Agreement Between Physical Activity Measured by Actical® Activity Monitor and as a Component of Total Energy Expenditure Measured by Doubly Labeled Water

By

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CERTIFICATE OF APPROVAL

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List of Abbreviations and Acronyms

^{18}O	Oxygen – 18
^{2}H	Deuterium
BMI	Body Mass Index
CO_2	Carbon Dioxide
CV	Coefficient of Variation
DEXA	Dual X-ray Absorptiometry
DLW	Doubly Labeled Water
kcal	Kilocalorie
kg	Kilograms
L-T_4	Levothyroxine
MET	Metabolic Equivalents Per Time
O_2	Oxygen
PAEE	Physical Activity Energy Expenditure
$PAEE_{AC}$	Physical Activity Energy Expenditure Measured by Actical®
$PAEE_{CALC}$	Physical Activity Energy Expenditure Estimated by Doubly Labeled Water
REE	Resting Energy Expenditure
RQ	Respiratory Quotient
TEE	Total Daily Energy Expenditure
TEF	Thermic Effect of Food
VO_2	Volume of Oxygen Consumed

VCO_2	Volume of Carbon Dioxide Produced

ABSTRACT

Researchers frequently use accelerometers to measure physical activity energy expenditure (PAEE) in free-living persons. Although accelerometers are promising tools for this purpose, few studies have validated accelerometry against gold standard methods, such as the doubly labeled water (DLW) method. To address this gap in research, this cross-sectional study compared direct measurement of PAEE with the Actical® Activity Monitor to PAEE calculated from the DLW method. Total energy expenditure was measured over a seven-day period using DLW. PAEE was estimated by subtracting resting energy expenditure and thermic effect of food from total energy expenditure. Simultaneously, PAEE was measured by accelerometry with an Actical® Activity Monitor. PAEE measured by each technique were compared using Student's paired *t*-tests, linear regression models, and the Bland-Altman method.

Sixty-two L-T_4 treated euthyroid women and healthy control women completed all measurements. Compared to the DLW method, the Actical® underestimated PAEE by an average of 193 ± 350 kcal/day. Using linear regression, there was a negative correlation between BMI ($p = 0.031$) and fat mass ($p = 0.048$) and the difference in PAEE estimated by the two methods.

In this sample of participants, PAEE estimated by Actical® was lower than PAEE estimated by the DLW method among 74% (n = 46) of participants. The large differences observed between the two measures of PAEE may limit the ability of the Actical® to accurately measure PAEE in free-living conditions. Future research is needed to optimize accelerometer accuracy.

CHAPTER 1

Introduction

Low levels of physical activity and sedentary behaviors are widespread throughout the United States (1) and are associated with excessive weight gain among the population. Approximately two-thirds of American adults are overweight or obese (1). Obesity is associated with an increased risk of developing several chronic diseases such as cardiovascular disease, and cancer (2). Additionally, obesity is linked to many endocrine abnormalities, including diabetes and thyroid dysfunction (3).

Obesity results from an imbalance between energy intake and energy expenditure. The balance between energy intake and energy expenditure determines an individual's energy stores. When energy intake and energy expenditure are not matched, changes in body weight occur. Positive energy balance results in weight gain, and occurs when energy intake exceeds energy expenditure. In contrast, negative energy balance results in weight loss, and occurs when energy expenditure exceeds energy intake.

In 2003, Hill et al. proposed that unintentional weight gain related to positive energy balance can be targeted through interventions addressing the "energy gap," or "the required change in energy expenditure relative to energy intake necessary to restore energy balance" (4). This theory is based on the assumption that each pound of body weight a person gains represents a positive energy balance of 3500 kcal with energy derived from a mixed composition diet that is stored with a 50% efficiency. This means that for every 100 kcals of energy consumed in excess of expenditures, at least 50 kcals of energy are deposited in fat stores.

According to Hill et al., small increases in daily physical activity energy expenditure (PAEE) are sufficient to close the “energy gap” in 90% of the U.S. population (4). For example, walking an additional mile takes most people about 15 to 20 minutes each day, which burns about 100 kcals/day. Researchers have demonstrated the effectiveness of the“small-changes approach” for promoting increased physical activity by quantitatively measuring PAEE (5) (6).

However, measuring PAEE with nonintrusive, objective, valid and precise methods is challenging. Ideally, PAEE should be measured using objective techniques under free-living conditions, during a period of time that represents habitual activity level, with minimal discomfort to the user, and with inexpensive systems (7). PAEE can be measured by either subjective or objective methods. Subjective methods, such as activity logs and direct observations, are relatively inexpensive but are time-consuming, subject to assessment error and often provide an inaccurate assessment of PAEE. Objective methods to measure PAEE include portable indirect calorimeters and portable monitors like accelerometers. While these methods may provide an accurate assessment of energy expended through physical activity, portable indirect calorimeters require specialized equipment operated by trained personnel and as a result are more expensive. Accelerometers, however, provide a convenient and reliable direct measure of PAEE at a relatively low cost.

The low cost and simple technology of accelerometers has led to the increased use of accelerometers in field research and clinical trials to provide an objective estimate of PAEE. However, not all of the accelerometers available to researchers have been validated for estimating PAEE in free-living conditions. Additionally, validation of accelerometers is difficult because there is no "gold standard" to directly measure free-living PAEE.

Most studies that validate PAEE measured by an accelerometer are compared to indirect calorimetry (IC). One limitation of using IC to measure PAEE is that measurements are only taken for short periods of time and are usually performed in a laboratory setting, which may not represent free-living PAEE. One alternative comparison is the doubly labeled water (DLW) subtraction method, where the DLW technique used to measure total energy expenditure (TEE) is combined with IC to measure resting energy expenditure (REE) and thermic effect of food (TEF) (8). PAEE is then determined indirectly by subtracting the sum of REE and TEF from TEE (9). Since there is no "gold standard" to directly measure free-living PAEE, the DLW method is considered the criterion method for measuring PAEE. Due to the high cost of DLW, and the cost and technical complexity of analyzing DLW samples, its application in large-scale studies is limited.

To the best of our knowledge, there has only been one abstract published comparing calculated TEE using PAEE measured by the accelerometer we used in this study, the Actical® Activity Monitor (Philips Respironics, Bend, OR), to TEE estimated by the DLW method in free-living individuals (10). Blanton et al. compared TEE calculated as the sum of PAEE measured by the Actical® Activity Monitor and IC measured REE to TEE estimated by the DLW method in 10 normal-weight premenopausal women (mean age 29.9 ± 4.0 years; mean BMI 22.3 ± 1.8 kg/m^2) for 15 days. REE was measured using an IC at three time points each separated by one week. TEE calculated as the sum of PAEE measured by accelerometry and REE measured by IC (2160 ± 257 kcal/day) was not significantly different from TEE measured by the DLW method (2270 ± 408 kcal/day, $p = 0.77$). In this scenario, TEF was not accounted for in the calculation and may account for, at least in part, the 1.5% difference in TEE between methods. In addition, the generalizability of their findings are limited by the small sample size of 10 normal-weight, healthy, premenopausal women. Therefore, additional research is needed with larger samples of individuals across a wide range of weights, health status, and ages to determine or improve the accuracy of the measurement of PAEE using the Actical ® accelerometer.

To address this gap in accelerometry research, the research performed for this thesis used cross-sectional data obtained from participants in the "The Effects of Mild Hypothyroidism and Variations in Thyroid Function within the Normal Range on Metabolic Function and Body Composition" study. TEE was determined by the DLW method over a seven-day period. REE was measured on the first day of the DLW procedure by IC. TEF was estimated to be 10% of TEE. PAEE was calculated by the DLW subtraction method ($PAEE_{CALC}$). Simultaneously, PAEE was measured directly by accelerometry with an Actical® Activity Monitor ($PAEE_{AC}$) and then the two measures of PAEE were compared.

Significance

The health benefits of regular PAEE on body weight maintenance are well known. However, the CDC estimates that about 80% of American adults do not meet the recommended levels of physical activity outlined in the federal 2008 Physical Activity Guidelines for Americans (1). These lower levels of physical activity may account, at least in part, for why nearly 70% of Americans are classified as either overweight (BMI between 25.0 and 29.9 kg/m^2) or obese (BMI ≥ 30.0 kg/m^2) (1). Increasing physical activity is a key strategy to promote and maintain weight loss. Accurately monitoring PAEE is important to assess the balance between energy intake and energy expenditure. Accelerometry is widely used to measure PAEE, however the accuracy of this tool is not well established (11, 12).

Specific Aims

The primary aim of this study was to compare PAEE measured with the Actical® Activity Monitor ($PAEE_{AC}$) to PAEE calculated from the DLW subtraction method ($PAEE_{CALC}$) in euthyroid women.

The secondary aim was to explore how variables such as age, weight, body mass index, lean mass, percent body fat, and serum thyroid stimulating hormone concentrations within the normal reference range may influence the difference in PAEE measured by these two methods.

Hypotheses

We hypothesized that 1) the mean difference in PAEE measured by these two methods would be no more than 50 kcals/day, and 2) that BMI and lean body mass would influence the difference in PAEE determined by these two methods.

CHAPTER 2: BACKGROUND

Energy Balance

Body weight regulation relies on the maintenance of energy balance, whereby total energy intake is equal to total energy expenditure (TEE). In adults, TEE is comprised of three primary components: Resting Energy Expenditure (REE), Physical Activity Energy Expenditure (PAEE) and Thermic Effect of Food (TEF) as illustrated in Figure 1. REE is the energy expended to support obligatory physiological functions while at rest. Obligatory functions include respiration, cardiac function, maintenance of normal muscle tension and regulation of body temperature. REE accounts for about 75% of TEE in sedentary individuals and about 50% of TEE in very active males (13). TEF is the amount of energy required to digest, absorb, metabolize and store nutrients that are consumed. TEF reflects meal-induced thermogenesis and accounts for approximately 10% of TEE (14). PAEE is the energy expended because of intentional movement produced by skeletal muscles (15).

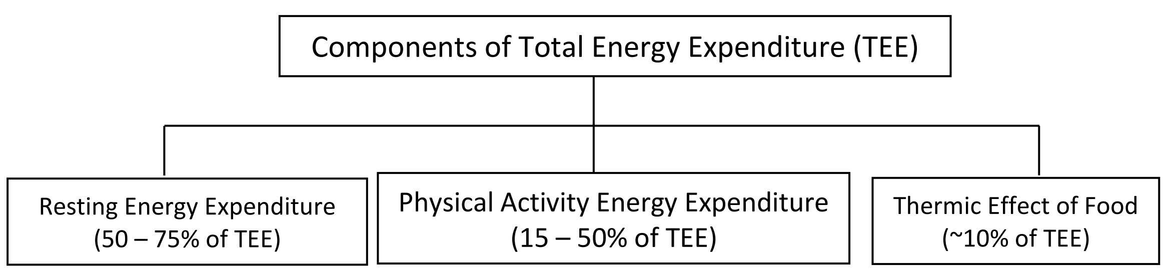

Figure 1. Components of Total Daily Energy Expenditure

*Variability in ranges is due to combining information from different studies (13-15).

Physical Activity Energy Expenditure

PAEE ranges from 15% in sedentary individuals to 50% or more of TEE in active individuals (13). The amount of energy a person expends during physical activity is determined by the duration and the intensity of the activity performed (15). Types of physical activity range from low-intensity daily activities, like occupational or household tasks, to short bursts of vigorous-intensity activities, such as running or carrying heavy loads uphill (16). The amount of energy expended as PAEE is also determined by muscle mass used for movement and the frequency, intensity, and duration of muscular contractions (15). PAEE varies dramatically from person to person as well as within the same person from day to day.

Thirty minutes of moderate-to-vigorous intensity physical activity five days per week (total 150 minutes per week) is recommended to improve health in previously sedentary individuals (17). The American College of Sports Medicine (ACSM) recommends that adults participate in 250 to 300 minutes per week of moderate-to-vigorous intensity physical activity (18). This amount of activity results in an energy expenditure of approximately 2,000 kcal per week and has been shown to promote and maintain weight loss in overweight and obese adults (17, 18). Accurate assessment of physical activity is critical for assessing the role of physical activity in body weight maintenance on an individual basis and as a tool for researchers to develop and validate public health recommendations for daily PAEE (19).

Methods of Estimating and Measuring Energy Expenditure

There are a few methods that researchers use to measure PAEE and each method has its own advantages and disadvantages. Objective methods to measure PAEE include IC, the DLW subtraction method, and accelerometry.

Indirect Calorimetry

Indirect calorimeters are machines that use a mouthpiece, facemask, or canopy to collect and analyze the amount of oxygen consumed (VO_2) and the amount of carbon dioxide produced (VCO_2) to measure TEE and each of its components. The amounts of O_2 and carbon dioxide (CO_2) exchanged in the lungs closely represent the body's composite utilization and release of O_2 and CO_2 by tissues and reflect the rate of transformation of chemical energy into heat, a process known as thermogenesis.

The VMax Encore 29N Indirect Calorimeter (SensorMedics Viasys Healthcare, Yorba Linda, CA) used in this study to measure REE has been validated and tested for reliability in several studies. Cooper et al., (20) validated the VMax Encore 29N and four other IC systems against the Deltatrac II Metabolic Monitor (SensorMedics Viasys Healthcare, Yorba Linda, CA) a well-established valid and reliable reference indirect calorimeter system (21-25). The study was performed at three different sites and included 38 participants. Reliability assessment for REE measured by the VMax revealed a mean within-subject coefficient of variation (CV) of 8.4% compared to the 3% CV for the Deltatrac. The authors noted that one of the limitations of their study is that although all of the indirect calorimeters were calibrated daily the flow rate of each instrument was not tested which may have contributed to the variation they observed.

Measurement of Resting Energy Expenditure by Indirect Calorimetry

REE can be measured by IC and is most accurately assessed, when an individual has fasted for a minimum of six hours, has refrained from physical activity for 12 hours, and has abstained from nicotine, caffeine and other stimulants for 24 hours (26). Under these standard conditions, the within individual CV of REE measured with a ventilated hood indirect calorimeter in healthy adults is 2 – 4% (26, 27). Lean mass accounts for approximately 80% of the interindividual variability of measured REE, with 20% of the variability unaccounted for (28).

Measurement of Thermic Effect of Food by Indirect Calorimetry

TEF can be measured by IC and is calculated as the energy expended during the post-prandial period (typically 5 – 6 hours after meal consumption) above the REE measured just prior to meal consumption. Size and macronutrient composition of the test meal, and the subject's body composition and physical activity level are strong determinants of TEF (29). Protein-rich meals result in higher and longer postprandial energy expenditure than carbohydrate-rich meals (30). Luscombe found that TEF was significantly higher after consuming a high-protein than a high-carbohydrate meal (0.064 vs. 0.05 kcal expended/kcal energy consumed/2 hours, $p = 0.003$) (31). Absolute TEF and REE are higher in healthy, habitually exercising adults compared to sedentary adults (30). Belinski et al. determined that TEF was 9% higher when a standardized meal was consumed after three hours of walking compared to no prior exercise (32).

Thermic Effect of Food as a Percentage of Total Energy Expenditure

In a study often cited for TEF comprising about 10% of TEE (9, 33, 34), Schutz et al. measured the components of energy expenditure in 20 obese, otherwise healthy women (mean body fat percentage: 38.6 ± 0.7%) and eight normal weight control women (mean body fat percentage: 24.7 ± 0.9%) over a 24 - hour period (14). TEE was continuously measured for 24 hours in a respiration chamber of which sleeping energy expenditure was measured for eight hours. Doppler radar simultaneously measured sedentary PAEE. REE was measured by IC for 30 minutes the morning after. For the determination of TEF, participants consumed three meals with identical macronutrient compositions (15% from protein, 40% from fat, and 45% from carbohydrates) that provided 41.2 kcal/kg of lean mass. TEF was calculated as the difference between TEE and the sum of PAEE and REE. There was an inverse relationship between percent body fat and TEF ($r = -0.613$, $p = 0.001$). Obese women had a mean TEF of 8.7 ± 0.8% of TEE whereas normal weight controls had a mean TEF of 14.8 ± 1.1% of TEE ($p < 0.001$) (14).

Measurement of Total Energy Expenditure by Doubly Labeled Water Method

The doubly labeled water (DLW) technique is the noninvasive "gold standard" for measuring TEE under free-living conditions for up to three weeks (35). The DLW technique involves the administration of the stable isotopes deuterium (^{2}H) and oxygen-18 (^{18}O) as water ($^{2}H_2{}^{18}O$) (36) to determine TEE. The DLW method has an accuracy of approximately 2% and a precision of 3 to 7% (compared to near-continuous respiratory gas exchange) (37). The intraindividual variation of TEE by the DLW method is 7.8% (38). Over the past three decades, the DLW method has been subjected to extensive evaluation and validation in human volunteers including infants, pregnant women and elderly patients (36, 39-41).

Following a dose of DLW, the stable isotopes ^2H and ^{18}O, rapidly mix with the hydrogen and O_2 in the body water and bicarbonate pools within four hours of ingestion. CO_2 and water are produced as energy is expended by the body. The ^2H is eliminated from the body as water through evaporative losses from skin and lungs and via waste. Most of the ^{18}O is eliminated from the body in one of two forms, as water and as CO_2. Thus, the slope of ^{18}O elimination is steeper than the slope for ^2H elimination and the difference between these two disappearance rates is proportional to CO_2 production. The elimination rates for both isotopes as their concentrations return to the pre-administration levels is determined by analyzing urine samples via mass spectrometry to measure CO_2 production. Established equations are used to calculate TEE from the amount of CO_2 produced (35).

Estimating Physical Activity Energy Expenditure by the Doubly Labeled Water Method

The use of DLW methodology provides a unique opportunity to measure the accuracy of accelerometers. PAEE can be estimated indirectly as the difference between TEE as measured by DLW minus REE measured by IC and an estimated 10% of TEE for TEF. This approach is nonintrusive, and objective. In spite of the high cost of the DLW and mass spectrometer instrumentation, and the need for technical expertise in measurement, DLW remains the criterion method for validating other methods to assess PAEE in free-living individuals.

In a classically cited study, Schoeller and Webb standardized the DLW method against nearly continuous respiratory gas exchange in three men and two women in 1984 (36). Respiratory gas exchange was measured with a ventilated facemask that was connected to a gas exchange-monitoring cart for 22 – 23 hours/day for five consecutive days. Subjects consumed the labeled water on the evening before the five-day study period and after collection of a base-line urine sample. Urine samples were collected overnight and the following morning before breakfast. The subjects lived in a 3000 ft^2 laboratory/apartment with a living room, kitchen, dining room, bedroom, office, exercise room, and bathroom. Subjects wore the mask for five days, except for 20 minutes each day at breakfast and lunch, and 60 minutes at suppertime. The energy content of each subject's meal equaled their estimated sedentary energy expenditure based on body fat-free mass plus estimated energy needs for activities, with the macronutrient composition of the diet comprising 20% protein, 40% fat, and 40% carbohydrate. Subjects exercised two or three times a day for a total of 1.5 to 2.5 hours/day, and the added PAEE was estimated to be 400 – 600 kcal/day. After the five-day study period, final urine samples were collected. Total body water and isotope elimination rates were determined by mass spectrometer analysis of urinary water after DLW administration relative to predose urine concentrations. Analysis showed good comparability of the two methods with Student's paired *t*-test showing that energy expenditures from the DLW method averaged only 6% more than the five day average calculated from daily respiratory gas exchange with an 8% CV ($p > 0.05$) (36).

In contrast, Leenders et al. compared PAEE measured by a Tritrac-R3D accelerometer to PAEE estimated by the DLW equation [PAEE = (TEE x 0.90) – REE] in 13 healthy women over seven days (9). Prior to the DLW part of the study period, subjects wore the accelerometer for seven days to ensure that: 1) physical activity reflected ambulatory activity and did not include weight-training or cycling activities; 2) subjects engaged in a wide range of physical activities from light intensity to vigorous intensity; and 3) they were familiar with appropriate wearing of the accelerometer. The evening before the study, subjects consumed their DLW dose and the following morning after an overnight stay at the laboratory, REE was measured for 45 to 50 minutes by a Deltatrac™ indirect calorimeter. Paired *t*-tests revealed that PAEE measured by the Tritrac-R3D was significantly different from the DLW calculated PAEE ($p > 0.05$). Specifically, PAEE measured by Tritrac-R3D significantly underestimated DLW calculated PAEE by 35% (-320 kcal/day: range; -780 to 89 kcal/day). The authors concluded that the difference between DLW calculated PAEE and Tritrac-R3D measured PAEE show that the accelerometers used were imprecise and unreliable predictors of individual PAEE assessment (9).

Predicting Physical Activity Energy Expenditure from Accelerometry Data

Accelerometry-based physical activity monitors, or accelerometers, are small portable sensor systems that quantify physical activity by measuring the acceleration of the body during movement. Accelerometers measure activity over time and quantify the intensity, frequency, and duration of bouts of physical activity that an individual performs. Each type of activity is assigned a metabolic equivalent (MET) value or range of values as published by the American College of Sports Medicine (ACSM) (16). The ACSM has designated standard ranges of METs for physical activity intensities from sedentary (1 – 1.5 METs), to light (1.5 – 3 METs), moderate (3 – 6 METs), vigorous (6 – 9 METs), and very vigorous (> 9 METs). MET ranges are used to quantify data collected by accelerometers to predict PAEE (42-44). The digital activity data collected by the Actical® are processed by proprietary software to estimate PAEE using linear regression models that predict METs from the activity counts (44). The Actical® proprietary software estimates REE, using age, sex, height and weight and estimates TEE as the sum of estimated REE and PAEE.

Prediction equations to estimate METs were developed using multiple-linear regression analysis that include activity counts measured by accelerometers and descriptive parameters for body size (BMI: kg/m^2) or body composition (fat mass and lean mass), as independent variables of the model (44). Cut-points, values of activity counts that discriminate between the MET ranges, are used to determine the amount of time a subject spends engaged in physical activity of a specific intensity. To establish cut-points, subjects perform specific types of physical activity and PAEE is measured simultaneously by IC and accelerometry. The activity count value corresponding to three, six, and nine METs were extracted from the regression model and these values were used to classify data into three or four physical activity intensity categories (44).

Heil et al. developed predictive equations to estimate PAEE for the Actical® (44). These equations were developed using linear regression models to determine the relationship between VO_2 measured by IC and activity counts for specific types of physical activity measured by accelerometry (44). Data was derived from 24 adults and 24 children, who performed 10 activities (supine rest, three sitting, three simulated house cleaning tasks, treadmill walking and running, and over-ground walking) while wearing Actical® monitors on the ankle, hip and wrist and a portable indirect calorimeter system in a laboratory setting. The portable indirect calorimeter system was used to determine energy expenditure during each activity. PAEE was derived from IC measures of VO_2. The energy expended during supine rest (REE) was set at 1.0 MET. Prediction algorithms to determine PAEE were created using the Actical® output. The PAEE variables were summarized by statistical software that included the total PAEE and activity counts corresponding to sedentary to light intensity activities, and moderate to vigorous intensity activities.

It is because of lack of data on the validation of objective measures of PAEE in varying populations that the current study focused on the emerging technique for measuring PAEE with accelerometry. Finding an accurate method to expand PAEE assessment in a variety of patient populations is critical to determine the differential impact of PAEE on health and disease risk.

CHAPTER 3: Research Design and Methods

General Study Design and Setting

This study utilized cross-sectional data obtained as a part of "The Effects of Hypothyroidism and Variations in Thyroid Function within the Normal Range on Metabolic Function and Body Composition" study. For the purpose of this sub-analysis, data from women with either no thyroid disease (controls; n=15) or from those who received levothyroxine (L-T_4), a medication used to treat hypothyroidism (n=49), were included. At the time of data collection, all participants had serum TSH concentrations that were essentially normal (0.27-4.87 mU/L; normal range = 0.34 – 5.60 mU/L). Weight, height, body composition (fat mass and lean mass), total daily energy expenditure (TEE), resting energy expenditure (REE), and physical activity energy expenditure (PAEE) were measured in each participant. All procedures took place at the Oregon Health & Science University (OHSU) in the Clinical & Translational Research Center (CTRC). This study was reviewed and approved by the OHSU Institutional Review Board (IRB) and all participants signed consent and Health Insurance Portability and Accountability Act (HIPAA) Authorization forms.

Study Participants

Subjects with no history of thyroid disease and with normal TSH concentrations were included as healthy controls. Women treated with L-T_4 were hypothyroid as a result of adult-onset disease due to radioactive iodine ablation, thyroidectomy for benign thyroid disease or Hasimoto's disease. L-T_4 treated euthyroid participants were included if they had little to no endogenous thyroid function, as evidenced by significantly elevated serum TSH concentrations before L-T_4 treatment. These same participants received stable L-T_4 doses for at least 3 months with documented serum TSH concentrations in the normal reference range of 0.34 – 5.60 mU/L before participating in study measurements. Participants did not have any other acute or chronic illnesses that could affect thyroid function, and were not taking medications that could affect thyroid hormone concentrations. Oral contraceptives and estrogen replacement therapy (ERT) were allowed, as long as the type and dose were stable for three months and no changes were anticipated during the study. Women were studied in the follicular phase of the menstrual cycle or in the first week of an oral contraceptive or ERT cycle. Peri- and post-menopausal women were included since they are among the most common patients with hypothyroidism. Participants were "free living" and were given instruction by a registered dietitian on how to follow a standard healthy diet (15% protein, 35% fat, and 50% carbohydrate) and to maintain a stable exercise regimen for two weeks before their study visit.

Anthropometric Measurements

Weight was recorded to the nearest 0.01 kg with a digital scale (Scale-Tronix, Model 5002, Wheaton, IL). Height was measured without shoes using a wall-mounted stadiometer (Harpenden Stadiometer, Holtain Ltd, Crymych, UK) and recorded to the nearest 0.1 cm. Body mass index was calculated as weight in kilograms divided by height in meters-squared (kg/m^2).

Measurement of Body Composition by Dual Energy X-ray Absorptiometry

Body composition was measured by Dual Energy X-ray Absorptiometry (DEXA) using a Hologic QDR Discovery A Densitometer (Hologic, Inc., Bedford, MA) following standard procedures (45). Study participants changed in to a hospital gown, removed all jewelry and laid horizontally on the DEXA scanning bed. The DEXA technician positioned the subject within the appropriate quadrants of the scanning bed and a total-body scan was performed to measure total body fat mass and lean mass. For women who did not fit completely within the DEXA scanning plane, a hemi-scan of the left side of the body was performed and measurements were multiplied by two to determine each body compartment measurement.

Measurement of Total Energy Expenditure by the Doubly Labeled Water Method

Total daily energy expenditure was measured by DLW method as described by Schoeller, et al (35). Participants consumed water enriched with stable isotopes for hydrogen (deuterium, ^{2}H; Sigma Aldrich, St. Louis, MO) and oxygen (^{18}O; Cambridge Isotope Laboratories, Andover, MA). Each subject drank a premixed dose of water that provided 1.7 gm of $^{2}H_2{}^{18}O$ per kg of body weight. The dose provided 1.6 g/kg of 94% $^{2}H_2{}^{18}O$ and 0.10 g/kg of 99.9% $^{2}H_2O$. Spot urine samples were collected before and two, three and four hours after consuming the enriched water to determine background isotopic exposure and whole body isotope equilibrium, respectively. Two additional spot urine samples were collected seven days later; upon waking and one hour later, to calculate the elimination rates of each stable isotope. Urine samples were stored at -20° C until sent for analysis.

The ratio of $^2H/^1H$ and $^{18}O/^{16}O$ in in urine samples was measured using a Europa 20/20 Isotope Ratio Mass Spectrometer in the laboratory of Dale Scholler, PhD, at the University of Wisconsin. Total body water and CO_2 production was calculated by the equation of Schoeller (35):

$$rCO_2 \text{ mol/day} = [(\text{TBW mol}/2.076)*(1.007k_{18}-1.041k_2)]-0.0253rG \text{ mol}$$

where rCO_2 is the rate of CO_2 production, TBW is total body water in moles, and k_{18} and k_2 are the respective isotope elimination rates calculated by the linear regression of the isotope enrichment over time and rG is a correction factor for the fractionated water loss associated with breathing and sweating over time.

$$rG \text{ mol}=1.05*\text{TBW mol}*(1.007k_{18}-1.041k_2)$$

Carbon dioxide production (rCO_2) was used to calculate total energy expenditure by the modified Weir equation (37):

$$\text{TEE kcal/day}= rCO_2\text{L/day}(1.1+3.9/\text{FQ})*22.4\text{L/mol } CO_2$$

where FQ is the food quotient, which for this study is a constant of 0.86. A constant of 22.4 is included to convert moles of CO_2 gas to L/day, resulting in final units of TEE in kcal/day.

<u>Measurement of Resting Energy Expenditure by Indirect Calorimetry</u>

Resting Energy Expenditure (REE) was measured by IC in a thermo-neutral room maintained at 70° F. A VMax Encore 29N Indirect Calorimeter (SensorMedics Viasys Healthcare, Yorba Linda, CA) was used to measure VO_c and VCO_2. This procedure was conducted after the participant fasted for 12 hours and before she performed any significant physical activity. Immediately before the procedure, each subject rested comfortably on a bed next to the indirect calorimeter for 20 minutes. A clear Plexiglas™ canopy was placed over her head and upper chest to ensure that air-exchange occurred only through the air intake and output valves. Airflow through these valves was adjusted to accommodate the participant. Expired air was sampled and analyzed to determine the $VO_2$and the VCO_2 produced each minute for 60 minutes. REE was calculated using the modified Weir equation:

$$REE\ (kcal/day) = [3.941\ (VO_2, L/min) + 1.106\ (VCO_2, L/min)] \times 1440\ min/day]$$

Estimation of the Thermic Effect of Food

Thermic effect of food was estimated as 10% of measured TEE for each participant based on the methodology of previous studies (9, 33, 34). This estimate of TEF was adopted by the Food and Agriculture Organization, the World Health Organization, and the United Nations University (46)

Measurement of Physical Activity Energy Expenditure by Doubly Labeled Water Subtraction Method

PAEE was estimated using the following equation:

$$PAEE_{CALC}\ (kcal/day) = TEE\ kcal/day – [TEF\ kcal/day + REE\ kcal/day]$$

where TEF (kcal/day) = 0.1 x TEE kcal/day.

Measurement of Physical Activity Energy Expenditure by Accelerometry

The omnidirectional Actical® Activity Monitor (Philips Respironics, Bend, OR) measured $PAEE_{AC}$. Participants wore the Actical® activity monitor at the waist during waking hours for seven days during the same time period in which TEE was measured by DLW. Data was downloaded from the Actical® using an ActiReader®, a PC serial port interface that facilitates telemetric data transfer from the Actical®, recorded as activity counts, average activity (counts per minute), time interval duration (minutes), activity intensity ranges during sedentary, light, moderate and vigorous activity, and accumulated time within each activity range (minutes). The Actical® used proprietary prediction equations to estimate the PAEE from the aggregated activity counts. Minute-by-minute PAEE values were reduced to an average for each day. The daily averages across the seven-day period were summed and divided by seven (or the number of days measured) to estimate average daily PAEE.

Measurement of Thyroid Stimulating Hormone

Serum TSH concentration was measured in mU/L by immunochemiluminometric assay (ICMA, Kaiser, Nichols Institute Kit 36577X, San Juan Capistrano, CA). The functional sensitivity of this assay is 0.008 mU/L; the analytical sensitivity of this assay is 0.003 mU/L. The intra-assay CV for the functional sensitivity is 9.5% (0.03 mU/L); the intra-assay analytical sensitivity CV is 4.7% (11.6 mU/L). The inter-assay CV for the functional assay is 17% (0.02 mU/L); the inter-assay CV for the analytical assay is 4.6% (14 mU/L) (47).

Security and Confidentiality

Demographic data and coded study data were stored on restricted OHSU network drives and coded study data was stored in a password protected REDCap database (Research Electronic Data Capture) (48). Blood and urine samples were coded for storage in the OCTRI Core Lab. Privacy and confidentiality were ensured by restricting access and coding data and samples whenever possible.

Once processed for the study needs, residual and additional samples were coded for storage with a nonderived code and no direct identifiers. Access to specimens was restricted to OCTRI lab personnel. The key to the code was held on a restricted OHSU network drive behind the OHSU firewall with access limited to study personnel. Source data in paper documents was held in locked filing cabinets in a locked office. Electronic data was stored on restricted drives on the OHSU network behind a firewall with standard back-up procedures managed by OHSU ITG and in a web-accessible REDCap database housed on an OHSU secure server. Access was restricted to study personnel by unique user ID and password. Audit logs include authentication, data changes, data exports and viewing by each user. Data and specimens were transferred only in coded fashion.

Data Cleaning and Evaluation

Data for TEE (kcal/day), REE (kcal/day), $PAEE_{AC}$ (kcal/day), and measures of body composition was exported from REDCap without identifiers into standard spreadsheets (Excel, Microsoft Office 2010) and imported into statistical analysis and graphing software (IBM SPSS Statistics, Chicago, IL and GraphPad Prism® version 5.04, La Jolla, CA). $PAEE_{CALC}$ was calculated on standard spreadsheets using REDCap data. Standard distribution curves were generated to assess normality of each set of outcome variables. Box-plots and histograms were used to identify outliers and skew. Values that stood out from the others by visual inspection were investigated further to ensure data was entered correctly and any mistakes were corrected.

Data Analysis

Descriptive statistics including mean, standard deviation, minimum, and maximum values, of age, weight, height, body composition parameters, energy expenditure variables and TSH concentrations were calculated and reported for the total sample. A Student paired *t*-test was used to determine if the mean difference in $PAEE_{AC}$ and $PAEE_{CALC}$ was greater than 50 kcal/day. The significance level was set at a p-value ≤ 0.05. The magnitude and direction of the mean difference, as well as the upper and lower bounds of the 95% confidence interval were determined.

To determine if there was a systematic difference between the two methods, the Bland-Altman method was used. Since this study compared two different measurements of PAEE within the same individual during the same time, the PAEE measurements were expected to be highly correlated and the mean difference between the two measurements (μ) was expected to be small. If the true differences between the PAEE measures are normally distributed, then approximately 95% of the difference values are expected to fall within the range established by the mean plus or minus two times the standard deviation ($\mu \pm 2\sigma$). The mean difference plus or minus two times the standard deviation (σ), designated as (μ - 2σ) and (μ + 2σ), were estimated using sample data. These estimates refer to the lower and upper limits of agreements, respectively (49). Since these limits are only estimates, 95% confidence intervals for both the lower limit (μ - 2σ) and upper limit (μ + 2σ) were obtained as described by Bland-Altman (49) using the following equation:

95% Confidence Interval = lower or upper limit of agreement ±

[(t statistic x standard error (SE)]

where SE = $\sqrt{[\{3(s^2)\}/n]}$

The SE of $\bar{x}$ is $\sqrt{[s^2/n]}$, where n is the sample size, and the SE of $\bar{x}$ - 2s and $\bar{x}$ + 2s is about $\sqrt{[\{3(s^2)\}/n]}$. The confidence intervals provide an estimate of the accuracy of the upper and lower limits of agreement.

To assess the agreement of PAEE measured by the two techniques, the differences between PAEE ($PAEE_{CALC} – PAEE_{AC}$) measured by these two techniques (y-axis) was calculated and plotted for each participant against the average PAEE ($[PAEE_{CALC} + PAEE_{AC}]/2$) measured by these two techniques (x-axis) (49). Two other y-axis reference lines were placed to designate the lower and upper limits of agreement of the mean difference between these two measures ($\bar{x} \pm 2\sigma$). SPSS software (IBM SPSS Statistics, Chicago, IL) was used to calculate descriptive statistics and to perform regression analyses and GraphPad Prism® version 5.04 (GraphPad Software, Inc., La Jolla, CA) was used to generate the Bland-Altman plots.

Univariate regression models were constructed to explore how independent variables such as age, weight, body composition parameters, and TSH concentrations influence the difference in PAEE measures. The difference in PAEE measures was entered into the model as the dependent variable. The relationships between each independent and dependent variable were analyzed.

RESULTS

Descriptive Statistics

Sixty-five participants had data sets that were considered for analysis. Three participants were excluded from analysis because of missing Actical® data (less than 5 days of PAEE data), leaving, 62 participants with adequate data for the subanalysis. Of these participants, all 62 were female; 54 were white (87%), four were Hispanic/Latino (6%), three were Asian (5%), and one participant (2%) did not provide details of her race/ethnicity. Participant characteristics including age, body composition parameters, and serum TSH concentrations are presented in Table 1.

There was a broad range in age and body composition parameters in the study population. In this study population, 28 women had BMIs in the normal range (45%; 18.5 – 24.9 kg/m^2), 13 were in the overweight range (21%; 25 – 29.9 kg/m2), and 21 were obese (34%; ≥ 30 kg/m^2).

Table 1. Participant Characteristics (n = 62).

Variable	Mean ± SD	Range
Age (yr)	45 ± 12	20 – 68
Weight (kg)	74.6 ± 17.7	48.6 – 137.8
Height (cm)	164 ± 6	149 – 177
Body Mass Index (kg/m^2)	28 ± 6	19 – 47
Lean Mass (kg)	47.7 ± 6.8	36.5 – 70.6
Fat Mass (kg)	27.3 ± 1.6	10.2 – 67.2
Percentage of Fat Mass (%)	34.6 ± 8	19.9 – 52.2
Thyroid Stimulating Hormone (mU/L)	2.00 ± 1.17	0.27 – 4.87

The mean values and range for each component of energy expenditure are presented in Table 2. Expressed as a percent of TEE, REE represented 56 ± 7%. $PAEE_{CALC}$ represented 34 ± 7% ,whereas $PAEE_{AC}$ was 26 ± 11% of TEE. $PAEE_{CALC}$ as a percent of TEE was within 20 – 29.9% for 20 participants, 30 – 39.9% for 30 participants, 40 – 49.9% in 9 participants, and ≥ 50% in three participants. $PAEE_{AC}$ was within a smaller percentage of TEE (9 – 19.9% in 20 participants; 20 – 29.9% in 22; 30 – 39.9% in 16; 40 – 49.9 in two; and ≥ 50% in two).

The percentages for the REE and $PAEE_{CALC}$ as a percent of TEE fall within normal expected ranges as outlined by other studies (10, 33). However, $PAEE_{AC}$ represents a much smaller percentage of TEE compared to other studies (10, 33).

Table 2.Components of energy expenditure.

Variable	Mean ± SD	Range
TEE (kcal/day)	2334 ± 448	1561 – 3354
TEE (kcal/kg/Lean Mass)	49 ± 8	34 – 73
REE (kcal/day)	1287 ± 180	1039 – 1798
REE (kcal/kg/Lean Mass)	27 ± 3	23 – 33
TEF (kcal/day)	233 ± 45	156 – 335
$PAEE_{CALC}$ (kcal/day)	815 ± 324*	363 – 1768*
$PAEE_{AC}$ (kcal/day)	621 ± 304*	223 – 1536*

TEE was determined by the doubly labeled water method; REE was measured by indirect calorimetry; TEF was estimated as 10% of TEE; PAEE was measured by Actical® ($PAEE_{AC}$) and estimated by calculation ($PAEE_{CALC}$).
**Indicates the means of these two measures were significantly different ($p = 0.002$).*

Differences in Physical Activity Energy Expenditure Measures

$PAEE_{AC}$ was lower than $PAEE_{CALC}$ by an average of 193 kcal/day (95% CI for the mean difference [$PAEE_{CALC}$ - $PAEE_{AC}$]: 104 – 282 kcal/day) which is larger than the hypothesized 50 kcal/day difference (Table 2). The means of the two measures of PAEE were significantly different (r = 0.380, p = 0.002).

Limits of Agreement

To evaluate our primary aim, the agreement between the two measures of PAEE was assessed using the Bland-Altman method (49), through which lower and upper limits of agreement and 95% confidence intervals of the lower and upper limits were calculated. Our findings suggest that, among women with TSH concentrations within the normal range, approximately 95% of the differences between $PAEE_{AC}$ and $PAEE_{CALC}$ are estimated to fall between -493 kcal to 879 kcals (width of 1372 kcal/day). The lower limit of agreement for the difference between $PAEE_{AC}$ and $PAEE_{CALC}$ has a 95% confidence interval of -658 kcal to -328 kcal (width of 329 kcal/day). The upper limit of agreement for the difference between $PAEE_{AC}$ and $PAEE_{CALC}$ has a 95% confidence interval of 715 kcal to 1044 kcal (width of 329 kcal/day). Both upper and lower limits of agreement are large in magnitude and suggest that there are considerable discrepancies between these two methods.

In addition, the lower and upper limit interval widths are wide suggesting that the limits of agreement are not precisely estimated. Therefore, the calculated limits of agreement are poor estimates of the lower and upper bounds for 95% of the differences expected among women with TSH concentrations within the normal range.

Bland-Altman Plots

To further evaluate the differences between the PAEE measures, a plot of the difference between the PAEE measures versus the average of the PAEE measures is shown in Figure 2. All individual data points, except for five points, which in this data represents 8% of all values, fell between the upper and lower limits of agreement. Four participants (6%) had a mean difference of ≤ 50 kcals/day between the two measures of PAEE. $PAEE_{AC}$ was greater than $PAEE_{CALC}$ by 50 kcal/day in 12 participants (19%). $PAEE_{AC}$ was less than $PAEE_{CALC}$ in 74% of the participants (n = 46), reflecting a positive trend in the Bland-Altman plots. With a normal distribution, 95% of the values are expected to fall within the upper and lower limits of agreement (± 2 standard deviations), and 5% should fall outside of these limits.

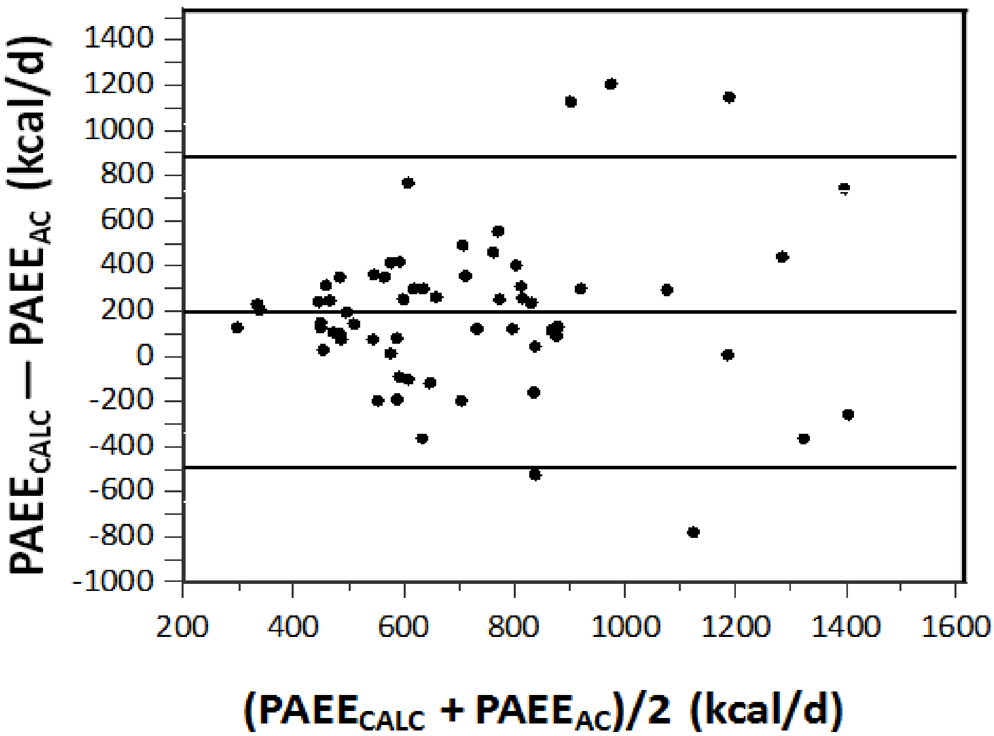

Figure 2. Bland-Altman plots for PAEE measured by an Actical® physical activity monitor (PAEE$_{AC}$) and PAEE$_{CALC}$ which was calculated as: PAEE$_{CALC}$ = (TEE x 0.90) – REE. The middle line reflects the mean differenceof 193 kcal/day between the two methods; the upper and lower lines represent the limits of agreement which are 1.96 standard deviations, about the mean difference between the two methods.

Univariate Linear Regression

Univariate linear regression models were used to assess the relationship between the difference in PAEE measures and several predictors. The coefficients of determination (R^2) and slope estimates from each of these univariate regression models are presented in Table 3. The plots of the difference in PAEE measures versus each of the predictors illustrate these relationships (Figures 3 – 10). Significant negative correlations were observed between the difference in PAEE measures and BMI and fat mass, suggesting that as BMI and fat mass increased the difference between the two PAEE measures decreased. A trend toward significance was observed between the difference in PAEE measures and percent body fat.

Table 3.Univariate regression models showing the association between the difference in PAEE measures and age, body composition parameters, and TSH concentration.

Variable	Slope estimate	R^2	p-value	95% CI
Age (yr)	2.35	0.006	0.549	-5.46 – 10.61
Weight (kg)	- 4.27	0.047	0.092	-9.52 – 0.72
Height	9.07	0.024	0.231	-5.94 – 24.07
Body Mass Index (kg/m²)	*-14.94*	*0.075*	*0.031*	*-28.46 – -1.42*
Lean Mass (kg)	- 5.61	0.012	0.401	-18.87 – 7.66
Fat Mass (kg)	*-7.915*	*0.063*	*0.048*	*-14.34 – -0.05*
Percent Body Fat (%)	- 10.26	0.055	0.066	-21.21 – 0.69
Thyroid Stimulating Hormone (mU/L)	49.95	0.028	0.195	-26.25 – 126.15

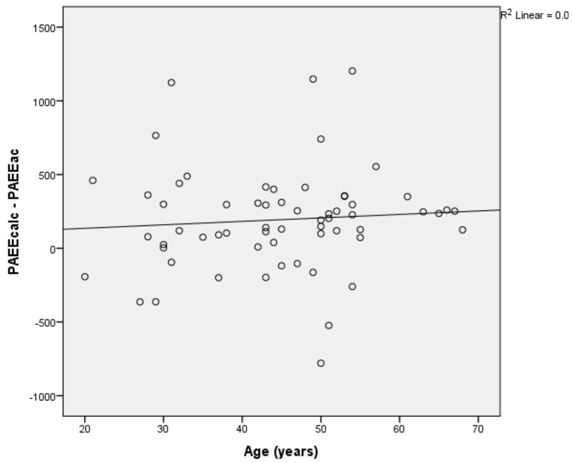

Figure 3. Relationship between difference in $PAEE_{CALC}$ and $PAEE_{AC}$ versus age in years.

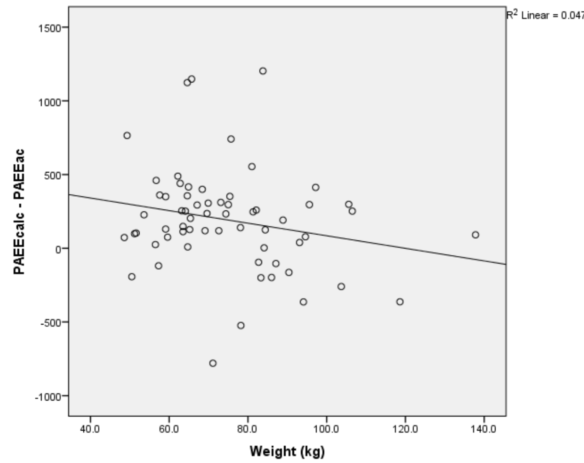

Figure 4. Relationship between difference in $PAEE_{CALC}$ and $PAEE_{AC}$ versus weight in kilograms.

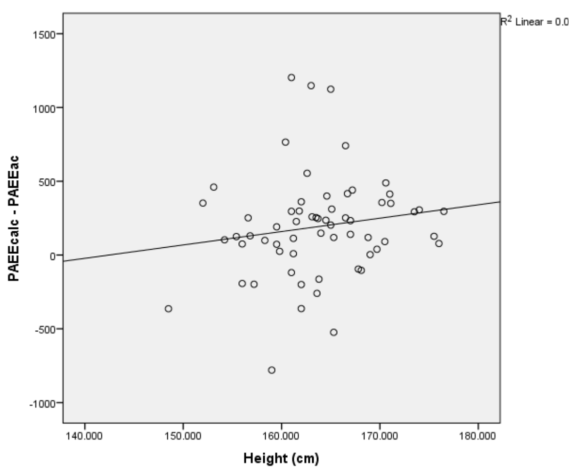

Figure 5. Relationship between difference in $PAEE_{CALC}$ and $PAEE_{AC}$ versus height in centimeters.

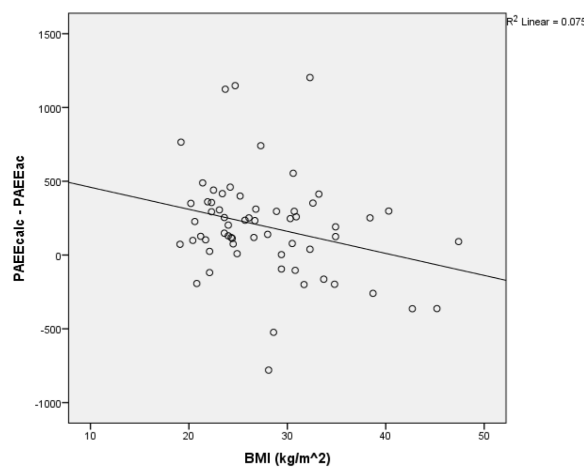

Figure 6. Relationship between difference in $PAEE_{CALC}$ and $PAEE_{AC}$ versus BMI (kg/m^2).

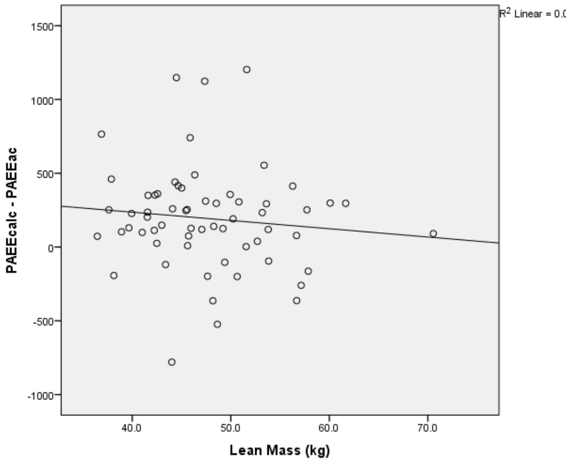

Figure 7. Relationship between difference in $PAEE_{CALC}$ and $PAEE_{AC}$ versus lean mass in kilograms.

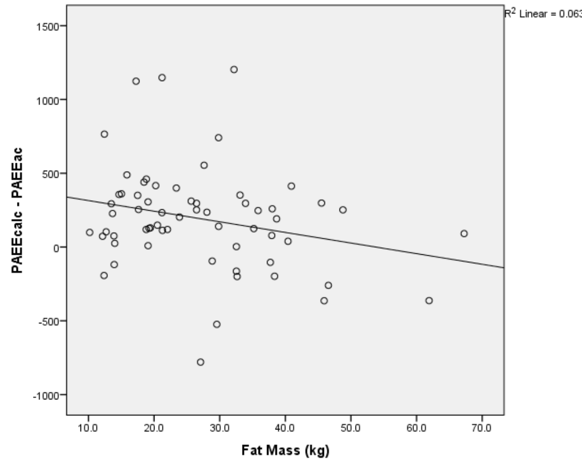

Figure 8. Relationship between difference in $PAEE_{CALC}$ and $PAEE_{AC}$ versus fat mass in kilograms.

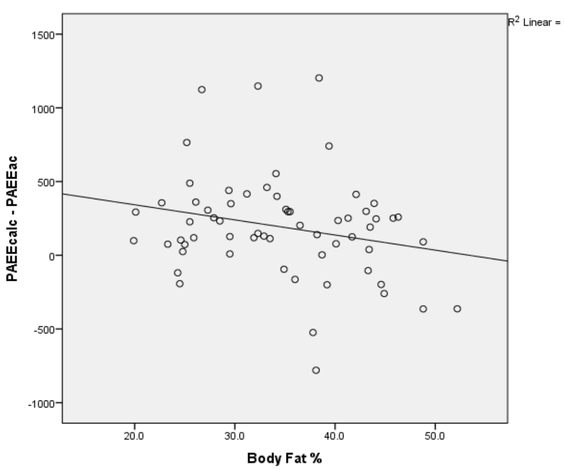

Figure 9. Relationship between difference in $PAEE_{CALC}$ and $PAEE_{AC}$ versus percent body fat in kilograms.

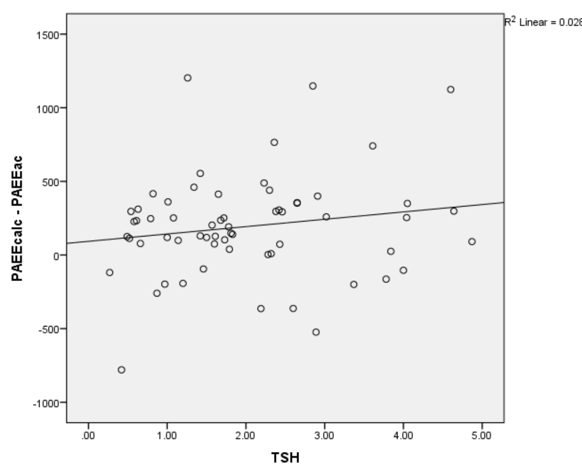

Figure 10 .Relationship between difference in $PAEE_{CALC}$ and $PAEE_{AC}$ versus thyroid stimulating hormone (TSH).

CHAPTER 5: DISCUSSION

Summary

This cross-sectional study compared PAEE measured by Actical® Activity Monitor ($PAEE_{AC}$) to the criterion measure for estimating PAEE by the DLW subtraction method ($PAEE_{CALC}$). The primary goal of this study was to determine if the mean difference in $PAEE_{AC}$ and $PAEE_{CALC}$ was within 50 kcal/day. The secondary goal was to determine the relationship between the difference of these two measures of PAEE and age, body composition parameters, and serum TSH concentrations, characteristics that may predict differences in PAEE measures between these two techniques.

The first study aim showed that the two measures of PAEE were related (r = 0.380, $p < 0.05$). However, compared to $PAEE_{CALC}$, $PAEE_{AC}$ was 193 kcals/day (95% CI: 104 – 282 kcal/day) lower which is higher than the 50 kcal/day acceptable limit ($p = 0.002$). The confidence intervals for the limits of agreement contain values that are large in magnitude. For example, the confidence interval for the lower limit of agreement was -658 kcal to -328 kcals. When measuring the PAEE of an individual with an Actical®, a difference from PAEE estimated by the DLW method of -658 to -328 kcals is significant. These potential limitations in accelerometry sensitivity and precision need to be taken into account clinical studies that utilize these devices.

The large difference in PAEE measurement methods observed may be due to instrument error in the Actical®, rather than calculation error for $PAEE_{CALC}$. The Actical® can be used to estimate PAEE only via the prediction equation provided by the manufacturer. This equation is proprietary and has not been validated in free-living conditions in the literature on this study's population. Even under controlled laboratory settings, the estimation of PAEE by the Actical® has been shown to result in under- and over-estimation in healthy populations when compared to IC (43).

Crouter et al. examined the validity of published regression equations for the Actical® and two other accelerometers by comparing them simultaneously against a portable indirect calorimeter during a variety of types of physical activity (43).. Twenty-four men (age 36 ± 12.8 years) and 24 women (age 35 ± 10.3 years) performed various activities that ranged from sedentary behaviors (lying, sitting, standing) to vigorous exercise while wearing the three accelerometers and a portable indirect calorimeter. In general, the Actical® gave accurate predictions of PAEE for sedentary activities and slow running, but overestimated PAEE of slow and fast walking and underestimated PAEE of all other activities. Figure 11 shows the difference between the portable indirect calorimeter measured MET values against the Actical® MET prediction equations.

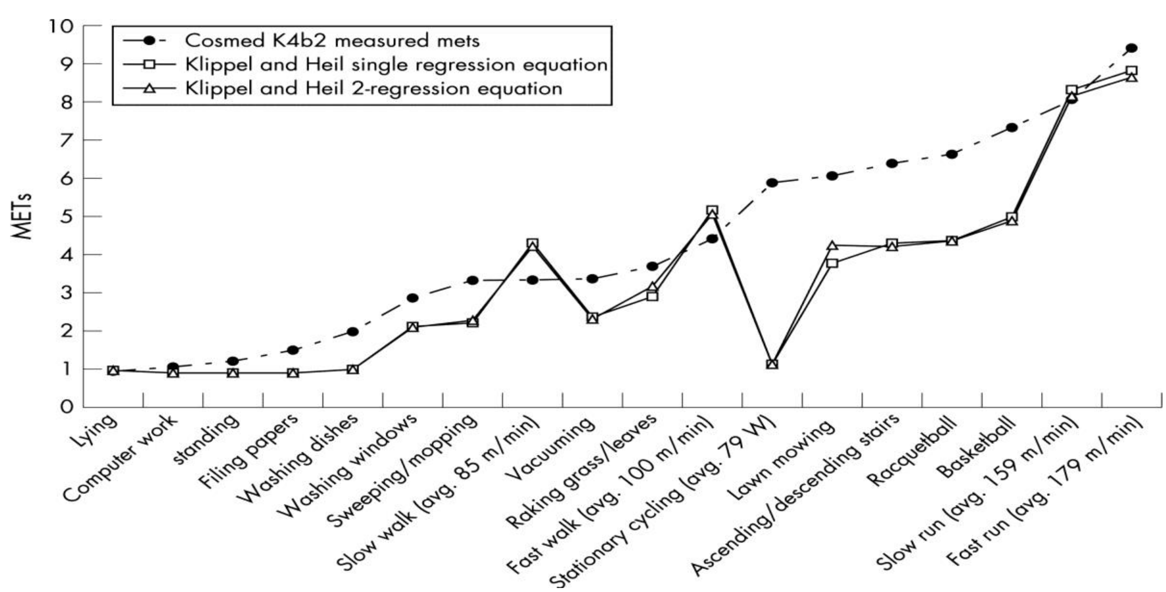

Figure 11. Indirect calorimetry measured METs and Actical® estimated METs (Klippel and Heil single regression and double regression equations) across 18 different activities (43).

Part of the underestimation by $PAEE_{AC}$ may be explained by the fact that the Actical® was designed to register ambulatory rhythmic activities, such as walking and running, and fails to register arm movements and weight bearing activities. When acceleration counts are registered at less than 50 counts/minute, the participant is credited with 1.0 MET. This would mean that an accelerometer would consider the efforts of a participant performing a vigorous activity of 25 pushups over one minute (~8.0 METs) to be worth 1.0 MET, or equal to sitting quietly watching television because the activity would only register 25 to 50 counts/minute (16). Another issue with accelerometry is that activity counts measured by accelerometers do not reflect the additional force generated by the body to overcome external forces. Servais et al. found that when climbing stairs, the body's acceleration is not proportional to PAEE, and accelerometry measurements of bodily movements underestimate PAEE (50). For example, walking uphill at 2.0 mph is considered ~6.0 METs or carrying a heavy load such as bags or groceries at that same speed represents 5.0 – 12.0 METs while walking at less than 2.0 mph on a flat surface represents 2.0 METs (16).

The secondary goal of this study was to explore how independent variables such as age, body composition parameters, and serum TSH concentration predict the differences observed between the two PAEE measurement techniques. Univariate regression models were used to determine whether age, weight, height, BMI, lean mass, fat mass, percent body fat, and TSH concentration explained differences in PAEE measurement techniques. Significant negative correlations were observed in the univariate regression model for BMI and fat mass, and a trend towards significance for percent body fat, suggesting that as the values for these variables increased the difference between the two measures decreased.

One explanation for the negative correlations between the difference in the two PAEE measures and the predictors, BMI and fat mass, is that Actical® predictive equations were developed using predominately moderate intensity lifestyle activities in normal weight participants (44). These predictive equations tend to overestimate the energy cost of walking, sedentary, and light activities and underestimate vigorous activities in healthy controls (43). Cross-sectional data indicates that obese individuals are normally less physically active and spend more time in sedentary and light activities and less time in moderate to vigorous activities than age-matched lean controls (51, 52). However, the metabolic cost of most activities is proportional to body weight and therefore, obese subjects expend more energy than normal weight subjects when performing the same physical task. For example, Chen et al. found that overweight and obese individuals exert higher levels of PAEE than lean individuals during normal-speed walking (53). Higher levels of PAEE associated with sedentary and light activities by overweight and obese individuals may result from additional loading forces from excess weight and postural deviations that place higher biomechanical demands for body adaptations in response to restricted movement patterns in average daily activities (54).

Anatomical differences between normal weight and overweight and obese subjects often results in differences in the placement of accelerometers. Overweight and obese subjects often display a protruding abdomen, which results in an anterior pelvic tilt placing the accelerometer at a diagonal angle instead of the vertical angle specified by the manufacturer. This variation in the placement of the Actical® might modify the accelerometer output and alter the PAEE estimates derived from it.

With improvements in accelerometer-based physical activity recognition, accelerometry can be a feasible method for quantitatively assessing individual activity behavior to quantify the dose of PAEE for related physiological outcomes (55). The CDC recommends that individuals participate in at least 30 minutes a day most days of the week of moderate intensity PAEE for maintenance of healthy weight and 60 minutes or more a day most days of the week of moderate intensity PAEE for weight loss and maintenance of weight loss (56). However, these guidelines were developed based on assumptions of the effects of regular physical activity rather than on the relationship between the dose of physical activity and health outcomes. This is because there is a lack of objective and accurate detailed measures on physical activity frequency, intensity, and duration of activities.

Strengths of Study Design

One strength of this study is the sample size. PAEE was measured by accelerometry and as an estimate by DLW in sixty-two free-living individuals. Further, we were able to measure energy expenditure parameters in participants with a wide range of body mass indices and ages. Finally, the DLW method used in this study is considered the gold standard for measuring TEE in free-living individuals.

Limitations

There are limitations to this research as well. The TEF value was estimated as 10% of TEE instead of measured by IC. Schutz et al. found a 6% difference in TEF measurements in obese women (8.7 ± 0.8% of TEE) and normal weight controls (14.8 ± 1.1%) (14). If TEF had been measured in this study and the TEF results matched those of Schutz, the difference between the two PAEE measures may have been smaller in normal weight participants and larger in overweight and obese participants.

Assessment of PAEE in free-living conditions is important for determining the relationship between physical activity and physiological outcomes (51). However, because of the accelerometer's limited ability to accurately recognize PAEE it is not possible to quantify the dose of PAEE for related physiological outcomes when using data obtained from accelerometry.

On average, participants wore the Actical® for ~14 hours a day for seven days, while the data collected by DLW represented 24 hours a day for seven days. The ~10 hours of data not collected by the Actical® may account for the difference between these two measures.

Future Research

Future research is needed to validate accelerometry to measure PAEE. Although this study expanded data on the Actical®, additional research is warranted to compare accelerometer measured PAEE to DLW in different populations. The discrepancies between PAEE measured by different accelerometers compared to DLW estimated PAEE may be attributed to the proprietary equations used by the manufacturer's software to calculate PAEE were developed in laboratory settings with healthy participants. The development of new predictive equations should be tested in different populations under free-living conditions to determine the reproducibility of PAEE prediction. Future accelerometers must be designed with increased sensitivity and precision to improve their ability to predict PAEE. Perhaps with future versions of accelerometer software, estimates in free-living PAEE will improve so that researchers can better determine the role of PAEE in chronic disease prevention and treatment.

Clinical Implications

As the rate of obesity increases in the US, the interest in understanding the process of maintaining a healthy body weight is increasingly important. Because PAEE is the only form of energy expenditure that can have major intentional alterations made to it, PAEE has become a key factor in individual weight loss prescriptions. In spite of its widely recognized importance, the ability to accurately quantify PAEE is limited with current measurement technology. One alternative for improving the assessment of PAEE is to combine accelerometer data with subjective measures such as activity and diet logs. This will enable clinicians and patients to better understand how physical activity affects energy balance and contributes to health promotion and disease prevention.

Overestimation of physical activity is common among US adults and accelerometers tend to underestimate PAEE. Considering the current rates of obesity in the US, some underestimation of PAEE may not be viewed negatively. However, underreporting PAEE may cause clients to make large increases in PAEE, which could lead to overexertion, injury or burnout making it harder for clients to want to continue or return to physical activity.

Accelerometers are growing in popularity with the general population; in fact some people are posting their accelerometry data on social media websites. These tools have great potential to promote social change focused on Hill's small behavioral changes. If society as a whole commits to making small changes to increase physical activity, the result can lead to the decline in the obesity epidemic.

Conclusion

In conclusion we reject our first hypothesis that PAEE measured by these two methods would be within 50 kcal/day. Instead, we found the average difference between these two techniques is 193 ± 350 kcal/day. Regarding our second hypothesis, we accept that BMI influences the difference in PAEE calculated by these two methods, be we reject that lean body mass influences this difference. Future studies as described above are needed to improve the ability to accurately measure PAEE and its contribution to promoting a healthy lifestyle.

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APPENDIX

Evidence Table

Citation	Study Design	Subjects/ Characteristics	Outcomes
Bonomi AG, Plasqui G, Goris AHC, Westerterp KR. Improving assessment of daily energy expenditure by identifying types of physical activity with a single accelerometer. *J Appl Physiol.* 2009;107(3):655-61.	Measured PA with a Tracmor triaxial accelerometer while simultaneously assessing TDEE with DLW for 2 weeks. PAL was determined by dividing TEE by sleeping metabolic rate which was measured overnight in a respiration chamber. Netherlands	N = 15 (men = 9; women = 6) • Ages 26 – 59 yr (41 ± 11) • BMI 19.6 – 29.5 (24.4 ± 3.0)	Accelerometer output used to calculate activity counts/day (AC_D) to determine duration of 6 activities. MET_D is mean of MET compendium value of each activity type weighed by daily duration. TEE predicted by AC_D and BWt and AC_D and FFM. These AC_D models replaced MET_D, which explained variation of TEE by 9%. Sedentary activities = >75% of the day.
Crouter SE, Churilla JR, Bassett DR. Estimating energy expenditure using accelerometers. *Eur J Appl Physiol.* 2006;98(6):601-12.	1. Compared Actical, AMP-331 and Actigraph simultaneously against a portable IC during all types of PA intensity. 2. Examined accelerometers' ability to predict light, moderate and vigorous PA.	N = 48 (men = 24; women = 24) • Age 21 – 69 yr • BMI 17.9 – 40.6	Actical and Actigraph overestimate walking and sedentary PA and underestimate most other PA.AMP-331 closely estimated walking but underestimated all other activities. All accelerometers underestimated vigorous PA ($p < 0.05$).

Heil DP. Predicting activity energy expenditure using the Actical activity monitor. *Res Q Exerc Sport.* 2006;77(1):64-80.	Developed algorithms for predicting PAEE in children and adults from Actical activity monitor data. Montana State University	N= 24 children N= 24 adults Subjects performed 10 activities (supine rest, 3 sitting, 3 house cleaning, and 3 locomotion) with Actical on ankle, hip and wrist.	PAEE was computed from VO2 and VCO2 consumption measured by a portable metabolic measurement system. Metabolic and Actical data were transformed and used to represent activity as: $PAEE_{ij} = (EE_{ij} - EESR_J)/M_{T(j)}$ $EE_i = 3.9 \times VO_{2(i)} + 1.1 \times VCO_{2(i)}$ Regression analysis was used to create PAEE prediction equations from Actical data. • Single linear regression models. • Multiple nonoverlapping linear regression models. Most of the algorithms accurately predicted PAEE intensity and duration ***(p>.05).***

Rothney MP, Schaefer EV, Neumann MM, Choi L, Chen KY. Validity of physical activity intensity predictions by ActiGraph, Actical, and RT3 accelerometers. *Obesity.* 2008;16(8):1946-52.	Compared 7 predictive equations for accelerometers on Actigraph, Actical and RT3 to the ones provided by the manufacturers and to MET values determined by whole room IC measures. Regression equations for each device were used to predict min-by-min METs and daily PAL Vanderbilt and NIH	N = 85 (men = 37; women = 48) • Ages 20 – 69 yr • BMI 16.9 – 42.1 • BF% 6.7 – 57	RT3 linear regression values best represented all activity. ActiGraph linear regression values underestimated sedentary PA and overestimated light activity. Actical linear regression estimates predicted moderate activity best.

APPENDIX B

Accelerometry

Accelerometry-based physical activity monitors, or accelerometers, are small portable sensor systems that quantify physical activity by measuring the acceleration of the body during movement. Accelerometers measure activity over time and quantify the intensity, frequency, and duration of bouts of physical activity that an individual performs.

Accelerometers measure physical activity based on the proportionality between force and acceleration as expressed in Newton's Second Law of Motion ($F_{NET} = m * a$). Theoretically, acceleration of the body is proportional to the muscular forces imposing movement and thus the amount of energy expended to generate this movement. Since force is correlated with mechanical work (work = force*displacement) and mechanical work requires energy input (work = change in energy) acceleration through all three orthogonal planes (anteroposterior, mediolateral, and vertical) is often used to estimate PAEE. Therefore, the data stored in the accelerometer is proportional to the intensity and duration of the measured accelerations which roughly correspond to changes in PAEE (1).

The accelerometers used in this study were the omnidirectional Actical® Activity Monitors (Philips Respironics, Bend, OR). It is equipped with a beam bending piezoelectric acceleration sensor, as shown in Figure B1.

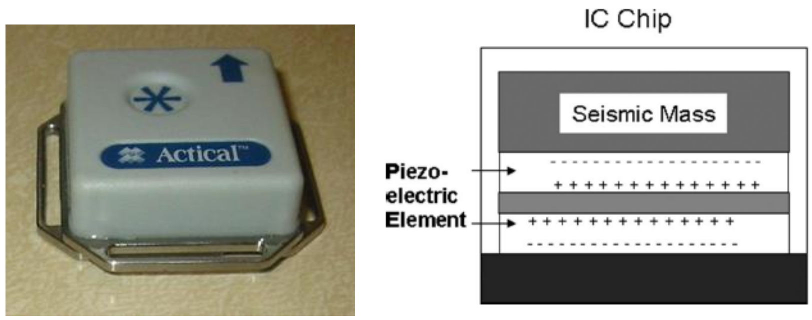

Figure B1. Image of the Actical® and a schematic of its piezoelectric accelerometer (2).

The piezoelectric acceleration sensor consists of a piezoelectric element attached to a seismic mass, housed in a small waterproof case. The piezoelectric element detects gravitational-forces related to movement, which cause the seismic mass to induce conformational changes in the piezoelectric element. These conformational changes result in a displaced charge that builds up on one side of the sensor. The charge differential generates an analog voltage signal that is filtered and amplified before being converted to a digital series of numbers (A/D conversion) at 32 hertz (Hz), or 32 cycles per second. The digitized values are averaged over one minute and the accelerometer counts are referred to as epochs (counts*min $^{-1}$) (2). See Figure A2. The amplitude of the digital acceleration signals are downloaded to a computer and analyzed by system software to identify the frequency, intensity and duration of physical activity. The Actical® software then uses prediction equations to estimate the metabolic cost, or PAEE, of physical activity from the aggregated epochs. The Actical® uses linear regression analysis for relating epochs to metabolic equivalent.

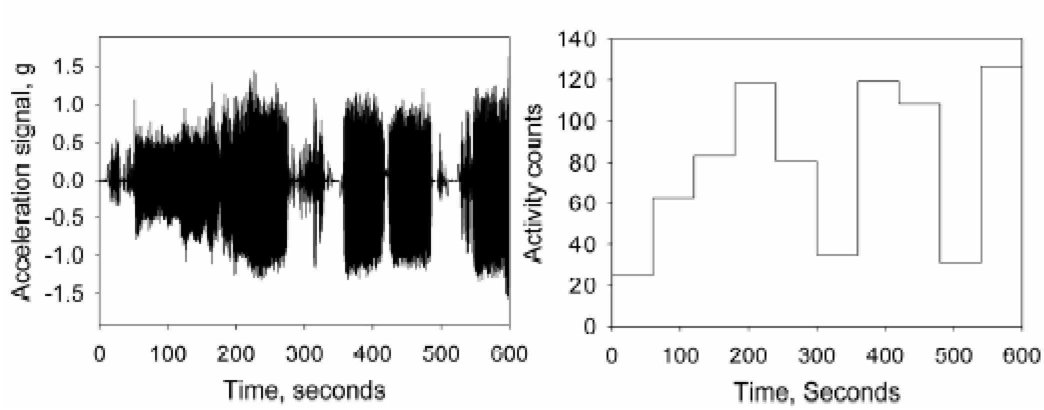

Figure B2. Analytical processing of the acceleration data. Image on the right is raw data and the image on the left is sum of the "raw counts." (2).

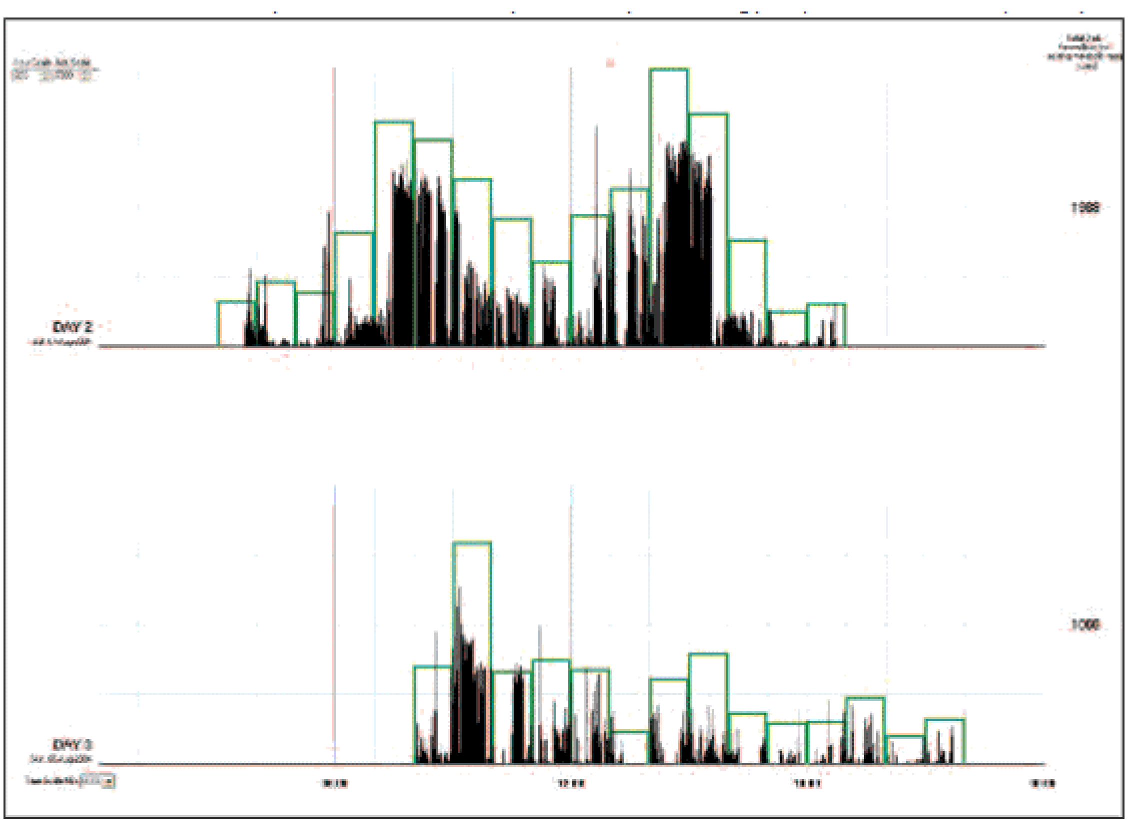

Figure B3. Intensity of the acceleration signal recorded with piezoelectric accelerometer and the resulting activity counts per minute.

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APPENDIX C

Metabolic Equivalent

A metabolic equivalent (MET), or the metabolic cost of activity, is a unit often used to classify physical activity intensity as multiples of one MET or the ratio of the associated metabolic rate for the specific activity divided by the REE. One MET reflects an oxygen consumption rate of 3.5 ml/kg/min or 1 kcal/kg/hour, which is the average energy cost associated with sitting in a chair at rest (1). Therefore, work at two METs requires twice the amount of energy expended at rest or 7.0 mL/kg/min and three METs requires three times the REE, ect. METs calculated in this way normalize data across subjects for a given type of physical activity and allows comparison of physical activity intensity despite differences in body size and composition. It is assumed that all subjects performing a specific type of physical activity exert approximately the same number of METs even though their PAEE measurement may be very different.

Each activity type has been assigned a MET value or range of values which is published by the American College of Sports Medicine (ACSM) (2). The ACSM has designated standard ranges of METs for physical activity intensities from sedentary (1 – 1.5 METs), light (1.5 – 3 METs), moderate (3 – 6 METs), vigorous (6 – 9 METs), and very vigorous (> 9 METs).

Sedentary (<1.0 – 1.0 MET)	Light (>1.0 – 3.0 METs)	Moderate (3.0 – 6.0 METs)	Vigorous (>6.0 METs)
Lying	Walking, slowly (1- 2 mph)	Walking, briskly (3-4 mph)	Walking, briskly uphill or carrying a load
Sitting, typing, writing or reading	Cycling, stationary (<50 W)	Cycling (<10mph)	Cycling, fast (>10 mph)
	Swimming, slow treading	Swimming, moderate effort	Swimming fast
	Light stretching	Calisthenics exercise	Climbing stairs
	Golf, power cart	Table tennis	Racketball or tennis
	Bowling	Golf, pulling cart or carrying clubs	Canoeing, rapidly
	Light house work, dusting	House work, vacuuming	Moving furniture
	Mowing lawn, riding mower	Mowing lawn, power mower	Mowing lawn, push mover

Table C1. Examples of Common Physical Activities by Intensity of Effort Required in MET Scores (3).

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