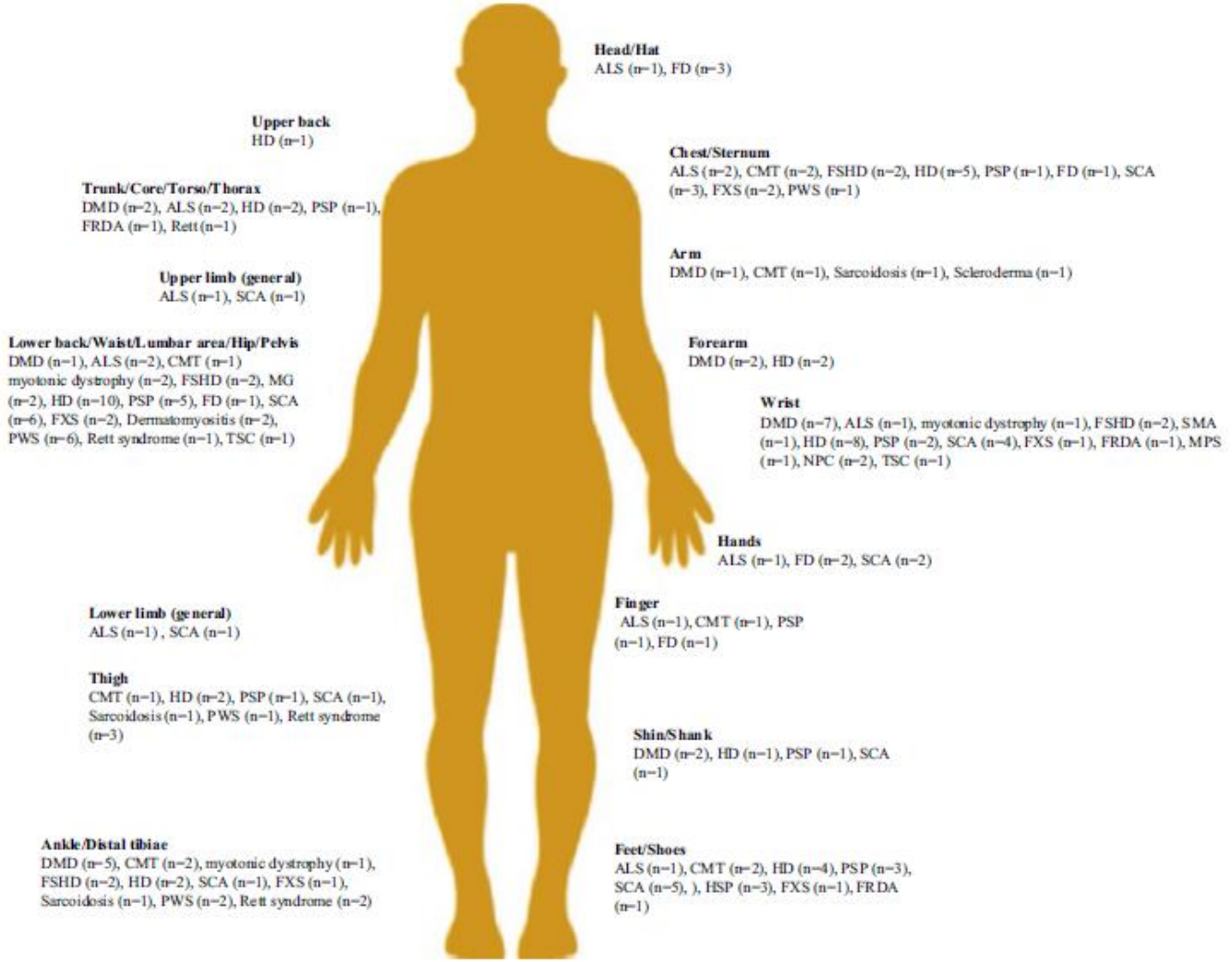
autonomy

- *Activity trackers*



Other
Wheelchair DMD (or trousers, n=1), SMA (n=1)
Bra/Belt/Pocket Pompe (n=1), HD (n=1)
Tee-shirt DMD (n=1)
Unknown ALS (n=1), HD (n=4), SBMA (n=1), Fabry (n=1), Narcolepsy (n=1), GM2 (n=1), Sarcoidosis (n=2)
Spoon FRDA (n=1)

from Poleur et al (2023)



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Daily life physical activity analysis

- *Activity trackers*

autonomy

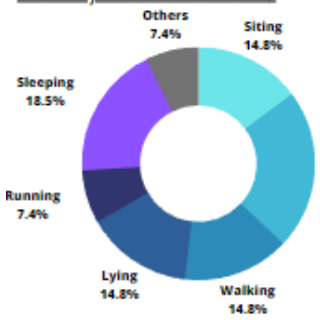
Daily activity report

Date : 16/05/2023
Subject ID: EJP144

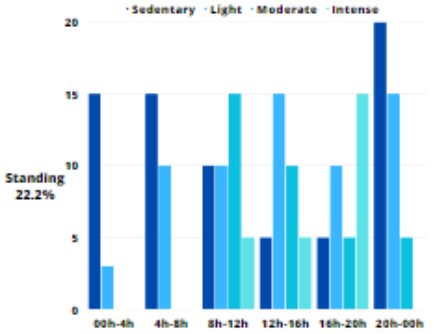
Global Physical Activity :

	Upper Limb	Lower Limb	Center of gravity
Linear activties index	323	786	233
Rotational activities	654	342	NaN

Acitvity Classification :

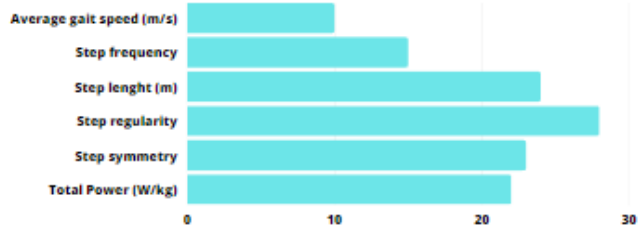


Time distribution activites



Movement intensity

Gait characteristics :



Tremors :

Yes ☐ *Average frequency* : 1.2 Hz
No ☐ *Max frequency* : 1.8 Hz

Falls :

Number of falls detected : 2 falls
Fracture : ☐ Yes ☐ No

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CURE THROUGH INNOVATION

Daily life physical activity analysis

- *Activity trackers*

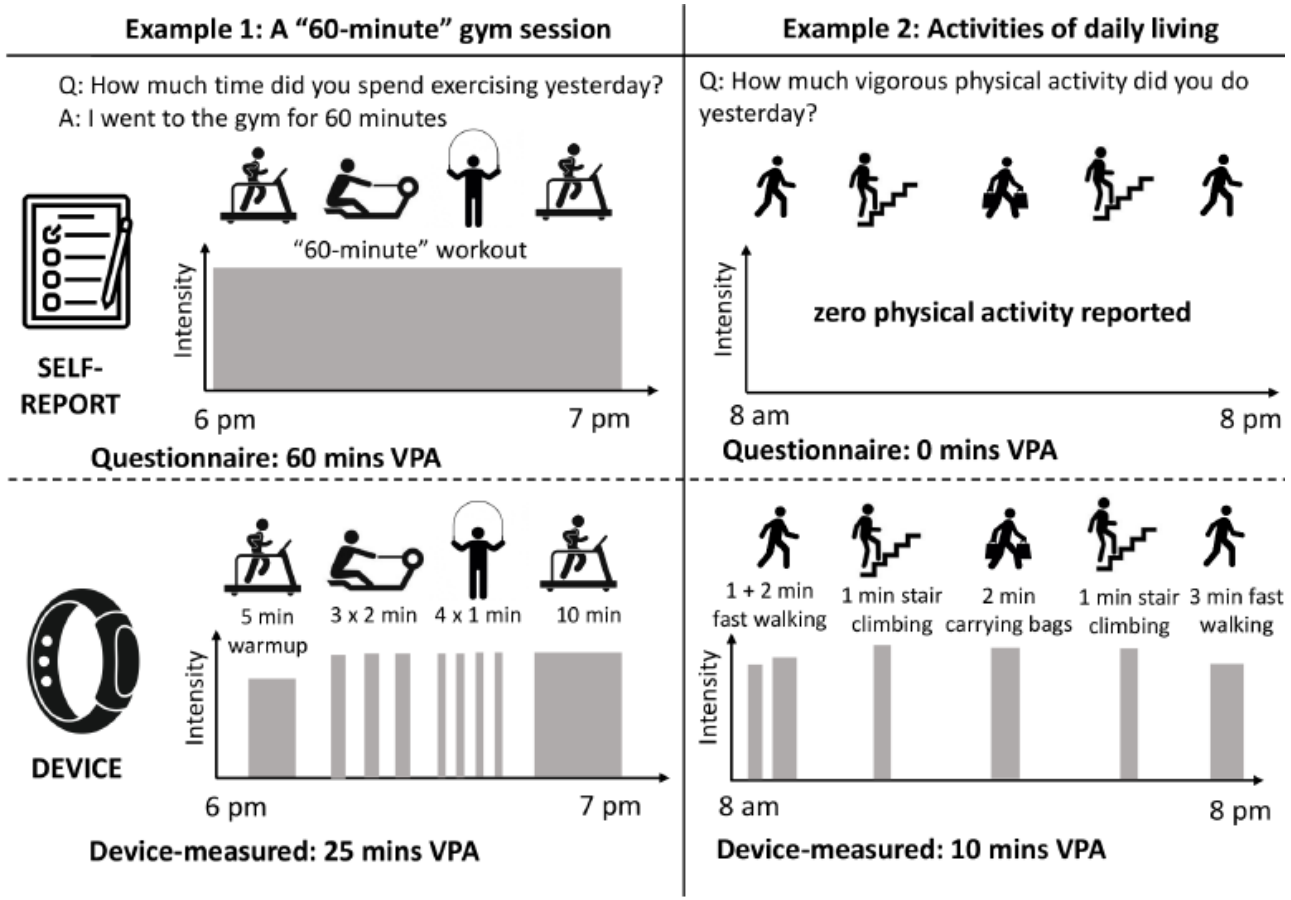
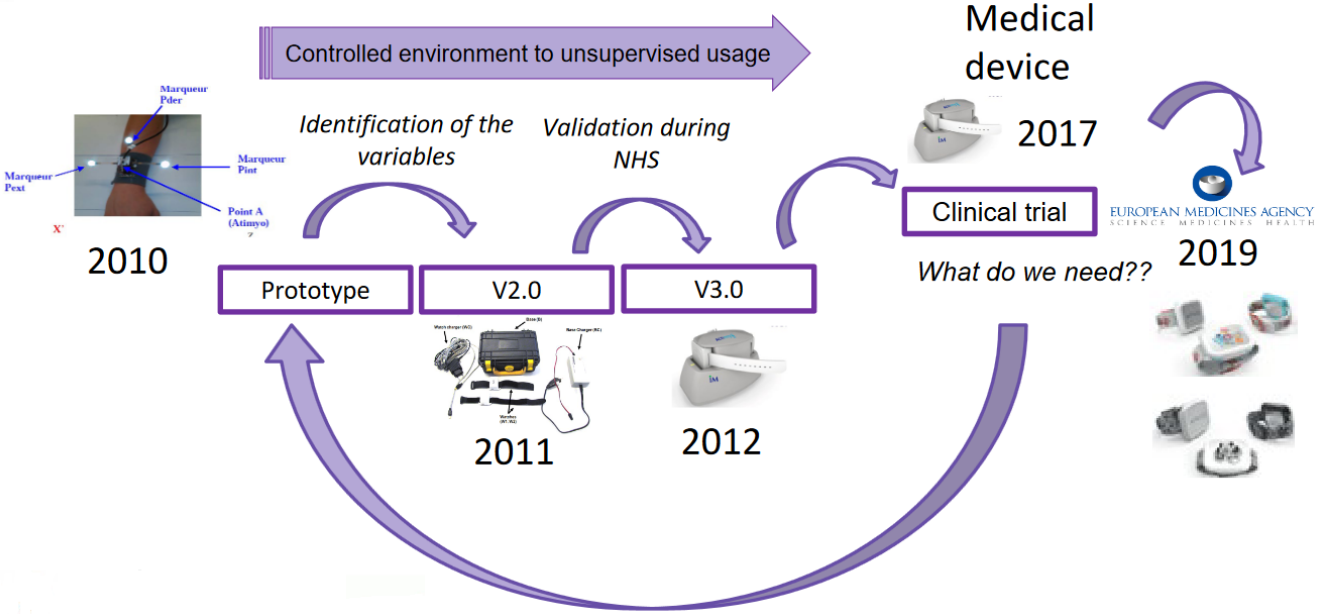


Figure 1 Physical activity captured by self-report questionnaire (top panels) and wearable device (bottom panels) in two different scenarios: a session in the gym (Example 1, left panels) and during intermittent activities of daily living (Example 2, right panels). Questionnaires overestimate physical activity in the former but underestimate physical activity in the latter. N.B. Simplified examples to illustrate the central point. VPA, vigorous physical activity.

from Gill et al (2023)

Daily life physical activity analysis

- *ActiMyo (then Syde)*



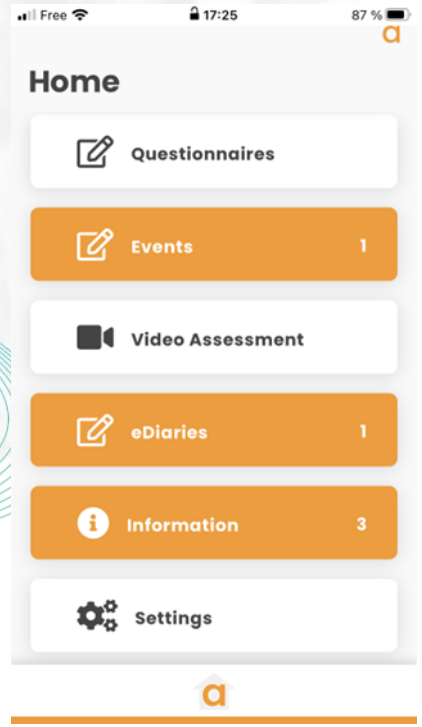
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

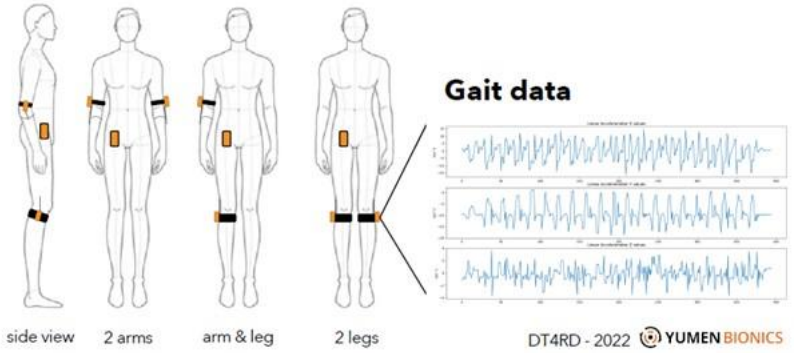
28 July 2023
EMADOC-1700519818-1127132
Committee for Medicinal Products for Human Use (CHMP)

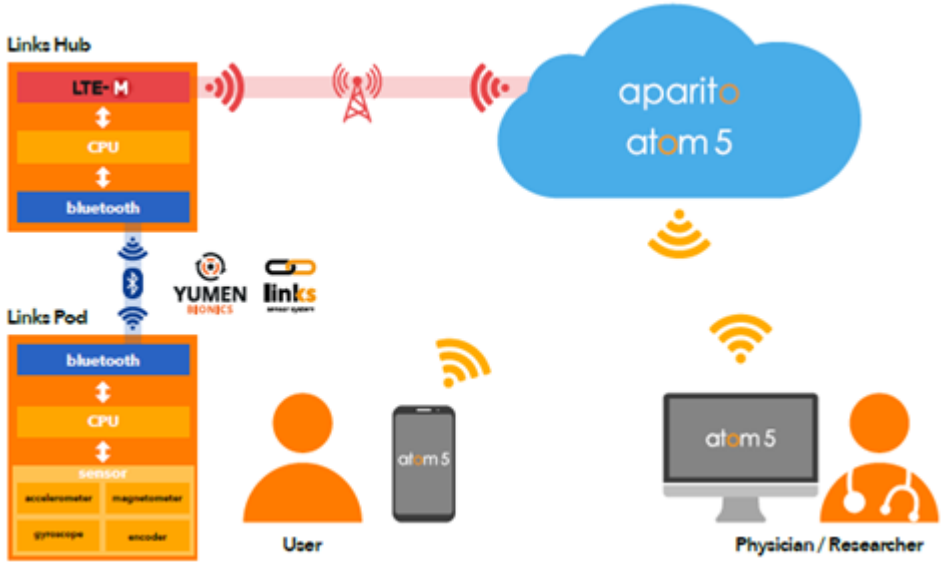
Qualification Opinion for Stride velocity 95th centile as primary endpoint in studies in ambulatory Duchenne Muscular Dystrophy studies

Connected objects, IOT, wearables, apps…

- *Centralised platform : example of Aparito platform*



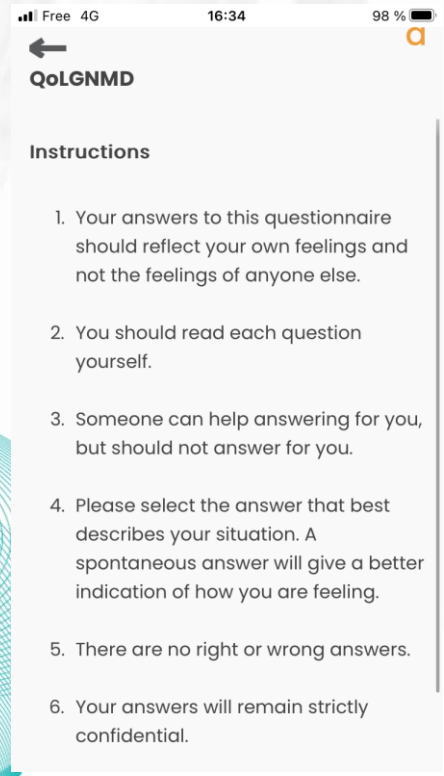


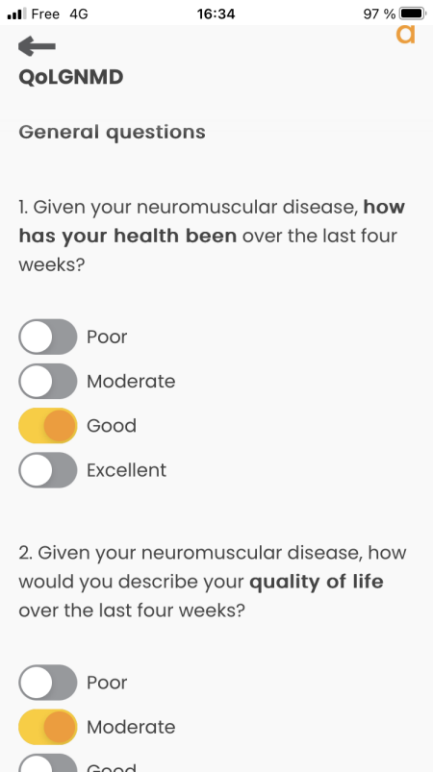


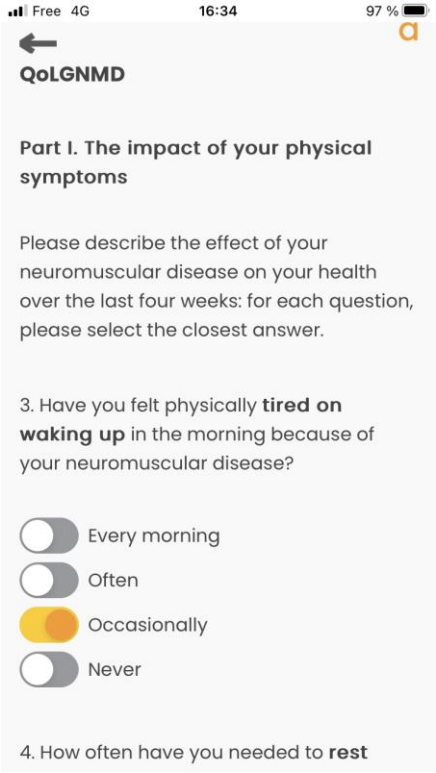
Digitalization of scales

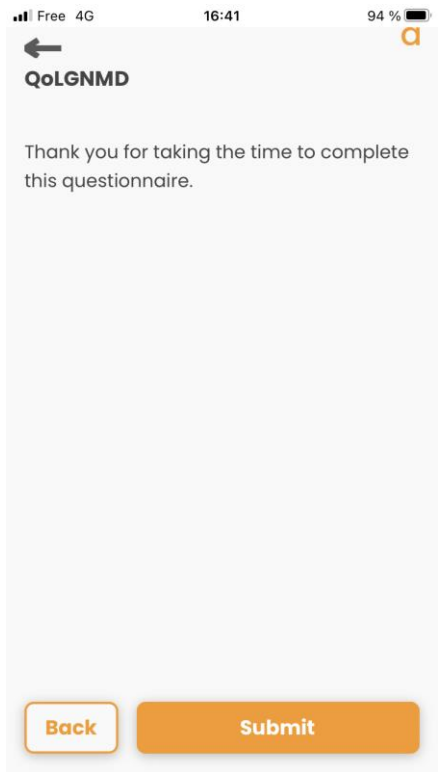
psychology
neuropsychology

Using Apps









Perspectives

- *Still place for many improvements in the domain of neuromuscular evaluations*
- *Many innovative devices in the pipeline*
- *Standardization, training and coaching are also key*
- *The place of AI will be growing*

from Damian (2021)

Thank you for your attention

3 November 2023

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