Quantitative assessment of multiple sclerosis using inertial sensors and the TUG test

Barry R. Greene, *Senior IEEE Member*, Michael Healy, Stephanie Rutledge, Brian Caulfield, *IEEE Member,* and Niall Tubridy

***Abstract*—Multiple sclerosis (MS) is a progressive neurological disorder affecting between 2 and 2.5 million people globally. Tests of mobility form part of clinical assessments of MS. Quantitative assessment of mobility using inertial sensors has the potential to provide objective, longitudinal monitoring of disease progression in patients with MS.**

The mobility of 21 patients (aged 25-59 years, 8 M, 13 F), diagnosed with relapsing-remitting MS was assessed using the Timed up and Go (TUG) test, while patients wore shank-mounted inertial sensors.

This exploratory, cross-sectional study aimed to examine the reliability of quantitative measures derived from inertial sensors during the TUG test, in patients with MS. Furthermore, we aimed to determine if disease status (as measured by the Multiple Sclerosis Impact Scale (MSIS-29) and the Expanded Disability Status Score (EDSS)) can be predicted by assessment using a TUG test and inertial sensors.

Reliability analysis showed that 32 of 52 inertial sensors parameters obtained during the TUG showed excellent intra-session reliability, while 11 of 52 showed moderate reliability. Using the inertial sensors parameters, regression models of the EDSS and MSIS-29 scales were derived using the elastic net procedure. Using cross validation, an elastic net regularized regression model of MSIS yielded a mean square error (MSE) of 334.6 with 25 degrees of freedom (DoF). Similarly, an elastic net regularized regression model of EDSS yielded a cross-validated MSE of 1.5 with 6 DoF.

Results suggest that inertial sensor parameters derived from MS patients while completing the TUG test are reliable and may have utility in assessing disease state as measured using EDSS and MSIS.

I. Introduction

Multiple sclerosis (MS) is a chronic, progressive neurological disorder affecting between 2 and 2.5 million people globally [1]. Impaired mobility is a common symptom of MS, even at lower levels of the disease, and has significant negative effects on quality of life [2]. Current best practice for clinical assessment of MS includes assessment of gait and mobility. Quantitative assessment of mobility using inertial sensors has the potential to provide objective, longitudinal monitoring of patients with MS. The Expanded Disability Status Score (EDSS) is one of the gold standard clinical measures of disability in MS with the higher end of the scales being very dependent on a patient's mobility. The relationships between quantitative measures of mobility and clinical status (as measured by the Multiple Sclerosis Impact Scale (MSIS-29) and the EDSS) in patients with relapsing remitting (RR) MS, has not yet been explored.

The Timed Up and Go test (TUG) is a standard mobility assessment [3]. The time taken to complete the test has been shown to be a threshold test for independent living and a predictor of frailty and falls. The TUG test is commonly used for assessing risk of falls in older adults [4]. Recent research has investigated the use of inertial sensors for quantitative evaluation of gait [5, 6] and to quantify movement in the TUG test [6, 7]. Spain *et al.* [8] used inertial sensors and the TUG test to compare the balance and gait of people with MS (with normal walking speeds), against healthy controls. They found that inertial sensor parameters could distinguish between MS patients and controls, whereas the stopwatch TUG time failed to distinguish the two groups. Higashi *et al.* [9] employed body-worn gyroscopes to evaluate movement in hemiplegic patients with pathological gait while performing the TUG test. Salarian *et al.* [6] showed that a TUG test quantified with inertial sensors was both a reliable and sensitive method for quantifying gait and mobility in Parkinson's disease patients. Similarly, Weiss *et al.* [7] used body-worn accelerometers to quantify the gait of Parkinson's disease patients during the timed up and go test.

This cross-sectional study aimed to examine the reliability of the quantitative measures derived from inertial sensors during the TUG test. Furthermore we aimed to determine if disease status for patients with relapsing remitting multiple sclerosis (as measured by the Multiple Sclerosis Impact Scale (MSIS-29) and the Expanded Disability Status Score (EDSS)) can be predicted by assessment using a TUG test instrumented with inertial sensors.

II. Data

The gait and mobility of 21 participants, (aged 25-59 years, 8 M, 13 F) were assessed at the Neurology outpatient department in St Vincent's University hospital, Dublin, Ireland. All participants were diagnosed as having clinically definite relapsing remitting multiple sclerosis (MS). Each

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B.R Greene is with the TRIL centre, University college Dublin, Ireland and Kinesis Health Technologies, Dublin, Ireland (e-mail: barry.greene@ucd.ie).

B. Caulfield, The Insight centre and School of Physiotherapy and Performance Science, University College Dublin, Ireland (e-mail: b.caulfield@ucd.ie).

N. Tubridy, S. Rutledge and M. Healy are with Dept. of Neurology, St Vincent's University Hospital, Dublin (N.Tubridy@st-vincents.ie).

participant received a comprehensive neurological examination which included a full medical and MS history, the Multiple Sclerosis Impact Scale (MSIS-29), the Montreal Cognitive Assessment (MoCA) and Symbol Digit Modalities Test (SDMT). Each participant's MS disease state was also assessed using the Expanded Disability Status Score (EDSS). Clinical information on the cohort is supplied in Table 1.

The inclusion criteria were participants aged between 18 and 60, diagnosed with clinically definite relapsing remitting MS and not initially on disease modifying therapy (DMT). The exclusion criteria were diseases other than MS, primary or secondary progressive MS or a participant on DMT. All participants provided written informed consent and ethical approval was received from the local research ethics committee.

Mobility was assessed using a 25 foot timed walk and the Timed up and Go (TUG); both of which were instrumented with inertial sensors.

TABLE I: CLINICAL DATA FOR MULTIPLE SCLEROSIS COHORT.

ID	Age	Height (cm)	Weight (Kg)	Gender	EDSS	MoCA	SDMT	MSIS-29
1	46	162.0	89.8	F	4.5	27	46	105
2	39	169.9	81.8	F	0	28	65	32
3	46	169.5	92.8	F	3	22	43	46
4	41	190.5	65.7	M	1.5	26	37	50
5	41	165.0	64.1	F	1	29	68	45
6	35	171.5	73.8	M	2	23	30	65
7	54	166.7	60.4	F	1	28	57	37
8	59	166.0	94.5	M	0	29	42	30
9	47	171.5	63.6	M	1.5	23	38	32
10	52	175.0	77.8	F	1.5	29	53	41
11	59	164.0	86.4	F	2	24	45	59
12	45	154.2	57.4	F	0	22	48	64
13	42	181.0	89.1	M	0	26	54	47
14	49	183.0	96.5	M	1.5	25	33	36
15	54	161.0	60.0	F	1.5	26	45	58
16	38	182.0	72.0	M	0	27	30	43
17	55	173.0	92.7	M	2	25	47	87
18	48	168.0	77.8	M	0	22	41	34
19	57	174.0	97.4	F	3	25	25	65
20	38	162.6	58.3	F	1	21	42	68
21	25	164.0	67.0	F	2	23	42	35
Mean	46.2	170.2	77.1		1.4	25.2	44.3	51.4

III. METHODS

A. Sensor data acquisition

The participants were asked to perform the TUG test [3], as fast as was safely possible, by getting up from a standard chair (46 cm high seat, 65 cm arm-rests), walking three meters, turning at a designated spot, returning to the seat and sitting down. The timer was started from the moment the clinician said 'go' to the moment the participants sat back on the chair. The task was demonstrated to each participant and participants were given time to familiarize themselves with the test, and allowed to rest between tests. Each participant completed three TUG tests.

For each TUG test, participants were fitted with two wireless inertial sensors (SHIMMER, Dublin, Ireland), which were attached by a clinician or research assistant, using elasticized bandages, to the mid-point of each anterior shank (shin)[10]. Each sensor contained a tri-axial accelerometer and a tri-axial gyroscope and sampled at 102.4Hz. Sensors were calibrated using a standard method [11]. The raw gyroscope signal was low pass filtered with zero-phase 2nd order Butterworth filter with a 20Hz corner frequency. Inertial sensor data were synchronously acquired in real-time via Bluetooth using a custom developed Android application, and aggregated using a 7" tablet computer (Acer Iconia, Android ver. 3.2). Each data acquisition application automatically connected to the relevant sensors, allowed the clinician/researcher to start and stop the recording manually. Data were automatically saved to text format for subsequent offline analysis.

B. Sensor data analysis

The mobility of each participant performing the TUG test was evaluated using a previously reported method for quantitative assessment of movement during the TUG test [10, 12]. Features were calculated from the angular velocity signals obtained from the tri-axial gyroscope sensors mounted on each shank. The 52 sensor-derived features can be grouped into four categories: temporal gait parameters, spatial gait parameters, tri-axial angular velocity parameters and turn parameters. Coefficient of variation (CV) features were transformed using a log-transform to ensure a more normal distribution. All features were then normalized to have zero mean and unity standard deviation.

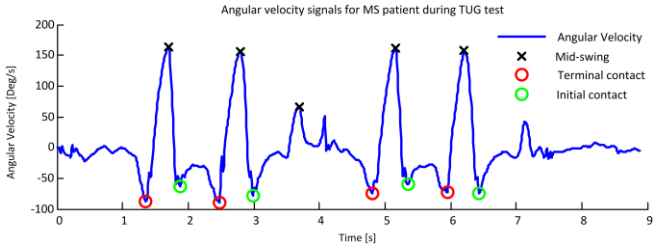

Figure 1: Sample medio-lateral shank angular velocity signal obtained from MS patient while performing a TUG test. Initial and terminal contact points (IC and TC) as well as mid-swing points are indicated.

C. Statistical analysis

Intra-class correlation coefficients (ICCs) were then calculated to assess the intra-session test-retest reliability; within-session reliability was calculated for each variable using ICC(2,1) and 95% confidence intervals supplied.

The elastic net regularization regression procedure [13] was used to derive a regression model of the EDSS score for all participants. This procedure was chosen due to the highly correlated nature of the features derived from the inertial sensors and the larger number of features (n=52) compared to observations (n=21). The lambda value for regularization was

chosen through 10-fold cross-validation as the minimum cross-validated mean squared error (MSE) that provided a non-null model. The alpha value for the elastic net procedure was set to 0.5 prior to analysis. The model fit provided by the elastic net procedure is quantified using MSE and degrees of freedom (DF). The coefficient of determination (R^2) was also calculated for the data set when applied to the model estimates produced. All analysis was performed offline in Matlab version 7.11 (Natick, VA, USA).

TABLE II: INTRACLASS CORRELATION COEFFICIENTS (ICC(2,1)) FOR INERTIAL SENSOR PARAMETERS.

Inertial sensor parameter	ICC(2,k)	(95% CI)
Mean Z-axis ang. vel. (deg/s)	0.99	(0.97-0.99)
Mean Z-axis ang. vel. x Height (deg.m/s)	0.99	(0.97-0.99)
Mean X-axis ang. vel. × Height (deg.m/s)	0.98	(0.97-0.99)
Mean X-axis ang. vel. (deg/s)	0.98	(0.96-0.99)
TUG recording time (s)	0.98	(0.95-0.99)
Mean Y-axis ang. vel. (deg/s)	0.96	(0.92-0.98)
Mean Y-axis ang. vel. × Height (deg.m/s)	0.96	(0.92-0.98)
Walk time (s)	0.95	(0.91-0.98)
Magnitude mean at mid-swing points (deg/s)	0.95	(0.89-0.98)
Mean stride length (cm/s)	0.94	(0.88-0.97)
Max X-axis ang. vel. × Height (deg.m/s)	0.94	(0.87-0.97)
Min Z-axis ang. vel. (deg/s)	0.93	(0.87-0.97)
Min Z-axis ang. vel. x Height (deg.m/s)	0.93	(0.86-0.97)
Min Y-axis ang. vel. × Height (deg.m/s)	0.93	(0.85-0.97)
Turn mid-point time (s)	0.93	(0.85-0.97)
Max X-axis ang. vel. (deg/s)	0.92	(0.85-0.97)
CV X-axis ang. vel. (%)	0.92	(0.84-0.97)
Number of gait cycles	0.92	(0.83-0.96)
Min Y-axis ang. vel. (deg/s)	0.92	(0.83-0.96)
Min X-axis ang. vel. × Height (deg.m/s)	0.90	(0.80-0.96)
Number of steps	0.90	(0.80-0.96)
Return from turn time (s)	0.90	(0.79-0.95)
Min X-axis ang. vel. (deg/s)	0.89	(0.77-0.95)
Mean stride time (s)	0.86	(0.72-0.94)
Cadence (steps/min)	0.86	(0.72-0.94)
CV Y-axis ang. vel. (%)	0.86	(0.71-0.94)
Max Y-axis ang. vel. × Height (deg.m/s)	0.86	(0.71-0.94)
CV Z-axis ang. vel. (%)	0.84	(0.67-0.93)
Max Y-axis ang. vel. (deg/s)	0.83	(0.66-0.93)
Mean step time (s)	0.81	(0.62-0.92)
Mean stride velocity (cm/s)	0.78	(0.56-0.90)
Time to stand (s)	0.78	(0.55-0.90)
Mean swing time (s)	0.66	(0.30-0.85)
Stride time variability (%)	0.65	(0.28-0.84)
Magnitude range at mid-swing points (deg/s)	0.63	(0.24-0.83)
Max Z-axis ang. vel. (deg/s)	0.62	(0.23-0.83)
CV stride length (%)	0.62	(0.23-0.83)
Max Z-axis ang. vel. x Height (deg.m/s)	0.62	(0.22-0.83)
Mean double support (%)	0.57	(0.12-0.81)
Mean single support (%)	0.56	(0.11-0.80)
Mean stance time (s)	0.54	(0.07-0.79)
Double support variability (%)	0.50	(0-0.78)
Ratio strides/turning time	0.43	(0-0.75)
CV stride velocity (%)	0.38	(0-0.72)
Step time variability (%)	0.37	(0-0.72)
Number of strides in turn	0.33	(0-0.70)
Walk ratio	0.22	(0-0.65)
Swing time variability (%)	0.21	(0-0.65)
Stance time variability (%)	0.16	(0-0.63)
Turn magnitude (deg/s)	0.08	(0-0.59)
Turning time (s)	0.07	(0-0.59)
Single support variability (%)	0	(0-0.52)

IV. RESULTS

The intra-session reliability of the inertial sensor parameters derived from participants performing three consecutive TUG tests was calculated using intraclass correlation coefficients (ICC(2,1)).

According to the levels suggested by Shrout and Fleiss [14], 32 of 52 inertial sensor parameters demonstrated excellent reliability (ICC≥0.7), while 11 of 52 parameters demonstrated moderate reliability (ICC≥0.4). Nine parameters exhibited poor reliability (ICC<0.4). The parameters exhibiting poor reliability were those based on gait variability or turn parameters, suggesting patients employed different turn strategies between iterations as well as a more variable gait patterns.

Using cross validation, an elastic net regularized regression model of MSIS-29 yielded a mean square error (MSE) of 334.6 with 25 degrees of freedom (DoF). The value of λ was chosen through 10 fold cross-validation (see Fig. 2(a)). When all data were applied to the model generated through the elastic net procedure, the coefficient of determination R^2 was 0.6 with a root mean square error of 12.0 (see Fig. 3(a)).

Similarly, an elastic net regularized regression model of EDSS yielded a cross-validated MSE of 1.5 with 6 DoF (see Fig. 2(b)). The value of λ was 0.57, with α set to 0.5 prior to analysis. When all data were applied to the model generated through the elastic net procedure, the coefficient of determination R^2 was 0.4 with a root mean square error of 0.9 (see Fig. 3(b)).

V. DISCUSSION

This study sought to investigate the utility of inertial sensors for assessing patients with relapsing remitting MS, as measured using the EDSS and MSIS-29 scales. The intra-session reliability of inertial sensor parameters derived from each TUG test for each participant was examined using intra-class correlation coefficients. Regression models of the EDSS and MSIS-29 scores were derived from the inertial sensor parameters using the elastic net regularization procedure.

The intra-session reliability of quantitative TUG parameters have been reported elsewhere [15], to our knowledge, however, this is the first attempt to quantify gait and mobility in patients with RR MS using inertial sensors.

The parameters used in this study were derived from tri-axial gyroscopes attached to both shanks, where difficulties related to sensor orientation were minimal. The macro gait variables, spatio-temporal gait parameters and angular velocity parameters demonstrate overall high levels of reliability, although some gait variability measures showed poor reliability suggesting high variability between trials. Salarian *et al.* [6] investigated the turn in their study and demonstrated good to excellent intra-session reliability, whereas certain turn variables in this study yielded much lower ICCs, e.g. turn magnitude, turning time.

Results suggest that quantitative assessment of mobility using inertial sensors may have utility in quantitatively assessing disease state in MS patients. We have demonstrated that parameters derived from a TUG test, instrumented with inertial sensors may have potential for use as a surrogate measure of MS disease state as measures by the MSIS-29 and EDSS scores.

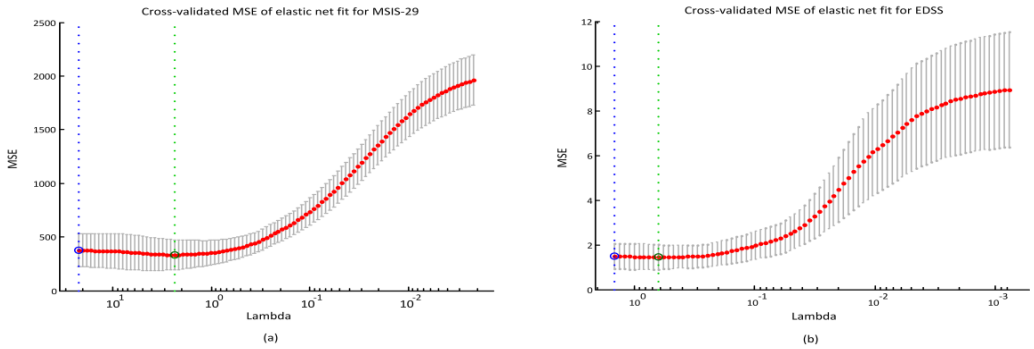

Figure 2. Plot of cross-validated MSE of elastic net fit for regression model of MSIS-29 (a) and EDSS (b). α parameter was set to 0.5, λ was chosen based on minimum value of MSE to yield a non-null model. Minimum MSE value is indicated by dotted blue line while, minimum MSE plus one standard error is indicated by the green dotted line.

Future work will examine longitudinal assessment of MS patients, in which changes in the quantitative parameters obtained from the sensor data during a mobility assessment would be mapped to clinical changes observed from application of the EDSS and MSIS-29 scales. Similarly, cognitive function could be assessed using Symbol Digit Modalities Test (SDMT) or Montreal Cognitive Assessment (MOCA) scales. Decline in cognitive function as measured by changes in these clinical scales could be used to determine if the instrumented mobility assessment can be used to quantify MS disease state and disease progression.

VI. References

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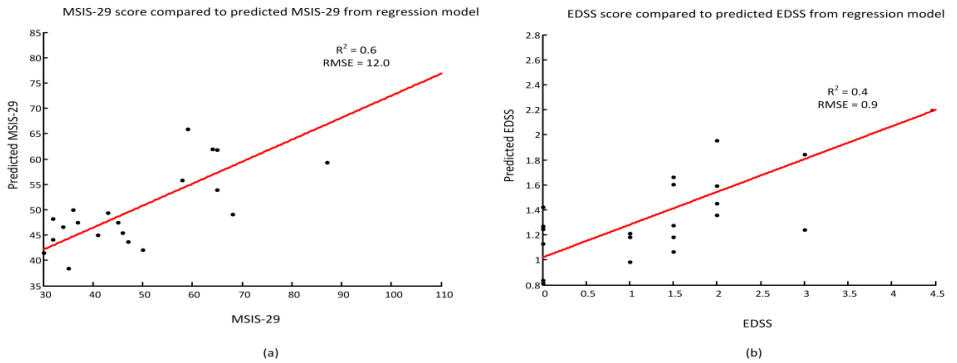

Figure 3. Predicted values of MSIS (a) and EDSS (b) obtained from regularized elastic net procedure, plotted against actual MSIS and EDSS.