

Measuring activity in patients with sarcoidosis - a pilot trial of two wrist-worn accelerometer devices

Running Title: Activity monitors in sarcoidosis – a pilot trial of devices

C P Atkins^{1,2}, A P Jones¹, A M Wilson^{1,2}

¹Norwich Medical School, University of East Anglia, Norwich, Norfolk, UK, NR4 7TJ

²Norfolk and Norwich University Hospital, Colney Lane, Norwich, UK, NR4 7UQ

Responsible Author: Dr C P Atkins, NIHR Doctoral Research Fellow, Norwich Medical School, University of East Anglia, Norwich, UK, NR4 7UY. E-mail: c.atkins@uea.ac.uk

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Abstract

Introduction

Increasing physical activity is associated with health benefits. Reduced physical activity has been noted in sarcoidosis, particularly where fatigue co-exists. Monitoring physical activity is possible with wrist-worn devices. This study compared two available devices to determine patient preference and compare wear-time, with a secondary outcome of comparing device outputs with fatigue scores.

Methods

Patients with sarcoidosis wore two wrist-worn activity monitors (GENEActiv actiwatch and Actigraph GT3X-bt) separately for seven days each. Participants were randomly allocated to receive either device first. Participants completed the Fatigue Assessment Scale (FAS) questionnaire immediately before wearing the first device. All participants completed a questionnaire of their perception regarding each device after the wear period. Data from the devices was analysed for total wear time, time spent in moderate or vigorous activity (MVPA) and for time spent in sedentary behaviours.

Results

Twelve patients with sarcoidosis were included. The GENEActiv device was preferred by ten (83.3%) participants. Wear time was greater with the GENEActiv device (1354 minutes/day vs 1079 minutes/day). Time spent in MVPA was slightly higher when recorded by the GENEActiv compared with the Actigraph. Moderately strong correlation was seen between FAS scores and sedentary time ($r = -0.554$), light activity ($r = -0.585$) and moderate activity ($r = 0.506$).

Discussion

A clear preference was demonstrated for the GENEActiv. This was reflected in higher wear time and suggests the device can be comfortably worn 24 hours per day. Data from this small cohort also suggests there is correlation between fatigue and activity scores in patients with sarcoidosis.

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Introduction

Increasing physical activity is associated with a wide-range of health benefits(1) and therefore assessing physical activity is important when evaluating interventions to support individuals to be active. Unfortunately, activity questionnaires are associated with recall bias and therefore other methods, including the use of accelerometry-based activity monitors, are required.(2). Accelerometers have been shown to produce comparable results to double-labelled water, the gold-standard measurement of energy expenditure, and can provide information on activity patterns rather than total energy expenditure over a set period(3). Some accelerometers are also able to measure sedentary behaviours, comparable to the gold-standard measure of inclinometers(4-6).

Activity monitors can either be worn proximally on the hip or upper arm, or distally on the wrist or ankle. The wrist position is associated with a reduction in accuracy when classifying activity intensity compared with the hip position, potentially due to constraint of movement at the wrist when performing certain activities(7). However, wrist-worn devices benefit from being more acceptable to participants may lead to better compliance and improved wear time(8). For this reason, the UK Biobank and the USA National Health and Nutrition Examination Survey (NHANES) now use wrist-worn devices to measure activity in participants. There are a number of wrist-worn devices available, yet it is unclear how much impact the individual design has on the comfort of wearing the device, as well as the subsequent effect on wear time.

Sarcoidosis is a multi-system, granulomatous disease of unknown origin(9). It can affect any organ or system within the body and can present with a range of symptoms that can persist in a chronic form(10, 11). A large number of patients with chronic disease suffer non-specific

manifestations, including fatigue in up to 80% of sufferers(12). It has been suggested that activity levels are reduced in patients with sarcoidosis, particularly when suffering from fatigue(13), and that improving physical activity can improve fatigue scores(14, 15).

Although the link between sedentary behaviours (defined as sitting or lying with low energy-expenditure) and fatigue has not been investigated in patients with sarcoidosis, an inverse correlation between them has been seen in other conditions where fatigue is a prominent symptom, such as fibromyalgia(16) and rheumatoid arthritis(17). Furthermore, it has previously been suggested that when considering choice of device for future studies within a patient group that a pilot study be performed to determine the ideal accelerometer device(18). Sarcoidosis patients have lower levels of activity than health individuals, even when the disease is in remission (13); it is therefore important to compare how potential devices will perform.

This study investigates the relative acceptability of two widely-used wrist-worn, accelerometry-based activity monitors, the GENEActiv original and the Actigraph GT3X-bt, in patients with sarcoidosis. These two devices are different in design but both output raw data which can be analysed in an identical fashion (5, 19). Both have also been shown to be able to measure sedentary behaviours(4, 5). The primary outcomes of interest are patient preferences relating to device comfort and wear time of the devices. The secondary outcomes of interest are patterns of activity and sedentary behaviours in these patients and the correlation between these outputs and the fatigue questionnaire scores.

Methods

Subjects

The study was undertaken at the Norfolk and Norwich University Hospital, in the UK.

Patients with a diagnosis of sarcoidosis were eligible for inclusion. The requirement for a diagnosis of sarcoidosis was either (1) a previous biopsy confirming non-caseating granulomas consistent with sarcoidosis, or (2) previous discussion by multi-disciplinary interstitial lung disease meeting panel with consensus diagnosis of sarcoidosis. All participants must have been aged over 18 years old and able to provide written consent. Ethical approval for the study was gained from the South West – Central Bristol Research Ethics Committee, reference number 15/SW/0363. The trial was registered on clinicaltrials.gov, reference NCT02626897.

Seventeen patients were approached to take part in this study; twelve consented to participate. All participants wore both devices for seven days each in a cross-over manner. The order in which the devices were worn was allocated randomly based on a computer-generated code.

Clinical Assessments

Data regarding body mass index (BMI), forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC) and FEV1/FVC ratio were taken from the most recent clinic attendance. Data was recorded on current immunosuppression use, organs affected by sarcoidosis (stratified into pulmonary and extrapulmonary disease), and duration since diagnosis. All participants completed the Fatigue Assessment Scale (FAS) questionnaire, a ten question fatigue score with a maximum score of 50, as a measure of present levels of fatigue. The threshold for significant fatigue in the FAS score is 22 points or greater(20).

Recording of device preference

All participants were asked to complete a survey documenting their impression of each device immediately after completing the period of wear for each. The questionnaire consisted of four 100mm visual analogue scales (VAS), with participants asked to mark on the 100mm scale their response to each of the following questions; (1) How comfortable was the device to wear? (2) How aware of it were you? (3) Would you have any objection to wearing it again? and (4) To what extent did it interfere with daily life? The VAS was scored by measuring the distance along a line from the left-hand side that the mark was made; a score of zero (0mm) referred to no problems for each question and a score of 100 (100mm) indicated severe or constant problems for each question. In addition to these four questions, participants were asked to complete a free-text box detailing any difficulties that were encountered with either device.

Measurement of daily activity

The two wrist-worn devices chosen for comparison were the GENEActiv original device (Activinsights, Cambridgeshire, UK) and the Actigraph GT3X-bt device (Actigraph, Pensacola, Florida, USA). The GENEActiv is a tri-axial, accelerometer-based activity monitor with a dynamic range of +/-8g (where g is equal to the gravitational pull of the earth), measuring 43 x 40 x 13mm with a traditional plastic watch strap, and weighs 16 grams. The Actigraph GT3X-bt is also a tri-axial, accelerometry-based activity monitor with a dynamic range of +/-6g, measuring 46 x 33 x 15mm with a Velcro-fixing strap, and weighs 19 grams. It has been widely used for both hip-worn and wrist-worn monitoring of activity. Because the primary outcome was determining in the acceptability and comfort of the devices, devices were worn separately over consecutive periods rather than simultaneously.

Each device was worn for seven days by each participant on their non-dominant wrist.

Devices were initialised to record data over the seven day period and then returned via postal envelopes. They were set to record output from the accelerometer thirty times per second (i.e. sampling frequency 30Hz). Data was defined as 'valid' if the devices were worn for at least 10 hours per day for at least two weekdays and two weekend days; the number of patients meeting a higher threshold of 16 hours per day were also recorded in keeping with previous studies(21). Finally, the number of days with 24 hours of wear time within each recording period was noted.

Activity data was analysed for both time spent in thresholds of activity (light, moderate and vigorous), as well as sedentary time. The mean accelerometer outputs by magnitude of wrist acceleration (Euclidean norm minus one-g, ENMO) per 24 hour period, during the least active 5 hours (L5) and most active 5 hours (M5) were calculated using the *R*-statistics package GGIR(22). Time spent in moderate or vigorous physical activity (MVPA) was calculated using the threshold of 100milli-g as has been used previously(19, 23) and is close to the specific device outputs signifying the threshold for moderate activity for both the GENEActiv (93.2milli-g) and Actigraph (100.6milli-g) devices, which have been established in previous data(24). MVPA was also calculated by 'bout' criteria as per WHO recommendations of activity occurring in bouts of at least ten minutes(1), using thresholds of more than 80% of any ten minute epoch spent above the 100milli-g threshold to be counted (MVPA₁₀). Magnitude of difference in outputs between devices was calculated where minimum valid data was available from both devices for a participant.

In addition to the output from GGIR, data from the preferred device (from the reported preference and total wear-time) was analysed for time spent in sedentary behaviours using

the sedentary sphere custom spreadsheet (available elsewhere(4)) after raw data from the devices had been converted into .csv format in 15-second epochs. Thresholds for activity vigour within this spreadsheet were taken from previous data by Esliger et al(25) and adjusted for the sampling frequency of the accelerometers, leading to differences in calculated time spent performing moderate or vigorous activity compared with the GGIR output.

Statistical analysis

All data analysis was undertaken by SPSS Statistics version 22 (IBM Corp, Illinois, USA). Comparison of device outputs and participant experience by each brand of accelerometer were undertaken. Correlations between FAS scores and time spent in sedentary behaviours and each threshold of activity was calculated using data from the preferred device.

Results

Demographic data for the participants are shown in Table 1. All participants had pulmonary sarcoidosis and five participants (41.7%) had extra-pulmonary disease. Five participants were receiving immunosuppression at the time of inclusion. Nine participants (75%) scored more than 21 on the FAS score, indicating significant fatigue.

The GENEActiv device was preferred by ten (83.3%) of the participants in this study. The results from the VAS questionnaire regarding experience of the devices are shown in Figure 1. Statistically significant differences ($p < 0.05$) were seen between the devices, with the GENEActiv device being more highly rated by participants across all domains of comfort, awareness of the device, objection to wearing the device and interference with daily

activities. Comments against the Actigraph device included being 'too bulky' (three participants) and the 'Velcro strap was too uncomfortable' (three participants). Despite this, all but one of these participants recorded minimum valid data. Two participants disliked the GENEActiv device; one person found the strap uncomfortable and another developed a skin reaction to the strap, although both of these participants recorded sufficient data to be considered valid monitoring periods. Other comments against the GENEActiv referred to the lack of a watch-face on the device.

Amongst the twelve patients who wore an accelerometer, 11 (91.7%) of the GENEActiv devices and 9 (75%) of the Actigraph devices recorded the minimum 'valid' data (Table 2). Results for the number of devices returned with any data, the number of devices returned with valid data and the mean duration of daily wear time is shown in Table 2. Preference for the GENEActiv device was reflected in greater wear time compared with the Actigraph device (mean wear time 1354 minutes per day vs 1079 minutes per day, $p = 0.001$). A higher number of GENEActiv devices recorded valid data over the wear period, both at the minimum threshold (91.7% vs 75%) and higher threshold (75% vs 58.3%). A greater number of complete 24 hour wear periods were recorded within each 7 day period using the GENEActiv than the Actigraph device (5.1 vs. 3.7).

Despite the devices being worn over two separate periods rather than at the same time, the average output from the devices across 24 hours (ENMO), during the least active 5 hours (L5) and most active 5 hours (M5) showed no significant differences between devices (Table 3). Time spent in MVPA, using both bout and non-bout criteria, was higher when measured by the GENEActiv devices compared with the actigraph devices. Although this was not statistically significant, the magnitude of difference between the two devices was large with

over two hours more MVPA recorded by the GENEActiv device over the course of a week where participants had valid data for both devices. In total, only three participants met World Health Organization (WHO) recommendations on time in MVPA per week according to 'bout' criteria (MVPA₁₀).

From the GENEActiv data, participants spent 427.3 minutes per day in sedentary behaviour; over half of their awake time. The mean time spent within each activity threshold per day were 245.4 minutes in light activity, 118.1 minutes in moderate activity and 7.1 minutes in vigorous activity, although the time in vigorous activity was skewed because of a high outlying value. With the outlying value removed the mean time spent performing vigorous activity fell to 3.1 minutes per day. Correlations between FAS scores and time spent within activity thresholds are shown in Figure 2. Moderately strong associations were seen between FAS scores and time in sedentary behaviours ($r = 0.554$, $p=0.077$), and time in light activity ($r = -0.585$, $p=0.059$). Weaker correlation was seen between moderate activity ($r=-0.506$, $p=0.112$) and FAS scores.

Discussion

This study sought to clarify the preferred device by patients with sarcoidosis. A clear preference was demonstrated for the GENEActiv device, with the difference in scores on the VAS statistically significant across all domains. Comments received from participants suggested they disliked the size and the strap of the Actigraph. The design of the GENEActiv appeared more comfortable, although feedback suggested that participants would have liked a watch face to negate needing to wear both a watch and the accelerometer. Overall, the GENEActiv appeared much less intrusive, with participants noting reduced awareness of

the device with less interference with normal activity. This should provide a better reflection of daily activity through increased wear-time (which was seen in our results) and less disruption of normal daily activities. The high levels of wear time achieved from these devices is in keeping with benefits seen elsewhere; large population studies investigating activity, including the UK Biobank and NHANES, have switched from hip-worn accelerometers to wrist-worn devices due to increased wear time(26). Our results show that significant differences in wear time exist even within devices worn at the same location and reinforce the importance of choosing a device which is acceptable to the participants who will be wearing them.

The preferred device in this study, the GENEActiv, had a mean daily non-wear time of only 86 minutes per day averaged over the entire wear period. The ideal minimum wear time per day is debated with a number of different recommendations for valid wear time of accelerometers proposed. Our minimum validity definition was taken from previous recommendations(27). Other reviews and studies have suggested that 13 hours(28) or 16 hours(21) are preferable to achieve an accurate picture of daily activity. Part of the rationale for these definitions was based on how sleep would impact on measurements due to difficulty separating sleep from periods of low activity (29). Modern accelerometry-based activity monitors, such as those tested here, incorporate additional sensors into the device (temperature and light sensing) which can be analysed with accelerometer outputs to determine sleep periods(30). These complex sensor arrangements allow sleep time and non-wear time to be excluded from activity analysis, meaning these devices can be truly “fit and forget” for participants in these trials. This also gives the option of collecting data on sleep patterns in addition to activity levels.

We investigated if there was correlation between fatigue measured by FAS scores and time in activity thresholds. Previous studies looking at fatigue and sarcoidosis have used clinic-based measures of exercise capacity such as the six-minute walk test as predictors for fatigue, which have been shown to be poor at predicting fatigue scores (31, 32). Conversely, activity in free-living was shown to be affected by fatigue in one study of patients with sarcoidosis(13). In the small number of subjects monitored here, time spent in light activity strongly moderately correlated with FAS scores. Additionally, time in sedentary behaviours, which has not previously been investigated, showed association with FAS scores. This suggests that changes in fatigue may be reflected in changes in activity and sedentary behaviours. Assessment of larger cohorts of patients with sarcoidosis will help to confirm these associations, as well as whether a relationship exists between fatigue and moderate or vigorous activity. Furthermore, investigation into whether increasing a patient's activity levels reduces their fatigue scores could be made using devices such as the ones used here.

The results identified a clear preference between two of the most widely used devices, identifying the GENEActiv as an appropriate device for future studies investigating elements of activity behaviours in patients with sarcoidosis. The strong bivariate relationship between fatigue and both sedentary time and light activity time recorded by the GENEActiv was notable, especially given the small sample, and suggests that fatigue and activity may be closely linked. The small sample size prevents conclusions being made regarding the relative impact of other factors such as lung function, use of immunosuppression or pattern of organ involvement have on activity levels. Future research in larger cohorts will be able to further investigate the effect these factors play in daily activity and sedentary behaviours in sarcoidosis.

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Table 1 – Participant Characteristics

Age – years (S.D.)	54.5 (13.0)
Male gender (%)	7 (58.3)
BMI – kg/m² (%)	27.3 (4.7)
Years since diagnosis (S.D.)	8.9 (8.7)
Pulmonary disease (%)	12 (100)
Extra-pulmonary disease (%)	5 (41.7)
- Cardiac	- 2
- Cutaneous	- 2
- Ophthalmological	- 1
On immunosuppression (%)	5 (41.7)
- Prednisolone	- 4
- Methotrexate	- 1
- Azathioprine	- 1
- Methylphenidate	- 1
FEV1 – % predicted (S.D.)	78.9 (23.2)
FVC – % predicted (S.D.)	74.8 (40.5)
Ratio (S.D.)	75.1 (16.6)
Fatigue Assessment Scale (FAS) Score (S.D.)	28.8 (9.3)
- FAS >21 (%)	- 9 (75)

Table 2 - Number of devices capturing data, including valid data, and total wear time by device

	Actigraph	GENEActiv	p-value for diff
No. devices returned with any data captured (%)	9 (75%)	11 (91.7%)	0.197
Number of devices with minimum valid data* (%)	9 (75%)	11 (91.7%)	0.685
Number of devices with higher valid data† (%)	7 (58.3%)	9 (75%)	0.504
Number of full 24h periods recorded (S.D.)	3.7 (2.3)	5.1 (1.8)	0.150
Wear time/day – min (S.D.)	1079 (215)	1354 (102)	0.001

* More than 10 hours data for 2 weekdays and 2 weekend days

† More than 16 hours data for 2 weekdays and 2 weekend days

Table 3 - Device outputs

	Actigraph	GENEActiv	Within-patient magnitude of difference*
ENMO – milli-g (S.D.)	25.7 (6.3)	27.4 (7.7)	1.24 (6.8)
L5 – milli-g (S.D.)	4.2 (2.7)	4.3 (2.2)	0.62 (1.8)
M5 – milli-g (S.D.)	48.5 (15.0)	51.3 (17.2)	3.19 (9.9)
MVPA (week) – min (S.D.)	556.9 (308.4)	668.1 (345.2)	148.2 (239.8)
MVPA₁₀ (week) - min (S.D.)	56.1 (62.0)	72.2 (74.8)	30.4 (38.2)

*Where paired data available; 8 participants provided data from both devices

ENMO – Euclidean Norm Minus One-g (mean accelerometer output over 24 hour period)

L5 – Mean accelerometer output (in milli-g) during the least active 5 hour period per day, averaged across all valid days

M5 - Mean accelerometer output (in milli-g) during the most active 5 hour period per day, averaged across all valid days

MVPA – Moderate or Vigorous Physical Activity using 100milli-g cut-off; no bout criteria used

MVPA₁₀ – Moderate or Vigorous Physical Activity using 100milli-g cut-off; bout criteria of 80% of any 10 minute block spent above 100milli-g threshold used

Figure 1 – Box-whisker plots of Visual Analogue Scale scores for experience of Actigraph and GENEActiv devices.

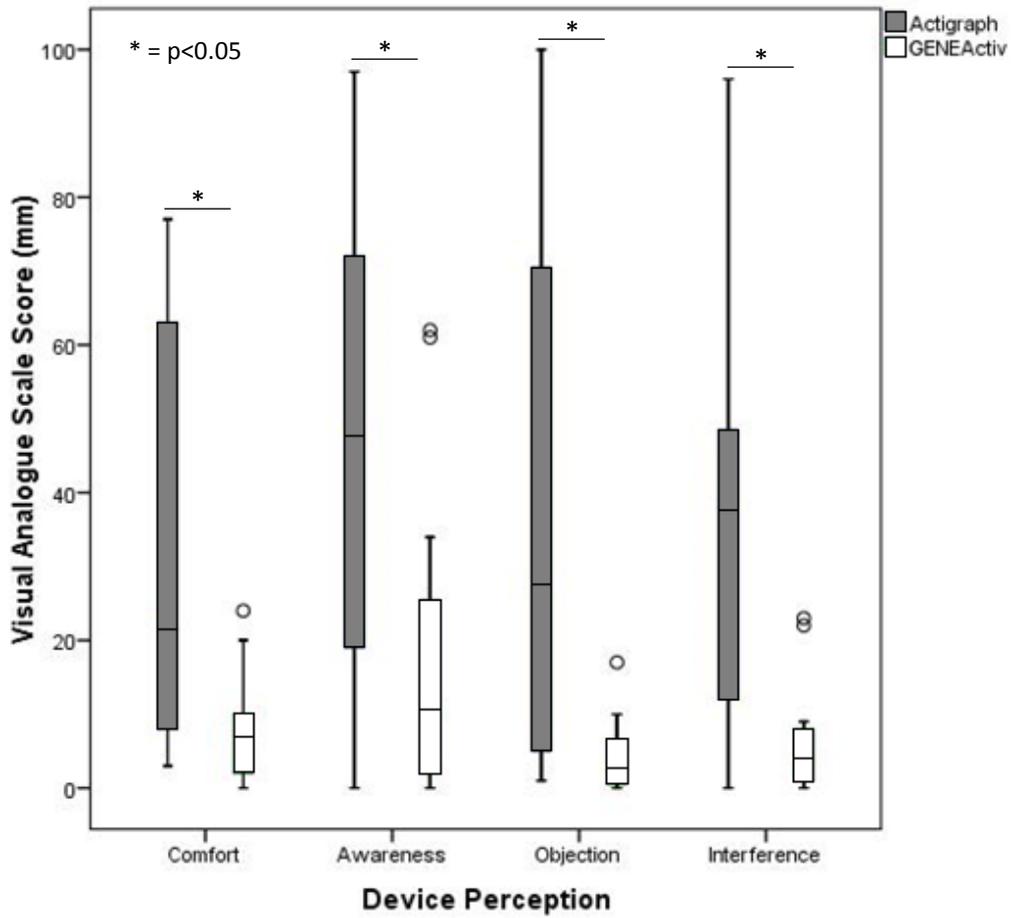
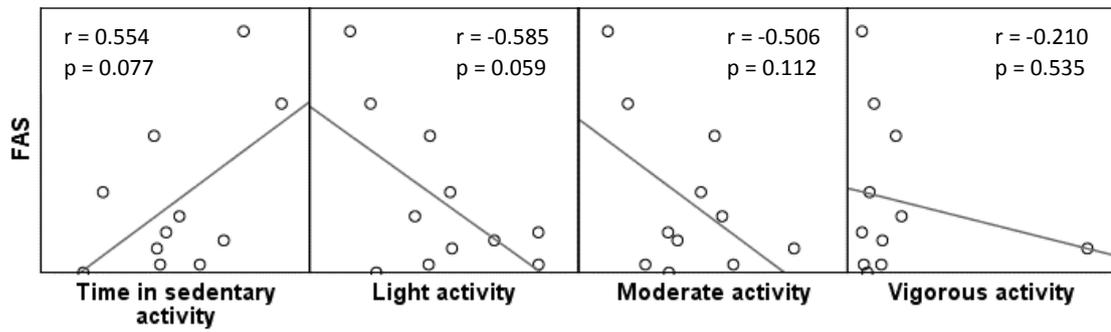


Figure 2 - Correlation of Fatigue Assessment Scale score and time spent in activity thresholds from GENEActiv data



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