Reliability and external validity of digital passive gait tracking in MS

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Background & methods | Concept model & data collection | Population characteristics, analytical validation & compliance | Reliability & validity | Longitudinal data | Conclusion | Acknowledgements & disclosure

BACKGROUND

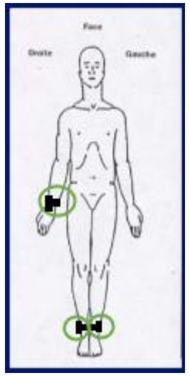
- Quantifying gait impairment, one of the main causes of disability in multiple sclerosis (MS), is an important step toward the quantification of disease progression
- The wearable Digital Health Technology (wDHT) is designed for patients' continuous assessment
- The 95th centile of stride velocity (SV95C) 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

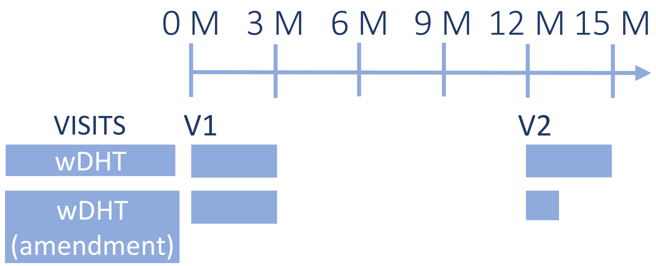
Analytical validation & selection of candidate variables in **controlled environment**

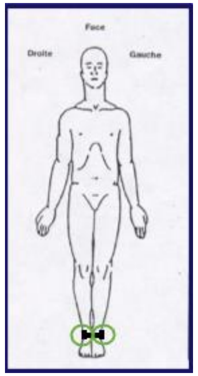
- 21 patients
- One visit: various gait exercices recorded with wDHT and a motion capture device



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

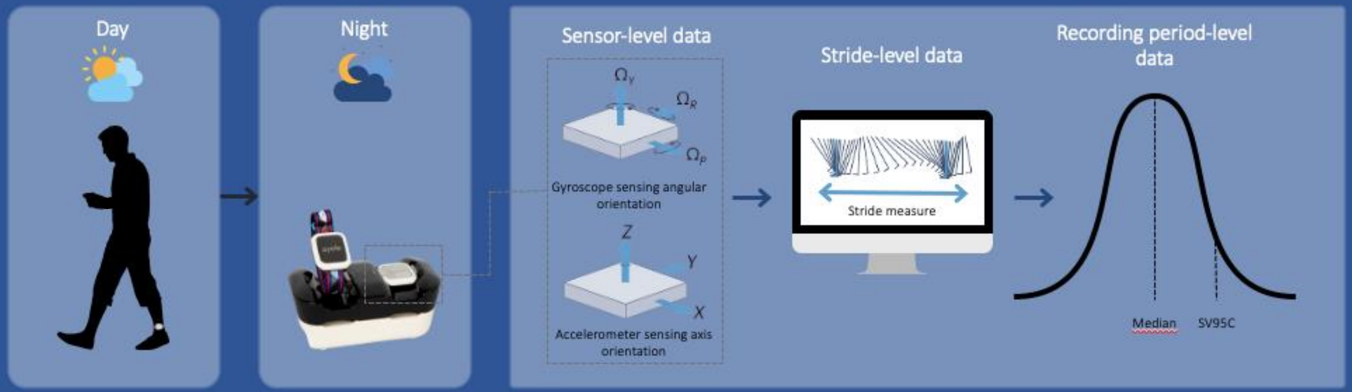
→ Gait impairment →

Concept of interest	Selected variables	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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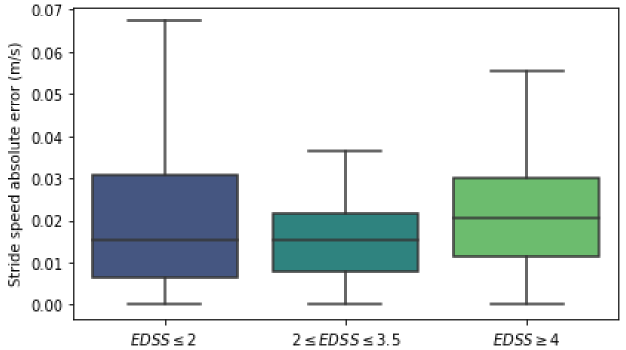
BASELINE CHARACTERISTICS

	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 published 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)
- No significant impact of the level of disability on the error

COMPLIANCE

Number of patients who recorded	**< 50 h of data**	**≥ 50 h of data**	**≥ 180 h of data**
Baseline, N (%)	1 (1%)	3 (4%)	74 (95%)
1 year, N (%)	3 (6%)	7 (13%)	44 (81%)

99% and 94% of patients at baseline and 1 year, respectively, have sufficient recorded data to compute digital endpoints

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

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RELIABILITY

- SV95C is reliable unlike WD90C

	ICC2
SV95C	0.88*
WD90C	0.4

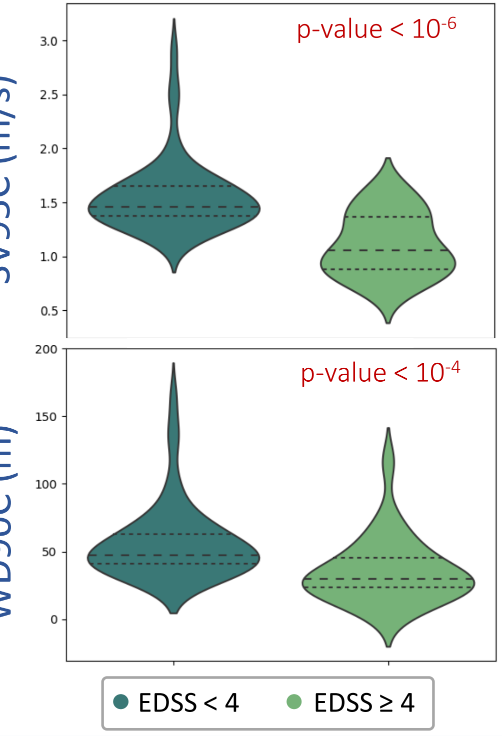
ICC2 = intraclass correlation coefficient (single random raters): describes how strongly two consecutive measures resemble each other

ICC2 is computed on 3 consecutive one-month periods at baseline

*The 3 outliers at baseline described on the next slide are included in the ICC2 computation

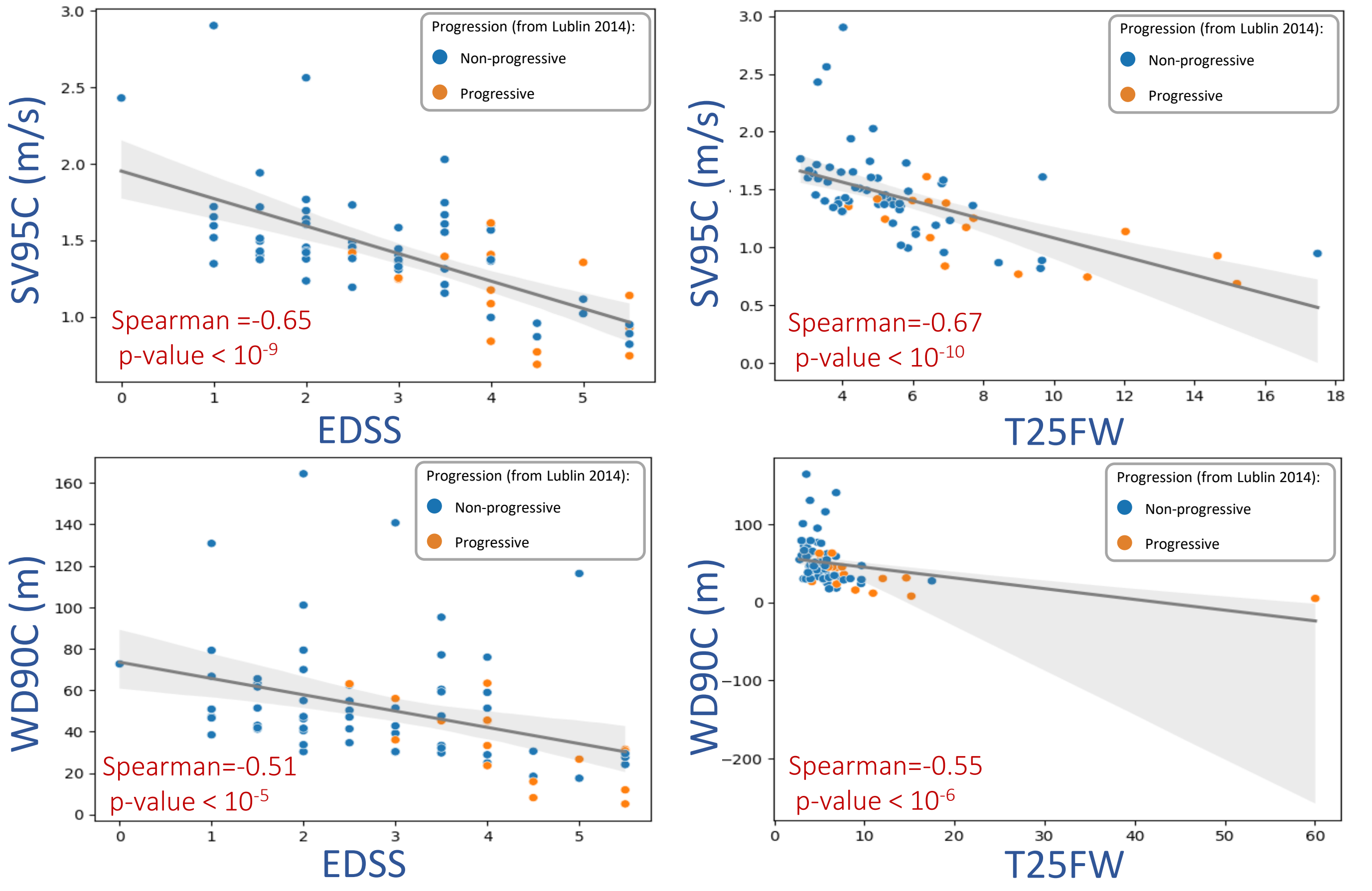
KNOWN-GROUP VALIDITY

- 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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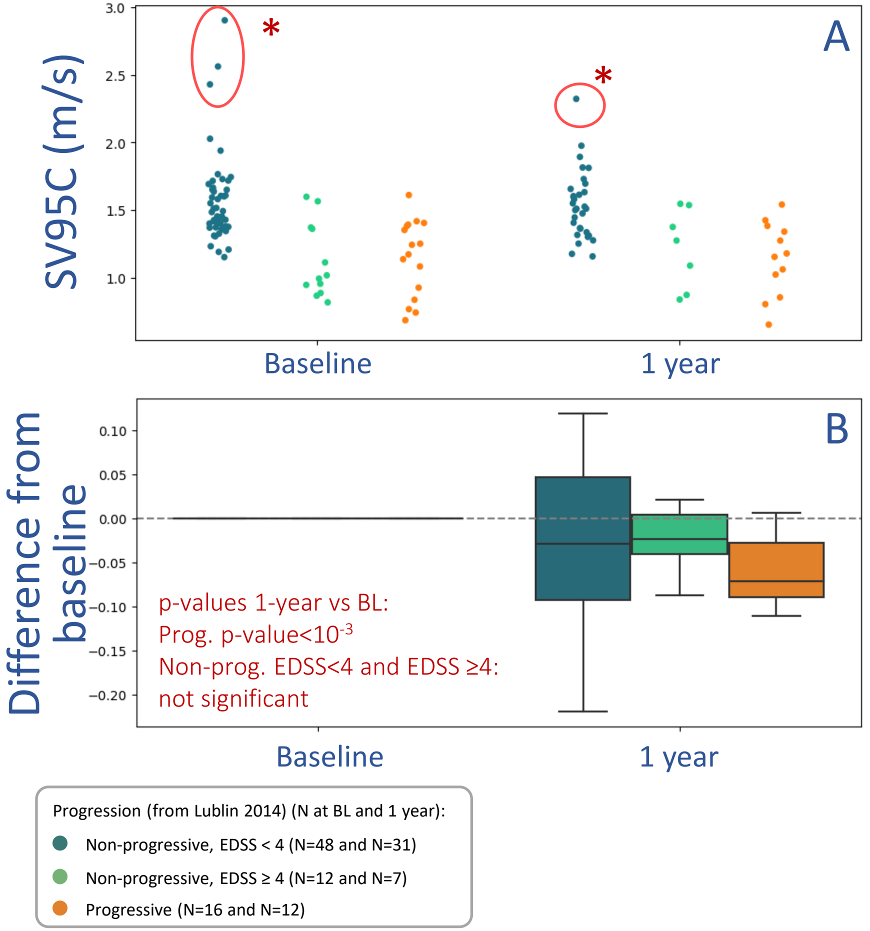
SV95C LONGITUDINAL DATA



- 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

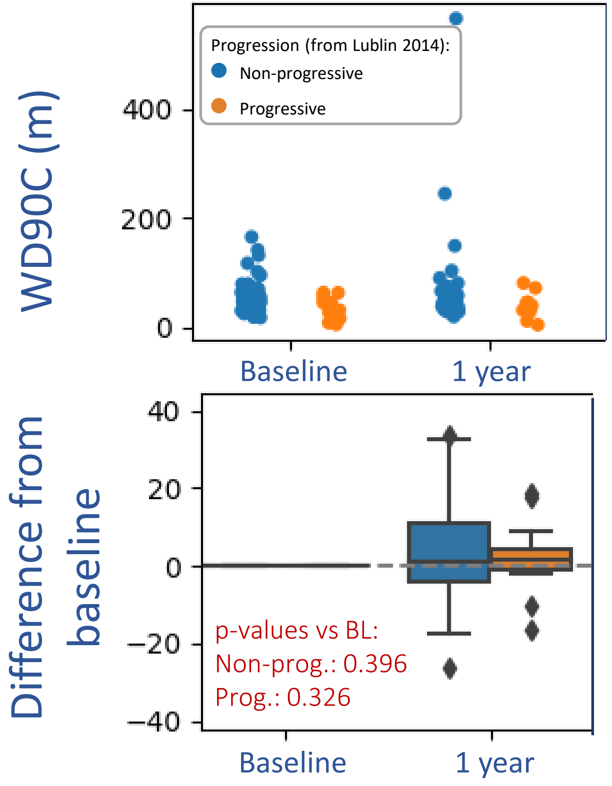
* 4 patients in red circles ran during one period (3 at baseline and 1 at 1 year), but did not wear the DHT while running at the other period: ongoing optimization to take into account this type of environmental factor. They were removed on figure B.

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

WD90C LONGITUDINAL DATA



- There is no evidence of decline based on WD90C from baseline for patients with a progressive course

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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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