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Free-living Monitoring of Ambulatory Activity after Treatments for Lower Extremity Musculoskeletal Cancers using an Accelerometer-based Wearable – A New Paradigm to Outcome Assessment in Musculoskeletal Oncology?

Running title: Ambulatory activity after sarcoma treatments

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Each author certifies that his or her institution approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.

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Abstract

Purpose of the study: Ambulatory activity (walking) is affected after sarcoma surgery yet is not routinely assessed. Small inexpensive accelerometers could bridge the gap. Study objectives investigated, whether in patients with lower extremity musculoskeletal tumours:

A) It was feasible to conduct ambulatory activity assessments in patient's homes using an accelerometer-based wearable (AX3, Axivity).
B) AX3 assessments produced clinically useful data, distinguished tumour sub-groups and related to existing measures.

Methods: In a prospective cross-sectional pilot, 34 patients with musculoskeletal tumours in the femur/thigh (19), pelvis/hip (3), tibia/leg (9), or ankle/foot (3) participated. 27 had limb-sparing surgery and 7 amputation. Patients were assessed using a thigh-worn monitor. Summary measures of volume (total steps/day, total ambulatory bouts/day, mean bout length), pattern (alpha) and variability (S_2) of ambulatory activity were derived.

Results: AX3 was well-tolerated and feasible to use. Outcomes compared to literature but did not distinguish tumour sub-groups. Alpha negatively correlated with disability [walking outside (r=-418, p=0.042*), social life (r=-0.512, p=0.010*)]. Disability negatively predicted alpha (unstandardised co-efficient = -0.001, R^2=0.186, p=0.039*).

Conclusion: A wearable can assess novel attributes of walking; volume, pattern and variability after sarcoma surgery. Such outcomes provides valuable information about people's physical performance in their homes, which can guide rehabilitation.

Level of Evidence Level III, diagnostic study

Keywords: Functional outcomes; sarcoma; cancer; quality of life; rehabilitation; ambulatory activity; ambulation; mobility

IMPLICATIONS FOR REHABILITATION

Routine capture of ambulatory activity by sarcoma services in peoples' homes can provide important information about individuals 'actual' physical activity levels and limitations after sarcoma surgery to inform personalised rehabilitation and care needs, including timely referral for support.

Routine remote ambulatory monitoring about out of hospital activity can support personalised care for patients, including identifying high risk patients who need rapid intervention and care closer to home.

Use of routine remote ambulatory monitoring could enhance delivery of evidence-based care closer to peoples' homes without disrupting their daily routine and therefore reducing patient and carer burden

Collection of data close to home using questionnaires and objective community assessment could be more cost effective and comprehensive than in-hospital assessment and could reduce the need for hospital attendance, which is of importance to vulnerable patients, particularly during the Covid-19 pandemic.

Introduction

Major surgery, chemotherapy and radiotherapy for lower extremity musculoskeletal tumours (bone and soft tissue) often leads to physical limitations [1-3]. Historically, cumbersome motion capture laboratory systems [4,5] were used to capture these, which provide important information about short periods of performance in a controlled environment. However they suffer from the inherent limitations of a patient's heightened attention, or the unintentional impact of testing known as the 'Hawthorne effect' [6]. While motion capture systems are currently the validated gold standard assessments for capturing gait deficits in a controlled laboratory environment [7], it is difficult to use these systems to capture performance at home and in the community, given that systems are not easily portable and are expensive. Recent studies have highlighted that physical activity and gait observations can be made in people's homes using small affordable body-worn activity monitors containing accelerometers which also provide information about features such as activity distribution, variability, steps per day, or energy expenditure [8-11]. Although the benefits of such wearable technology over laboratory systems include ease of use, portability and cost-effectiveness, they require validation prior to a clinical roll-out [3,9]. Despite these limitations, the potential benefits of remote monitoring using such wearable technology in people's homes and community [8] warrants exploration of its use in various clinical populations, to better reflect the real-life problems patients face.

Ambulatory activity (walking) in patient's homes is important, given the link between being active, survival and quality of life after cancer treatment [12,13]. Previous sarcoma studies have investigated sedentary activity or activity intensity [3]; which lacks completes understanding of ambulatory activity. Wearables could provide an efficient inexpensive

solution for assessing ambulatory activity [14,15] and indicate whether patients reach recommended activity targets [16].

More recently available wearables, triaxial accelerometers can provide additional detailed information about the volume, pattern and variability of ambulatory activity [9,17] . This novel information can facilitate personalised exercise programs [18], reduce traditional follow-up [19], identify patients at-risk [20,21] and allow a manageable way for stratifying patients [21] needing targeted rehabilitation when they may live a long way from specialist centres. In our recent publication on the same patient population in a different clinical setting, we showed a validated experimental triaxial accelerometer, axivity (AX3) successfully captured multiple attributes of function e.g balance and gait outcomes in a hospital after sarcoma treatments [22]. AX3 also offers a potent remote monitoring solution in the current covid-19 pandemic and reduce exposure to coronavirus.

The objective of our study therefore was to investigate the following in patients treated for lower extremity musculoskeletal tumours:

(1) Feasibility and acceptability of ambulatory activity assessments using AX3

(2) Early indicators of validity of ambulatory activity assessments using AX3 including face validity (the clinically usefulness of AX3 data compared to literature), discriminant validity (observe differences captured by AX3 between tumour sub-groups) and convergent validity (whether AX3 reflects findings from existing clinical scales)

Patients and Methods

Patients

The study was approved by the National Research Ethics committee (Reference: 13/NE/0296) and xxxxxxxxxxxxxxxxxx [anonymous hospital] (Reference:6801). Eligible patients were recruited from clinics and databases using convenience sampling. These were more than one year post-surgery for a lower extremity musculoskeletal tumour, and free of active disease/treatment [22].

Tumour Sub-groups

For purposes of this study, patients were classified by tumour type (bone tumour (BT) or soft tissue sarcoma (STS)) and surgery (limb sparing (LSS) or amputation (AMP)). Sub-groups were: LSS for above-knee BT; LSS for below-knee BT; LSS for above-knee STS; LSS for below-knee STS; above-knee AMP for BT or STS; below-knee AMP for BT or STS.

Assessments using Existing Clinic Scales

Established clinical measures in sarcoma; disability (Toronto Extremity Salvage Score, TESS) [23], impairment (Musculoskeletal Tumour Rating System, MSTS) [2], and quality of life (Quality of life-Cancer survivors (QoL-CS) [24] (Table 1) were used.

Equipment

A single wearable containing a tri-axial accelerometer (Axivity AX3; dimensions 23.0, 32.5 and 7.6 mm, weight: 11.0 g, sampling frequency 100Hz, range ± 8 g, Fig. 1A) was used to assess ambulatory activity. This sensor was selected as it has been validated for its suitability to capture high-resolution data for human movement analysis [25], is low-cost and provides open, high-resolution accelerometer data.

Wearable protocol: Measurement of Free-living Ambulatory Activity

Patients were asked to wear AX3 on the mid-thigh (Fig. 1B) of the dominant limb (directly against the skin, affixed with adhesive tape) during normal activities in their homes/community for 7 days [26,27]. Here, the dominant limb was considered as the classical understanding of the stronger, neuromotorically handier leg. A test was completed to determine the dominant leg, by asking the patient to stand on two legs and then instructing them to take a step. The first leg they use to do the test 3 times is considered as the dominant leg. Participants were asked to wear the accelerometer on the dominant leg on mid-thigh if below knee amputations and on other healthy thigh if it were an above knee amputation. This protocol was standardised and reported to the engineers working on the data analysis to account for the accelerometry analysis. The mid-thigh location was used as is known in a previous study to provide valid mobility/ambulatory activity outcomes in sarcoma patients [14]. After seven days, participants were asked to post back the AX3 to the study team [28,29]. Two reminder calls were made to prompt non-responders and feedback about AX3 use were collected using feedback forms.

Data Processing to obtain Ambulatory Activity outcomes

Data processing in three steps consisted: (1) Downloaded data from AX3 were processed using MATLAB® (R2012a). (2) Raw acceleration signals were segmented by calendar days (3) Periods of continuous walking [ambulatory bouts (ABs)] were extracted from raw data of upright positions (standing/stepping/walking). Established algorithms [30] were applied to ABs to derive ambulatory activity outcomes (Table 1). Outcome measures were described by a broad framework of macro behavioural outcomes [31] (A) Volume: total steps/day, total ambulatory hours/day, total ABs/day, mean bout length generated based on ABs detected over 7 days. A further set of nonlinear descriptors were derived: (B) Pattern of ABs derived using a

power-law distribution (alpha, α) which describes the distribution of ABs by evaluating the ratio of short to long ABs (e.g. a high alpha means that the total walking time is made up of proportionally short ABs compared to long ABs) (C) the within AB variability (S2) estimated using a maximum likelihood technique.

A logical heuristics paradigm was implemented into walking bout identification and quantification algorithm, which is accurate in detecting ABs in free-living conditions based on the concurrent use of a GoPro camera and AX3 [17]. The analytical pipeline automatically checked for 'non-wear time days' and discarded those from the analysis. Within each walking bout, a step detection method validated in older adults, sensitive and customised to each wearer was applied [32,33]. This allowed detection of differences due to natural cadence and anthropometric measurements. Validation of step count for our study patients in the hospital confirmed that sensor-derived step count showed excellent agreement with video step count [22].

Data Considerations

All bouts with more than three steps were used for evaluating ambulatory activity [34-37]. An initial inspection of total steps/day of individual cases was undertaken to investigate if ambulatory activity was reflective of patient's physical status. A technical and clinical viewpoint was taken towards these cases, they were investigated and excluded if values did not match the patient's known physical status. Patients with gait data ≥ 2 days were included in the final data analysis, to maximise the use of representative data [26]. We included full days and there was no threshold on number of hours on a particular day. Weekdays and weekends were captured together, to have a full view about the week.

Clinical interpretation of Good versus Poor Ambulatory Activity Outcomes

High values of total steps/day, total ambulatory hours/day, total ABs/day, mean bout length, variability and low values of alpha in a patient reflected a good clinical outcome (Table 1).

Study Outcomes

Our primary study outcome was measured by calculating the number of datasets successfully obtained, data loss encountered, and acceptability of use of the sensor. Our secondary outcomes were assessed by comparing ambulatory activity with reference values in the literature, across different tumour sub-groups and with existing clinical scales.

Statistical Analysis

Statistical analysis was carried out using SPSS v19 (IBM). Parametric data was represented as mean ± standard deviation (SD) and non-parametric data as medians with interquartile ranges (IQR) and/or minimum - maximum. Ambulatory activity outcomes were compared between tumour sub-groups using Independent t or Mann-Whitney U tests. Effect sizes were estimated using Z-statistic and sample size (N) from the Mann-Whitney U tests [38-40]. The formula for calculation of r-square proposed by Rosenthal and Rubin in 2003; $r = z/\sqrt{N}$ was utilised and after calculating r, it was squared to obtain r-square [40]. r-square measures the proportion of variance (%) in the dependent variable which is explainable by the independent variable [39]. So, the effect sizes derived can provide a quantitative capture of the magnitude of the effect of the independent variables [39]. The greater the effect size, the larger is the effect of the independent variable, however in human behaviour research small values might also hold significance [39]. For this study, effect sizes were utilised to investigate the effect of the independent variables such as tumour type (bone or soft tissue tumour) and surgery type (limb sparing or amputation) on ambulatory activity outcomes. Although a p-value will tell us

whether groups are significantly different, the effect size using r-square will tell us what the extent (size) of this difference is [40]. For the purposes of the study we have utilised the classification, r-square of 0.1 is considered as small effect, 0.3 medium effect and 0.5 and above as large effect [39,40].

We used the Bonferroni correction to address correction for multiple measures for the between group comparisons and set the alpha level at 0.05/6 = 0.008. In order to assess convergent validity. Pearson and Spearman's rho correlations were used to investigate relationships between ambulatory activity and existing measures. Correlations were classified as strong (-1.0 to -0.5 or 0.5 to 1.0), moderate (-0.5 to -0.3 or 0.3 to 0.5) or weak (-0.3 to -0.1 or 0.1 to 0.3) [41]. Regression models were run to assess the influence of wearable measures on existing clinical measures and vice-versa. Confounding factors identified were accounted for using significant relationships between variables and confounders identified were adjusted in the regression analysis. Significance was taken at the 0.05 level.

Results

Patient characteristics

34 adults of mean age 43 ± 20 years participated. The height of patients was 1.8 ± 0.10 meters (1.6-1.9 m), weight 78.4 kg (IQR, 66.0-101.1) and Body Mass Index 25.9 kg/m^2 (IQR, 21.7–31.6 kg/m^2). 25 males and 9 females were treated for BT (n=21) or STS (n=13) in the femur (n=19), pelvis/hip (n=3), tibia (n=9), or ankle/foot (n=3). BTs comprised of 10 osteosarcomas, 1 Ewing's sarcoma, 6 chondrosarcomas, 2 Malignant fibrous histiocytoma, 1 malignant pilomatrixoma and 1 metastatic cancer and STS comprised of 4 myxofibrosarcomas, 4 synovial sarcomas and 5 others (one each of leiomyosarcoma, myxoid

liposarcoma, primitive neuroectodermal tumour, soft tissue chondrosarcoma and soft tissue sarcoma (high grade) [22]

27 underwent LSS; 11 had excision only, 12 had excision + endoprosthesis and 4 had other types of LSS (allograft/autograft and flaps) and 7 patients undergoing AMP included 1 hindquarter amputation, 3 above-knee and 3 below-knee. Median time from surgery was 79 months (33 – 108). 15/34 patients received chemotherapy, and 13/34 received radiotherapy.

Feasibility of Ambulatory Activity Assessments

The thigh-worn monitor was feasible to use and quick to set up. Data downloading/processing were straightforward to perform, and outcomes was derived successfully. Problems were encountered for 6 patients including; loss of data due to failure to return monitors, technical issues and ambulatory activity values not being representative (less days captured or not matching the clinical picture); ultimately leaving 28 datasets for final analysis. Patients reported the monitor use at home as easy and did not find that the monitor hindered their activity or caused problems. Out of 28 patients whose datasets were available, 8 patients failed to complete a feedback form leaving us with 20 feedback forms. So although there were 28 data sets for final analysis, all 28 patients returned the device but 8 of these patients failed to complete and return a feedback form leaving us ultimately with 20 feedback forms for analysis. Of those who returned feedback forms (n=20), 20/20 (100%) found the monitor acceptable, 17/20 (85%) user-friendly and 19/20 (95%) comfortable to wear at home/community. Limitations reported the monitor was easy to lose when not being worn, and it sometimes got detached. One patient forgot to put on the monitor till later on in the day and another found its method of application confusing, with respect to its orientation

for correct use.

Indicators of Validity of Ambulatory Activity Assessments

Patients with lower extremity sarcoma presented with a wide range of ambulatory activity values; patients accumulated total steps/day of 10953 (5960 – 13790), total ABs/day of 463 (363 – 745), mean bout length of 3.16 (1.73 – 3.74) seconds, alpha of 1.59 (1.57 – 1.61) and variability of 0.92 (0.86 – 0.97) (Table 2).

Ambulatory Activity in Tumour Subgroups

Patients in the BT group accumulated fewer total steps/day [9189 (4918 – 13059) than those in the STS group [13393 (8004 – 15308)] ($p=0.03$); but this was not statistically significant after application of Bonferroni correction (Table 2, Fig. 2A). No significant differences were seen between BT group and STS group for rest of the variables ($p>0.05$) (Fig. 2B-2F). The monitor did not distinguish between LSS and AMP groups ($p>0.05$) (Table 2). Weak (trivial) or small effect sizes were observed in groups (Table 2).

Wearables versus Clinical scales in Sarcoma

TESS scores were 83.6 (IQR 62.1 to 93.8 [8.3 to 100.0]), MSTS scores 24.5 (SD 7.9 [5.0 to 35.0]), and QoL-CS scores 7.1 (IQR 6.1 to 7.8 [2.7 to 9.1]). No significant correlations were observed between MSTS, TESS, QoL-CS total scores and ambulatory activity outcomes ($p>0.05$) (Table 3). Yet TESS sub-scales [standing ($r=0.514$, $p=0.010$*), walking outside ($r=0.613$, $p=0.001$*), social life ($r=0.464$, $p=0.022$*)] showed significant moderate positive associations with total steps/day (Table 3). Alpha showed moderate negative associations with TESS sub-scales [walking upstairs ($r=-0.405$, $p=0.050$*) walking outside ($r=-418$, $p=0.042$*)

and social life (r=-0.512, 0.010*)] (Table 3). TESS was a negative predictor of alpha (p=0.039*) (Table 4).

Discussion

This is the first study to investigate the pattern and variability of ambulatory activity alongside volume, in patients treated for lower extremity sarcomas using a triaxial accelerometer.

Feasibility of Ambulatory Activity Assessments

The study findings on free-living monitoring of ambulatory activity adds valuable knowledge in conjunction with our recently published research about the use of an AX3 in a hospital set-up [22]. Since modern wearables are small and easy to lose, a two-step process of double securing with a band or tape and provision of a case for the monitor might be useful. Labelling monitors and information sheets (with pictures) to remind patients the correct direction of the port; might overcome problems on wearability [42]. Since some patients report that they forget to wear monitors; providing reminders could be an effective solution to improve wear time [43].

Indicators of Validity of Ambulatory Activity Assessments

Comparison to Reference Literature and across Tumour Subgroups

Ambulatory activity outcomes in patients showed broad clinical sense and some variables were comparable to data in the literature [42,44]. In our study, patients accumulated a total steps/day of 10953 (5960 – 13790), which was higher than those in a study by Sugiura et al, 2001 [7119 ± 3563], and comparable to healthy controls [10,206 ± 1338] from the same study [44]. The reason for different readings could be because Sugiura et al, 2001, used a simple pedometer, whereas our study used a triaxial accelerometer. Other likely reasons for differences in results

could be depending on how previous work has defined ambulatory bouts and if they use all steps captured or just considered bout durations, for example: ambulatory bouts over 60s. These methodological approaches could affect volumetric metrics and results comparison. Accelerometers are highly accurate superior devices in capturing short stepping episodes compared to older pedometers, which provide only basic information on step count [45]

Comparisons to a previous study using AX3 at the L5 level in retired older adults [42] revealed that our study patients showed a lower alpha [(1.58 ±0.03)] compared to retired adults [2.49 (2.39 to 2.59)] [42]. Variability (S_2) in our patients [0.920 +/ 0.081] was higher than that of retired adults [0.61 (0.54 to 0.68)] and total ABs/day in our study [503±252] was also higher than retired adults [31 (17 to 45)] [42]. These findings could be explained on the basis that our patients tended to be younger and a proportion were in employment compared to the retired adults in the other study.

Although no statistically significant differences were seen, trends in the data were present and were described. The lack of significance may be because of a small sample size and the heterogeneity of the group. For example, there was a trend for the BT group to have a lower number of total steps/day compared to the STS group which reflects the greater magnitude of surgery for bone tumours [44]. Similarly amputees demonstrated trends towards an absolute low volume and higher alpha of ambulatory activity compared to those in the LSS group, which would be expected because of the disability associated with limb loss and the disrupted sensory and proprioceptive inputs in the residual limb [46,47]. As trivial or small effect sizes were observed, it can be ascertained that a small proportion of variance (%) in the dependent variable was explainable by the independent variable [39,40] such as the tumour or surgery type. To demonstrate a significant difference would likely require larger studies in future with a greater

number of classifications of patients by surgery level, tumour type or surgery type to investigate if differences are significant or because of a Type 2 sampling error. proportion of variance (%) in the dependent variable which is explainable by the independent variable

Wearables vs Clinical scales in Sarcoma

No significant relationships between existing clinical scales and ambulatory activity, agrees with previous research [14]. In our study, TESS sub-scales mainly of standing, walking and social life related to ambulatory activity, which made broad clinical sense, as the more people tend to stand, walk or socialise; they are expected to present with a higher ambulatory activity. In addition, TESS was a significant negative predictor of alpha, indicating that greater disability is associated with a lower volume of ambulatory activity and also predict an accumulation of shorter distribution of walking bouts. These relationships are sensible as per an international health standard: the International Classification of Functioning Disability and Health (ICF) [48,49], confirming convergent validity and is novel information which can guide designing of rehabilitation programmes.

Strengths, limitations and future work

Strengths of the study are that the use of a wearable in a range of tumour sub-types confirms its applicability across this heterogeneous population. The algorithms worked successfully, except for certain patient types (wheelchairs users), suggesting need for personalisation of algorithms for these groups. An AX3 being an open-source sensor has openness to develop, modify and personalise systems/algorithms.

Major study limitations in drawing firm conclusions is a small sample size and that a Type 2 sampling error, investigator bias and selection bias cannot be eliminated, although appropriate

measures were taken during data analysis to minimise bias. Although wearables seem promising for objective, continuous, unobtrusive free-living monitoring of patients in their homes/communities, clinicians will always be blinded to the context of real-life situations. Whilst useful, quantifying ambulatory behaviour has its own challenges, as ambulatory behaviour can vary between different age groups [16,50], weather conditions, time of the year, socio-economic background [51], gender [51] and geography [52]. Attributes of, level of occupation, participants in sports, socio-economic factors and activities in daily life (athletes or farmers, for example, have to be active when taking care of their training regime or daily tasks) must also be carefully examined. Hence blanket recommendations about the achievement of specific targets may not be ideal: it might be more useful to take a more personalised approach and stratify activity levels by clinical and demographic factors. Furthermore, no consensus currently states a specific suitable algorithm, which reduces consistency across studies [53]. Wearables have important applications in healthcare but requires standardisation of valid algorithms and validation in free-living conditions. Although we have shown that a single monitor is useful, some studies [54] suggest that multiple monitors might help overcome limitations of current algorithms.

Recommendations for future work

In order to rigorously test validity; research is warranted in larger homogenous samples. Work is needed to assess reliability of wearable measurement on different occasions and across the week, and sensitivity to change over time to confirm these devices are fit for purpose in clinical practice. Capturing longitudinal pre and post-treatment ambulatory activity status can allow tracking of functional outcome progress over time and impact of sarcoma surgery.

Although only a type of Physical activity ‘Ambulatory Activity’ is being quantified here and we are not capturing other types of physical activity, energy expenditure or intensity of physical activity; capturing these other attributes alongside ambulatory activity in future work will allow clinicians to understand the relationships between different functional activities.

Work is required to explore the use of this novel information to inform personalised rehabilitation strategies and routinely monitoring patients after surgery as this data can be processed promptly and be available within hours/days of having an assessment. Future work will aim to target derivation of outcome measures directly from the device automatically to facilitate its clinical usefulness. Until this is achieved, the AX3 can be a useful research tool to guide assessments, capture complex problems, guide treatment choices and rehabilitation in musculoskeletal oncology.

Conclusion

A thigh-worn monitor is feasible to use to quantify ambulatory activity remotely in patients' homes and communities. Novel insights about ambulatory activity (for example: alpha, variability (S_2)), acceptability to patients with some limitations which can be overcome using simple solutions, and significant associations with sarcoma scales showed promise. A single wearable after further validation could form a low-cost solution to remotely assess free-living ambulatory behaviour and guide personalised rehabilitation in patients treated for lower extremity musculoskeletal tumours.

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Tables

Table 1: Summary of existing clinical scales and extracted ambulatory activity measures

S.No	Clinic measures	Sub-domains	Scores
Existing clinic measures			
1.	Musculoskeletal Tumor Society score (MSTS) version developed in 1987 (MSTS-1987) for the Lower Limb [17]	7 sub-domains range of motion, stability, deformity, pain, muscle strength, functional activity and emotional acceptance.	The MSTS total score is expressed from 0-35 (worst to best physical functioning). Individual sub-domain score is 0-5.
2.	Toronto Extremity Salvage Score (TESS) [12]	30 self-reported items.	Scores range from 0 to 100 (worst to best outcomes).
3.	Quality of Life for Cancer Survivors (QoL-CS) [19]	41-item questionnaire.	Scores range from 0 to 100 (worst to best outcomes).
Volume of Ambulatory Activity			
1.	Total steps/day	Total number of steps taken over a 7 day period divided by number of days recorded.	A higher volume of ambulatory activity reflects higher amount of ambulatory activity accumulated by an individual, whereas a lower volume of ambulatory activity reflects lower amount of ambulatory activity accumulated by an individual
2.	Total ABs/day	Total number of ABs (continuous periods of walking >3 steps) over 7 days was divided by the number of days recorded.	
3.	Total ambulatory hours/day	Total number of hours spent walking was measured over a period of 7 days was divided by the number of days recorded.	
Pattern/Distributions of ABs			
1.	Mean bout length (seconds (s))	Mean length of walking time in seconds (s), over a 7 day period. Mean bout length is calculated using the maximum likelihood ratio technique, as the data were log normally distributed [23].	A higher mean bout length reflects higher periods of continuous walking, whereas a low mean bout length reflects shorter periods of pottering around.
2.	Alpha (α) of ABs	Alpha is the distribution of ABs and was quantified using the power law distribution exponent alpha (α). Alpha (α) is defined as the accumulation (by bout length) of walking time [39].	A low alpha indicates a greater accumulation of longer bouts and a high alpha of shorter bouts [34].
Variability of ABs			
1.	Variability (S_2)	The 'within person' variability of AB length and examines the dispersion of AB lengths in the same patient. This was also measured using the maximum likelihood method, as the data were log normally distributed [23]. Variability (S_2)	A higher variability indicates a greater variation in the pattern of walking, whereas a lower variability indicates a smaller variation of ABs [34].

Table 2: Ambulatory behaviour in tumor patients, BT vs STS, LSS vs AMP

Ambulatory Activity measures	Tumor patients (n=28)	BT group (n=16)	STS group (n=12)	p-value for BT vs STS groups	LSS group (n=23)	AMP group (n=5)	p-value for LSS vs AMP groups
	Median Values (25^{th} – 75^{th} percentile, 1QR)	Median Values (25^{th} – 75^{th} percentile, 1QR)	Median Values (25^{th} – 75^{th} percentile, 1QR)		Median Values (25^{th} – 75^{th} percentile, 1QR)	Median Values (25^{th} – 75^{th} percentile, 1QR)	
Total steps/day	10953	9189	13393	0.03	13047	9577	0.569
	(5960 – 13790)	(4918 - 13059)	(8004 - 15308)		(5653 – 13877)	(7054 – 12089)	
Total ABs/day	463	409	581	0.13	552	403	0.569
	(363 – 745)	(316 - 663)	(403 - 885)		(363 – 771)	(360 – 622)	
Total ambulatory hours/day	3.16	2.41	3.58	0.06	3.23	2.30	0.418
	(1.73 - 3.74)	(1.32 - 3.46)	(2.26 - 4.18)		(1.65 – 3.79)	(1.93 – 3.32)	
Mean bout length (s)	19.13	19.02	19.45	0.58	19.05	20.00	0.610
	(16.57 - 21.47)	(16.75 - 20.32)	(16.41 - 22.02)		(16.53 – 21.73)	(15.56–26.25)	
Alpha (distribution)	1.59	1.59	1.57	0.10	1.58	1.60	0.529
	(1.57 – 1.61)	(1.58 - 1.64)	(1.56 - 1.61)		(1.57 - 1.62)	(1.56 – 1.63)	
Variability (S_2)	0.92	0.92	0.90	0.85	0.92	0.97	0.294
	(0.86 – 0.97)	(0.87 - 0.97)	(0.85 - 0.98)		(0.86 – 0.96)	(0.85 -1.04)	

p-value – correlation between variables (*=statistically significant with and without Bonferroni correction)

Table 3: Spearman's correlations between ambulatory activity and existing clinical scales

Clinical scales	Ambulatory Activity Measures	Sample no (n)	R value	p-value	TESS sub-scales		Ambulatory Activity measures	Sample no (n)	R-value	p-value
MSTS (Impairment)	Total steps/day	28	0.032	0.870	TESS activities and social sub-scales with significant relations	TESS Sitting	Total steps/day	24	0.541	0.006*
	Total ABs/day	28	0.057	0.774			Total ABs/day	24	0.530	0.008*
	Total ambulatory hours/day	28	-0.006	0.978			Total ambulatory hours/day	24	0.541	0.006*
	Mean bout length (s)	28	0.071	0.721		TESS Standing	Total steps/day	24	0.514	0.010*
	Alpha	28	-0.107	0.587			Total ABs/day	24	0.439	0.032*
	Variability (S_2)	28	-0.025	0.900			Total ambulatory hours/day	24	0.597	0.002*
TESS (disability)	Total Steps/day	24	0.321	0.126			Mean bout length (s)	24	0.406	0.049*
	Total ABs/day	24	0.225	0.290			Alpha	24	-0.585	0.003*
	Total ambulatory hours/day	24	0.277	0.190		TESS Walking upstairs	Alpha	24	-0.405	0.050*
	Mean bout length (s)	24	0.214	0.315		TESS walking outside	Total steps/day	24	0.613	0.001*
	Alpha	24	-0.282	0.182			Total ABs/day	24	0.474	0.019*
	Variability (S_2)	24	0.090	0.676			Total ambulatory hours/day	24	0.566	0.004*
QoL-CS total score (QoL)	Total Steps/day	24	0.131	0.543			Alpha	24	-0.418	0.042*
	Total ABs/day	24	0.068	0.751		TESS Walking ramp	Total steps/day	24	0.430	0.036*
	Total ambulatory hours/day	24	0.097	0.653			Mean bout length (s)	24	0.414	0.044*
	Mean bout length (s)	24	0.254	0.231		TESS social	Total steps/day	24	0.464	0.022*
	Alpha	24	-0.179	0.402			Alpha	24	-0.512	0.010*
	Variability (S_2)	24	0.147	0.494						

Table 4: Regression Models: TESS vs Ambulatory Activity (n=24)

Model number	Independent variables	Unstandardised coefficients	Standardised regression coefficients (Beta)	R square	F-statistic change	Significance of regression model (p-value)	Excluded variables
Model 1: Total steps/day as a dependent variable							
	Constant	3114.352		0.130	0.084	0.084	N/A
	TESS	99.701	0.360				
Model 2: Total ambulatory hours/day as a dependent variable							
2.	Constant	0.985		0.120	0.097	0.097	N/A
	TESS	0.026	0.347				
Model 3: Alpha as dependent variable, adjusted for age							
3.	Constant	1.666					Age, level of tumor and time
	TESS	-0.001	-0.443	0.196	0.039*	0.039*	since surgery
Model 4: Alpha as dependent variable with TESS and age as independent variables							
4.	Constant	1.725					
	TESS	-0.001	-.434				
	Age	-0.001	-0.596	0.551	0.001*	0.000492*	BMI, Months post surgery

Figures

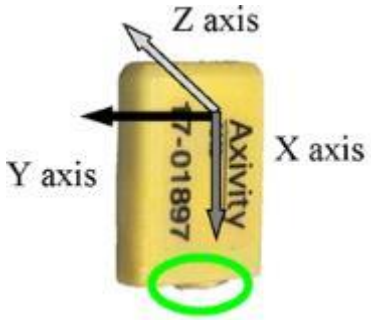

Figure 1

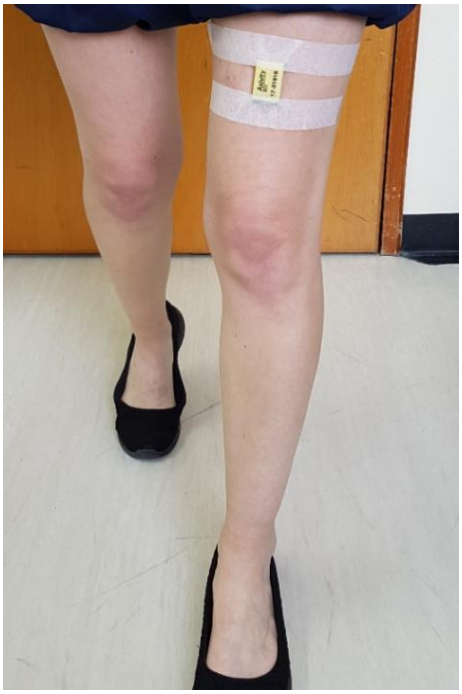

Figure 2

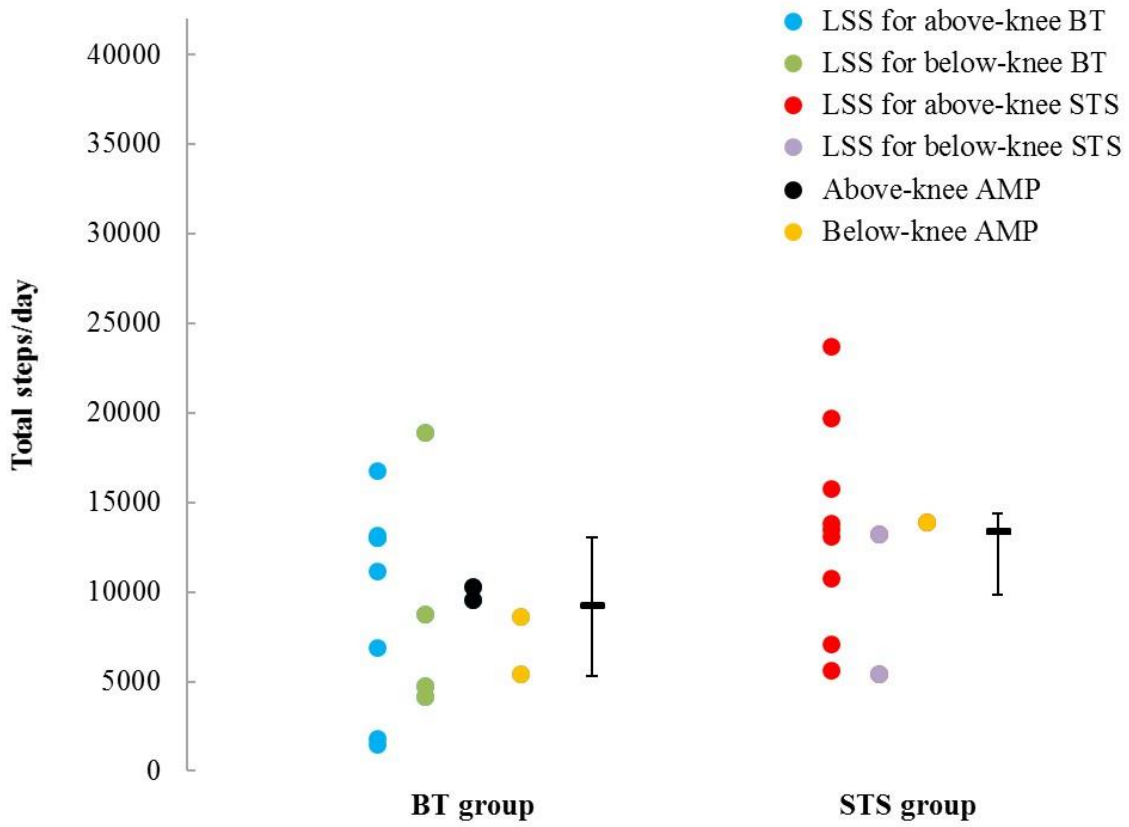
LSS for above-knee BT
LSS for below-knee BT
LSS for above-knee STS
LSS for below-knee STS
Above-knee AMP
Below-knee AMP
Total steps/day
40000
35000
30000
25000
20000
15000
10000
5000
0
BT group
STS group

Figure 2A

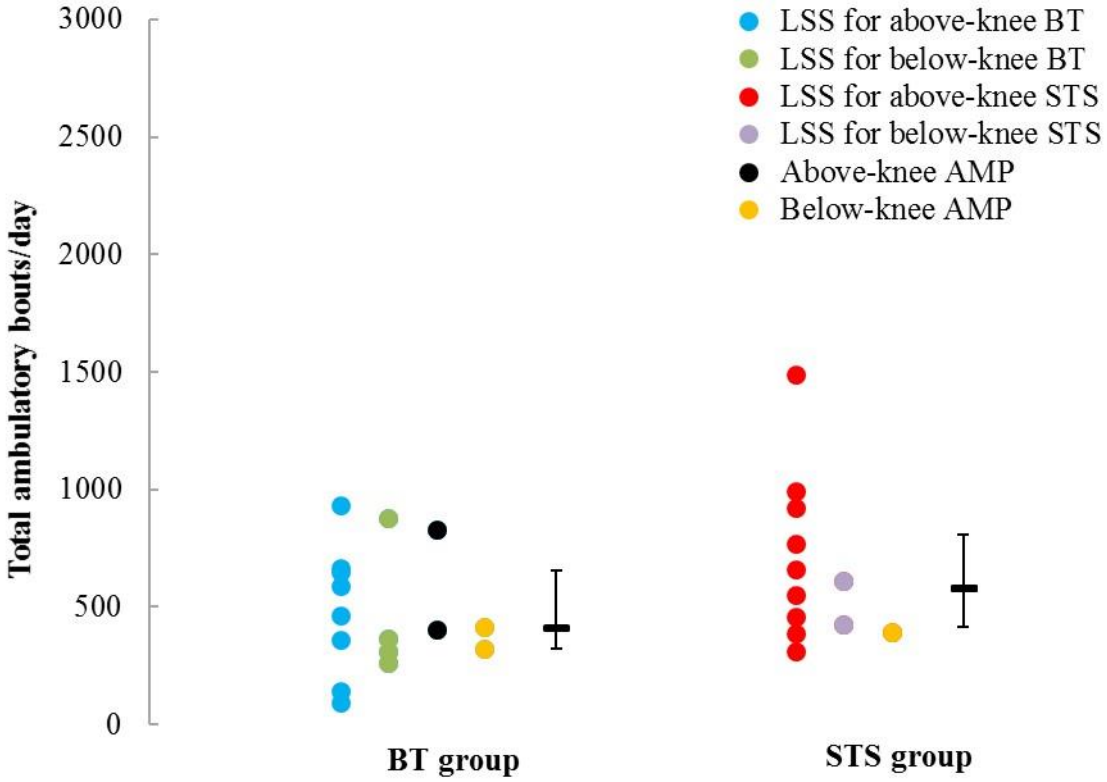
3000
2500
2000
1500
1000
500
0
Total ambulatory bouts/day
LSS for above-knee BT
LSS for below-knee BT
LSS for above-knee STS
LSS for below-knee STS
Above-knee AMP
Below-knee AMP
BT group
STS group

Figure 2B

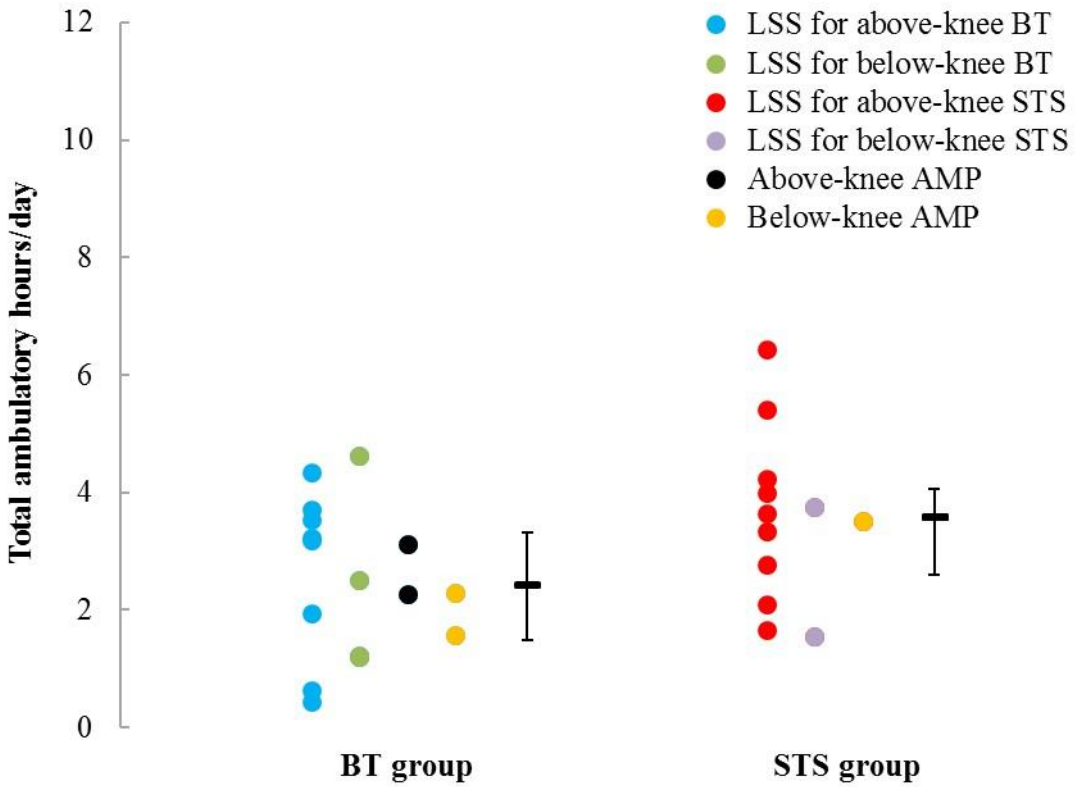
12
10
8
6
4
2
0
Total ambulatory hours/day
LSS for above-knee BT
LSS for below-knee BT
LSS for above-knee STS
LSS for below-knee STS
Above-knee AMP
Below-knee AMP
BT group
STS group

Figure 2C

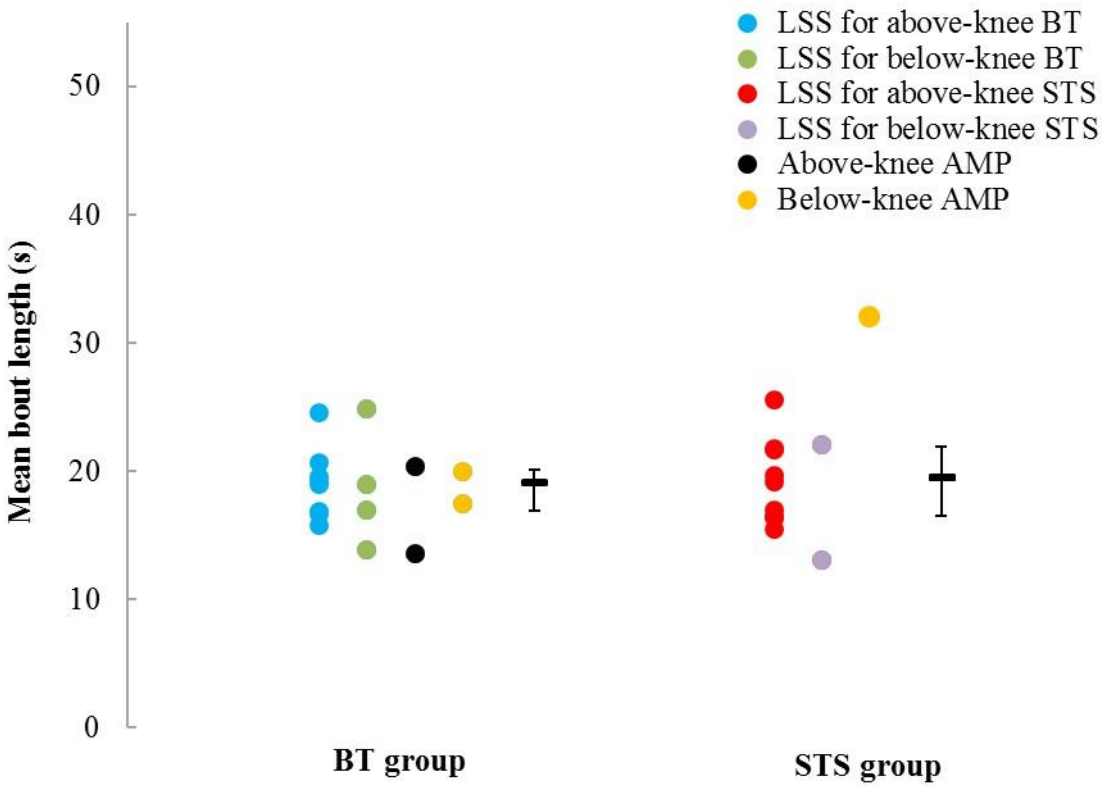
LSS for above-knee BT
LSS for below-knee BT
LSS for above-knee STS
LSS for below-knee STS
Above-knee AMP
Below-knee AMP
Mean bout length (s)
50
40
30
20
10
0
BT group
STS group

Figure 2D

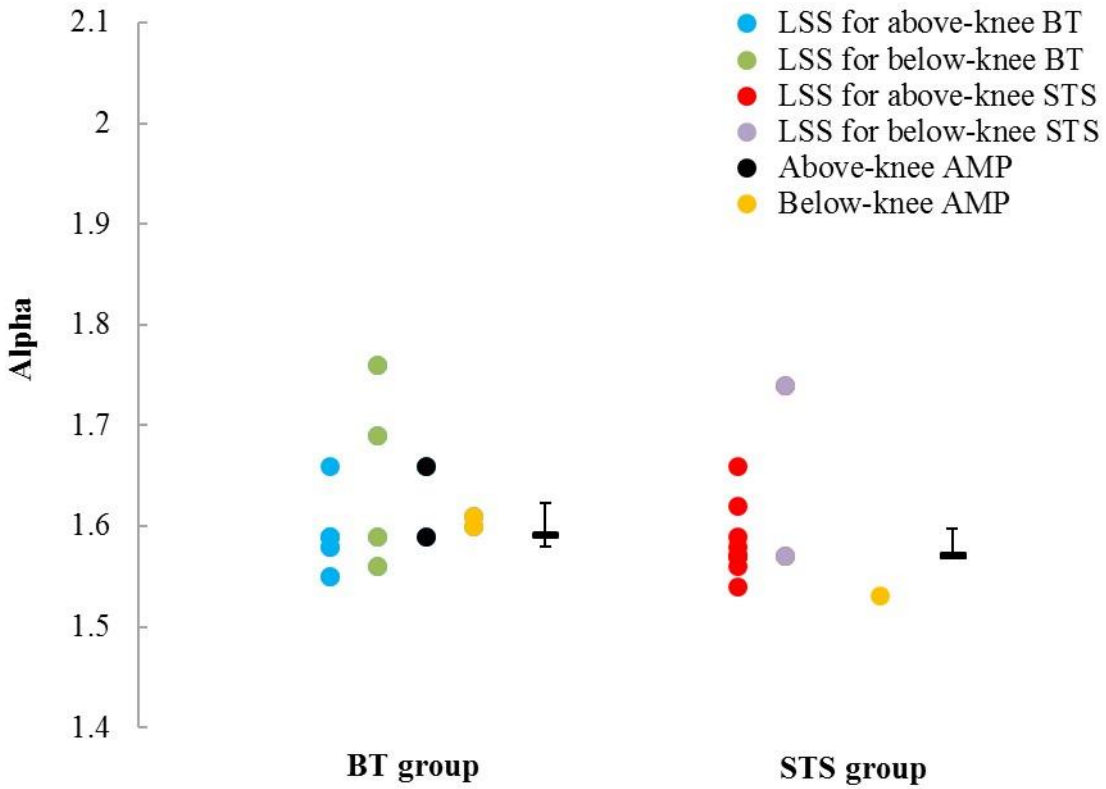
2.1
2
1.9
1.8
1.7
1.6
1.5
1.4
Alpha
LSS for above-knee BT
LSS for below-knee BT
LSS for above-knee STS
LSS for below-knee STS
Above-knee AMP
Below-knee AMP
BT group
STS group

Figure 2E

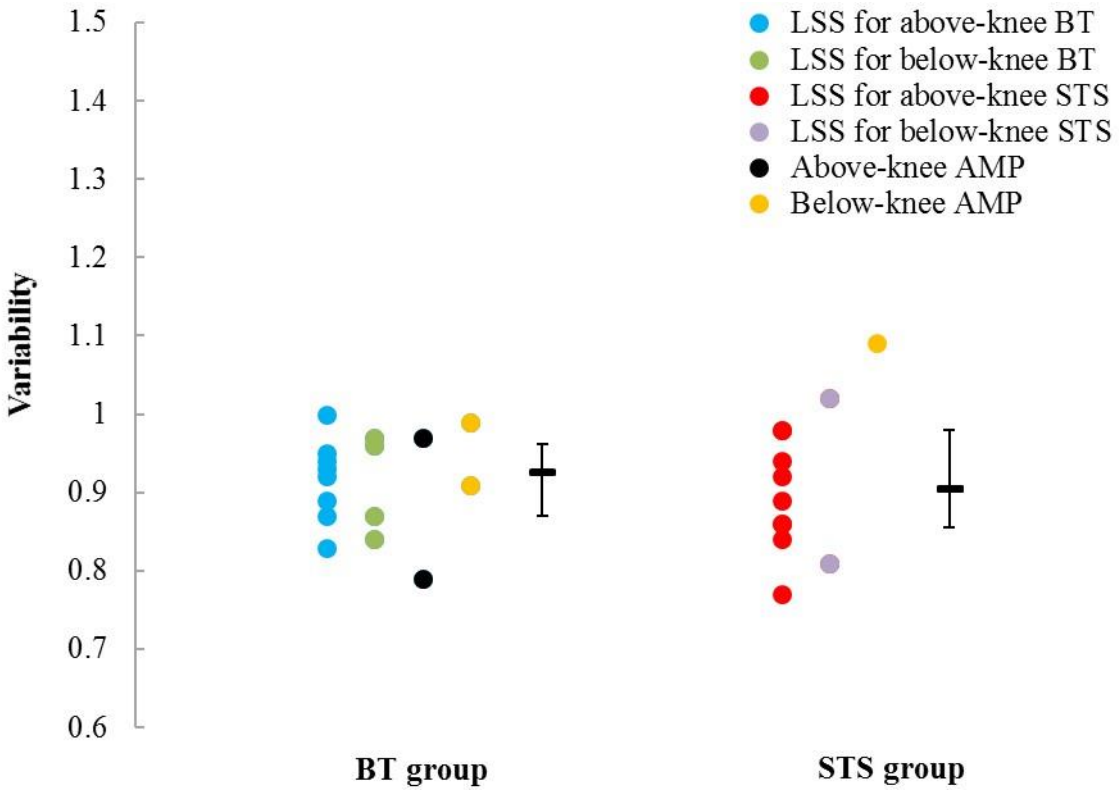
1.5
1.4
1.3
1.2
1.1
1
0.9
0.8
0.7
0.6
Variability
LSS for above-knee BT
LSS for below-knee BT
LSS for above-knee STS
LSS for below-knee STS
Above-knee AMP
Below-knee AMP
BT group
STS group

Figure 2F