Reliability and external validity of digital passive gait tracking in MS

Background & methods	Concept model & data collection	Population characteristics, analytical validation, compliance & reliability	Validity	Longitudinal data	Conclusion	Acknowledgements & disclosure

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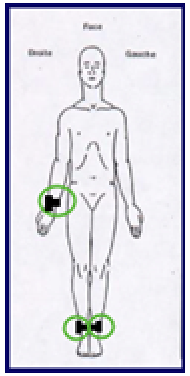
BACKGROUND

- Quantifying gait impairment, one of the main causes of disability in multiple sclerosis (MS), is an important step toward the quantification of disease progression
- The wearable Digital Health Technology (wDHT) is designed for patients' continuous assessment
- The 95th centile of stride velocity (SV95C) is the first digital clinical outcome measure qualified as a primary endpoint in Duchenne muscular dystrophy by the European Medicines Agency

METHODS

ActiMS : one project, two study protocols

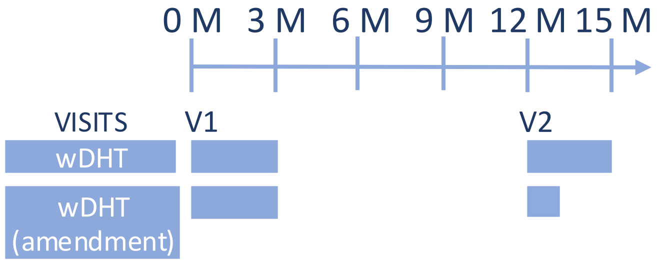
Analytical validation & selection of candidate variables in **controlled environment**

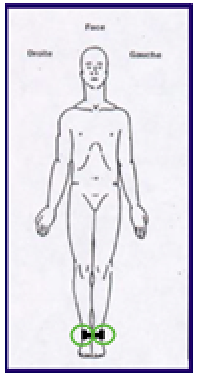


- 21 patients
- One visit: various gait exercices recorded with wDHT and a motion capture device

Validation of digital outcomes in **non-controlled environment**

- **78 patients**
- **5 sites** in Belgium and France
- Evaluation at baseline and at 1 year
- DHT worn for 3 months after the 1st visit and 1-3 months after the follow-up visit





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DATA COLLECTION AND VARIABLE IDENTIFICATION

What is meaningful for patients?

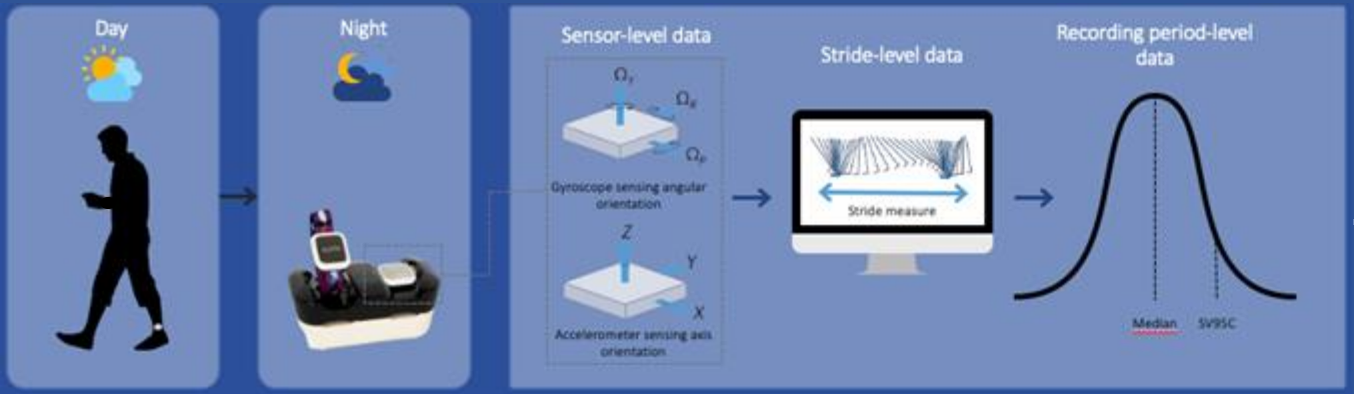
- **Measure "how patient functions"**
- **Overall disability burden**
- **Quantification of symptoms of disease**

→ **Gait impairment** →

Concept of interest	Selected variable	Variable definition
Reduced gait speed	95th centile of stride velocity (SV95C)	Top 5% of fastest strides
Reduced walking perimeter	90th Centile of walked distance (WD90C)	Top 10% of distance covered by the patient in a single bout

How to measure it in real life?

Data collection | **Data analysis**



Continuous collection of raw sensor data (ankle-ankle configuration)

Transfer of encrypted & anonymized data to a secure web cloud via a docking station

Regular monitoring and processing of data to extract stride-level information and compute digital endpoints, such as SV95C and WD90C

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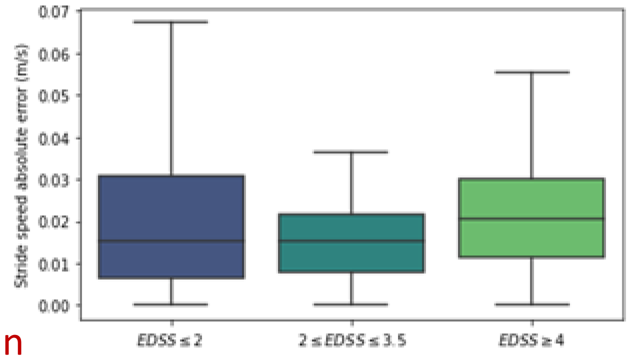
BASELINE CHARACTERISTICS

	Controlled environment	Non-controlled environment
Number of patients	21	78
Age (years): median ± SD [range]	39 ± 11.7 [22-62]	48.5 ± 11.7 [22-65]
Sex: female (%)	12 (54.5)	43 (55.1%)
EDSS: mean ± SD [range]	2.6 ± 1.3 [1.5-5.5]	3 ± 1.4 [0-5.5]
T25FW (seconds): mean ± SD [range]	5.3 ± 2.3 [3.1-13.7]	6.5 ± 6.7 [2.8-60.0]

ANALYTICAL VALIDATION

Analytical validation on 21 patients:

- Over 99% of strides identified using the Motion Capture were accurately detected by the wDHT



- Centimetric precision (median error on stride speed : 0.017 m/s) with no significant impact of the level of disability

COMPLIANCE

- 99% and 94% of patients at baseline and 1 year, respectively, have sufficient recorded data (>50h) to compute digital endpoints.
- 95% and 81% of patients at baseline and 1 year, respectively, have optimal recorded data (>180h)

Notes:
- 14 patients withdrew, 5 patients with no follow-up visit due to the departure of an investigator in one site, 5 patients are still collecting data

RELIABILITY

	ICC2
SV95C	0.88
WD90C	0.4

- SV95C is reliable unlike WD90C

ICC2 = intraclass correlation coefficient, computed on 3 consecutive one-month periods at baseline

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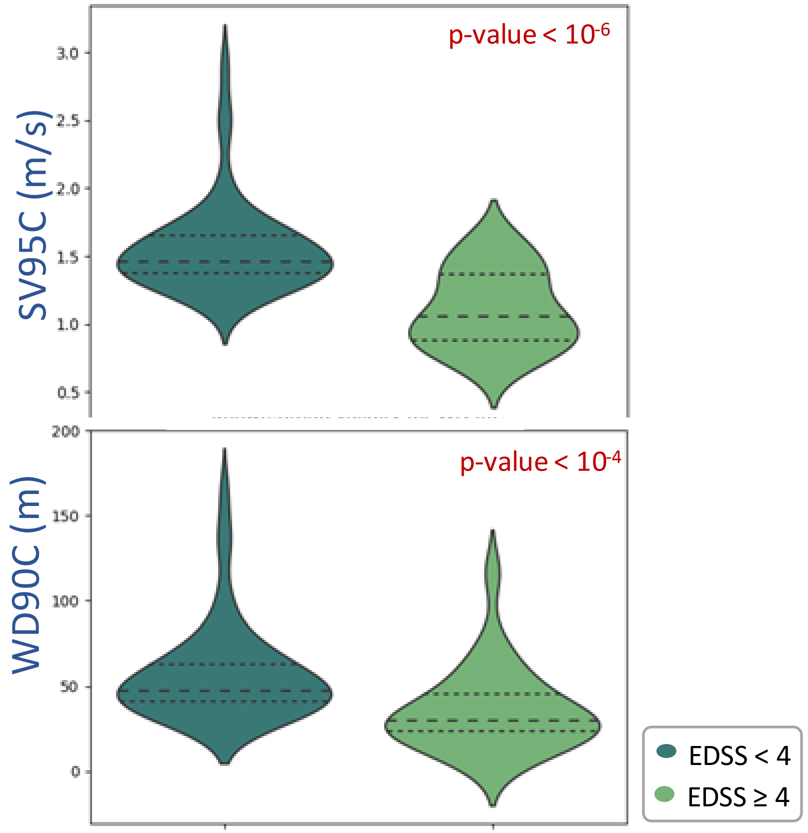
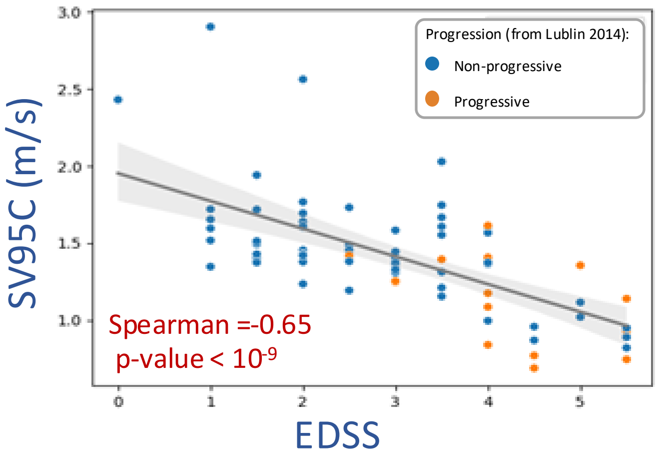
KNOWN-GROUP VALIDITY

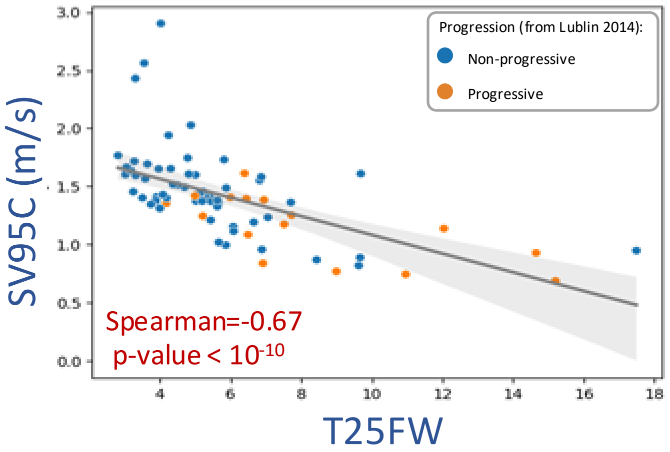
- SV95C and WD90C differentiate patients who are fully ambulant and those who are not

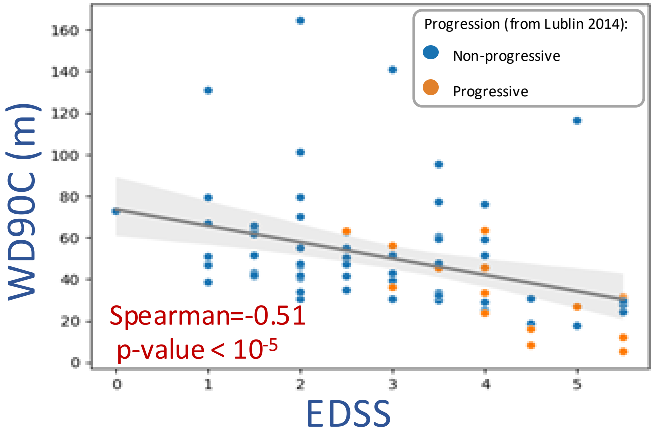


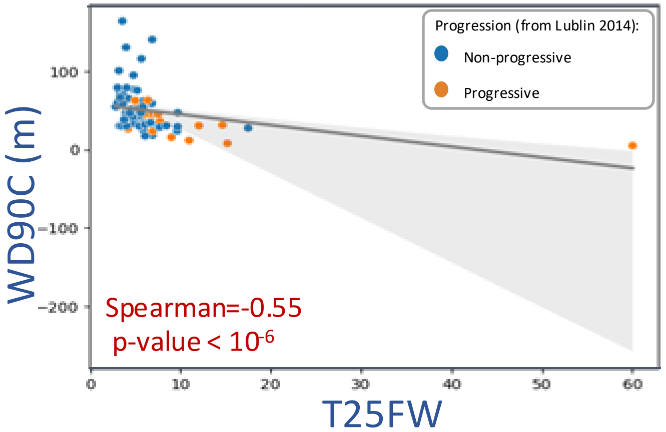
EXTERNAL VALIDITY

- Both SV95C and WD90C show significant correlation with EDSS & T25FW









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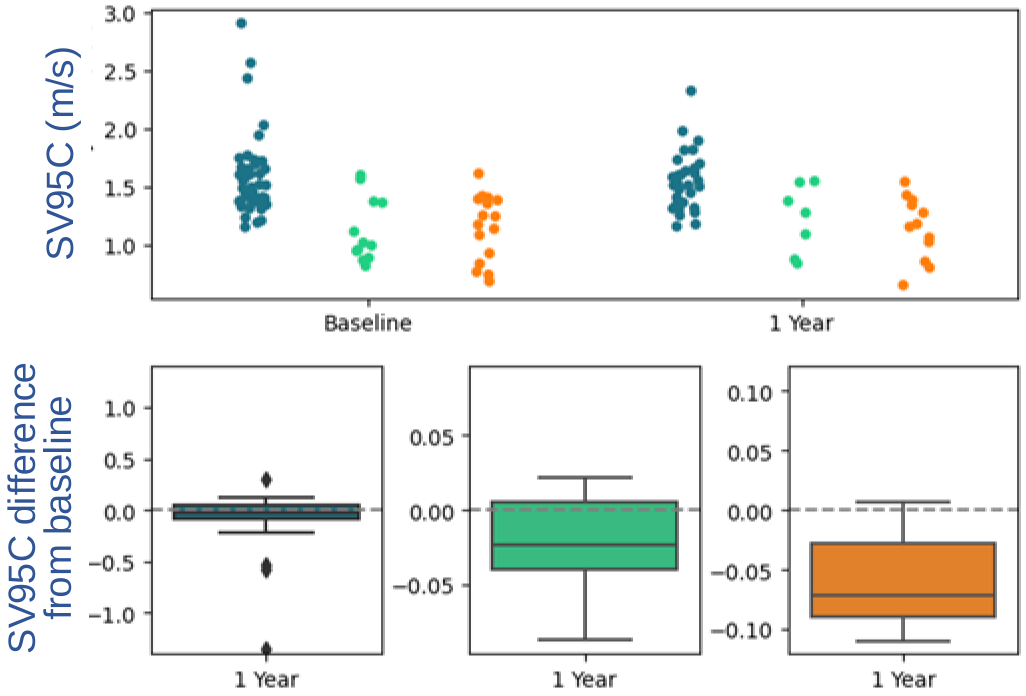
LONGITUDINAL DATA



Progression (from Lublin 2014) (N at BL and 1 year) [p-value of Wilcoxon signed-rank test on evolution]:

- Non-progressive, EDSS < 4 (N=48 and N=31) [p > 0.05]
- Non-progressive, EDSS ≥ 4 (N=12 and N=7) [p > 0.05]
- Progressive (N=16 and N=12) [p < 0.001]

- Unlike EDSS & T25FW, statistically significant SV95C decline ($p<10^{-3}$) at 1 year for progressive patients (Lublin 2014 definition)
- Non significant SV95C progression at 1 year for non-progressive patients regardless of baseline EDSS total score
- There is no evidence of decline from baseline based on WD90C for patients with a progressive course

In progressive population

	Wilcoxon (p value)	SRM
SV95C	**9.77e-4**	-1.584
WD90C	0.326	N/A
EDSS	0.059	N/A
T25FW	0.588	N/A

SRM = standardized response mean

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CONCLUSION

- Wearable monitoring is feasible and patient burden is limited
- Selected wDHT is precise & accurate for stride detection & stride speed measurement in a heterogeneous ambulant population
- Digital outcomes derived from wDHT show internal and external consistency with gold standard measures of MS disability
- SV95C is sensitive to change over a 1-year period. Long-term data with shorter intervals between recording periods are currently being collected.

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Disclosure:

Laurent Servais has given consultancy in the DMD field for Biogen, Novartis, Astellas, Evox, PTC, BioHaven, Zentech, MitoRX, Pfizer, Sarepta, Dyne, Santhera, Italfarmaco, **Roche and SYSNAV.**

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