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Towards a methodology for improving the comparability of accelerometer-based results for physical activity measurements in older adults

Lukas Stefan Gorzelniak

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Ich versichere, dass ich diese Dissertation selbständig verfasst und nur die angegebenen Quellen und Hilfsmittel verwendet habe.

München, den 20. März 2013 Lukas Stefan Gorzelniak

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Abstract

Introduction: Accelerometry has become an established method for objective physical activity (PA) measurements in medical and epidemiological research. However, current accelerometer types record PA in proprietary, manufacturer-dependent representations called "activity counts". Studies comparing these outputs or PA classification differences caused by varying positions or applied device-types are widely lacking. Therefore, the following main research question was formulated: "Are reported physical activity results in older adults affected by the selected devices and their associated proprietary outputs, their sampling location and the applied data reduction methods, and how can the comparability of results be eased or enabled?" In order to address this question, the following objectives have been defined for this thesis:

Objective I: *Compare the output of three widely used commercial accelerometers in order to derive conversion factors between units, and to select the most reliable device for the KORA-Age field study;*

Objective II: *Explore the differences in activity counts acquired at different positions, their location-dependent correlations to medical outcomes in COPD, as well as their positional effect on the estimated time spent in different intensity levels in the elderly, and to enable comparability by means of conversion factors between positions;*

Objective III: *Develop individualized uniaxial and triaxial cutpoints in a data-driven approach for the PA classifications in the elderly and compare the acquired results with published thresholds at two different sampling intervals.*

Material and Methods: The reliability and output of 11 RT3 (Stayhealthy), 5 GT1M and 5 GT3X (Actigraph) accelerometers was examined using repetitive motions carried out by means of a Stäubli TX90 robot. For the position-specific count output comparisons, PA was assessed at ankle, wrist (both GT1M) and hip sites (RT3) in 58 patients (62.2 $\pm$ 9.6y) with very severe COPD, and at ankle and hip sites (GT3X) in 190 healthy elderly subjects (75.1 $\pm$ 6.6y) of the KORA-Age cohort. PA data of 166 elderly subjects was used to derive individualized intensity cutpoints. Descriptive statistics were applied including reliability and correlations analysis, as well as multivariate regression models, agreement measures and statistical hypothesis tests.

Results: The vector magnitude unit (VMU) device output was significantly different between the three device types, with the GT3X showing the highest inter-device reliability. The device output was significantly different between all sampling locations in both study groups and the position affected the associations to medical outcomes in subjects suffering from COPD. From the KORA-Age PA data, differences were observed in the position-dependent intensity classification using published thresholds, but not for the developed

uniaxial performance-based quartile classifier (AQ) for the time spent in moderate-to-vigorous PA (MVPA). Uniaxial and triaxial classifications yielded different results in the estimated MVPA time in published and derived classification methods, and all MVPA classifications were strongly affected by the chosen sampling interval.

Discussion: Regarding Objective I, different device types with proprietary data outcomes were found to generate considerably different outcomes in the laboratory assessment in terms of acceleration magnitudes and codomains, preventing a direct translation of counts. These differences hinder a comparison of results between studies, and they likely affect the derived intensity thresholds in calibration studies. In terms of the device reliability, the inter-unit coefficient of variation increased with decreasing movement speed of the robot, but was still acceptably low in the GT3X accelerometers.

Concerning Objective II, the magnitude of the reported PA was shown to be dependent on the sampling location in the field-based examinations. A comparison of position-dependent count outputs was enabled by means of derived conversion factors for ankle and hip in the elderly and, likewise, for ankle and wrist positions in patients suffering from COPD. Despite enabling count-based comparisons between sampling locations, associations between position-wise PA data and medical outcomes should only be compared with caution, as each position seems to contain unique PA information, leading to different correlations. In order to enable comparable PA classifications of ankle and hip recordings in sedentary, light, moderate, vigorous intensity levels in the elderly, a method was developed (AQ) which classified moderate, vigorous and MVPA based on uniaxial recordings independent of the position ankle or hip. In contrast, using ankle and hip-derived cutpoints from a published calibration protocol resulted in different estimates between ankle and hip in all PA levels.

Concerning Objective III, the calculated time spent in MVPA varied considerably when different published cutpoints were applied to the cohort data. This underlines the need for standardization in calibration studies, as differences in the protocols typically lead to differences in the reported guideline adherence. Depending on the selected epoch and MVPA threshold, 12% to 100% of the elderly KORA-Age subjects met a current PA recommendation. The uniaxial AQ was found to classify MVPA fairly well, when compared to the median of all included published thresholds. The AQ can be simply calculated, relies only on PA data without complicated translations to energy expenditure estimates, and therefore, can be a means to enable comparability between studies.

Conclusion: The results of this thesis highlight the limited comparability due to lack of standardization in the assessment and processing of PA. The reported PA behavior was shown to be strongly depending on the device-specific proprietary outcome measure, the position of the device and the applied intensity cutpoints. To increase standardization, a PA classifier was developed in the scope of this thesis.

Future studies using raw data output will presumably enhance the comparability between devices and sampling locations and ease the calculation of conversion factors, despite remaining technical sensor differences. Moreover, using of high-sampled raw data recordings during the calibration process will likely lead to less device-dependent thresholds, and produce more comparable results concerning the adherence to PA guidelines between different clinical and epidemiological studies.

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List of Abbreviations

6-DOF	6-degrees of freedom
ACSM	American College of Sports Medicine
ADC	analog-to-digital converter
ADL	activities of daily living
AHA	American Heart Association
ANN	artificial neuronal networks
AP	anteroposterior plane
AQ	activity quartiles
CDC	Centers of Disease Control and Prevention
CHD	coronary heart disease
CI	confidence interval
COPD	chronic obstructive pulmonary disease
CPA	Compendium of Physical Activities
CSA	Computer Science and Applications Inc.
CV	coefficient of variation
dB	decibel
DHHS	Department of Health and Human Services
DIT	diet-induced thermogenesis
DLW	doubly labeled water
EE	energy expenditure
FEV_1%pred.	forced expiratory volume in 1s in % predicted
FEV_1%VC	forced vital capacity
FP	frontal plane
GOLD	global initiative for chronic obstructive lung disease
HMM	hidden Markov model
HR	heart rate
HST	hydraulic shaker table
Hz	hertz
IC	integrated circuit
ICAD	international children's accelerometry database
ICC	intraclass correlation coefficient
kcal	kilocalories
kJ	kilojoules

km/h	kilometer per hour
LSI	large scale integrated motor activity monitor
LTOT	long-term oxygen therapy
MA	mediolateral axis
MEMS	micro-electromechanical system
MET	metabolic equivalents
MVT	motorized vibration table
NHANES	National Health and Nutrition Exanimation Survey
NHLBI	National Heart, Lung, and Blood Institute
Nm	Newton meters
Ns	not significant
PA	physical activity
PAEE	physical activity energy expenditure
PLM	periodic leg movements
PR	pulmonary rehabilitation
RMR	resting metabolic rate
ROC	receiver operating characteristics
rpm	rounds per minute
SD	standard deviation
SEE	standard error of estimate
SNR	signal-to-noise ratio
SP	sagittal plane
TEE	total energy expenditure
VMU	vector magnitude units
WHO	World Health Organization

Glossary

6MWD Originally developed as a 12-minute walk test and adapted for chronic bronchitis, around the 1970s, the 6MWD was found to be a better tolerated, and easy to administer one-time measure of functional capacity of patients *(ATS Statement Guidelines for the Six-Minute Walk Test. Am. J. Respir. Crit. Care Med. July 1, 2002 vol. 166 no. 1 111-117)*. As the 6MWD was reported to be a predictor of morbidity and mortality in COPD, it has been integrated in the multidimensional disease grading score (BODE). In this BODE index, a 6MWD performance of $\geq$350 meter does not increase the rating, whereas a range from 250 to 349 meter increments the score by 1, 150 to 249 meter by 2, and $\leq$149 meter by 3 points.

BODE is a multidimensional disease grading index in chronic obstructive pulmonary disease published in the New England Journal of Medicine by Celli et al. in 2004 *(doi:10.1056/NEJMoa021322)*. Disease severity is rated from 0 to 10, in which the higher score presumably correlates with an increased risk of death. The BODE index consists of the body-mass index (0 to 1 points), airflow obstruction (FEV_1%pred., 0 to 3 points), self-reported dyspnea (mMRC, 0 to 3 points), and exercise capacity index (6MWD, 0 to 3 points) and is calculated by building the sum of the points in each assessment. Zero points are equivalent to a BMI of >21, a FEV_1%pred.: $\geq$65, a mMRC score between 0 to 1, and a 6MWD of: $\geq$350 meter. Ten points are generated by values of <21, <35, 4, and <149, respectively.

Borg CR 10 is a clinical tool for the assessment of perceived exertion published by Gunnar Borg in 1982 *(Psychophysical basis of perceived exertion. Med Sci Sports Exerc 1982; 14:377-81)*, which has been modified by Elliott et al. for the assessment of dyspnea *(The language of breathlessness. Am Rev Respir Dis 1991; 144: 826-32)*. Perceived shortness of breath during the last 24 hours or after a certain task is rated from 0 (no breathlessness at all) to 10 (maximal), with 3 being moderately, 5 severely and 7 very severely out of breath. The scale increments by 1, with the exception of 0.5 described as very, very slight (just noticiable) dyspnea. Note, that the original Borg score of perceived exertion has 20 instead of 10 units.

DLW is the gold standard in measuring the average metabolic rate of an organism over a certain period. After non-radioactive forms of the elements deuterium and oxygen-18 are administered orally to a subject, the elimination rates of both markers are measured in the subject over time through regular sampling of heavy isotope concentrations in the saliva, urine, or blood (Jones PJ et al. Validation of doubly labeled water for assessing energy expenditure in infants. Pediatr Res. 1987 Mar;21(3):242-6). From the loss in carbon dioxide the respiratory qoutient can be estimated, and thus, the metabolism.

GOLD is short for the Global Initiative for Chronic Obstructive Lung Disease which published a classification to describe the severity of the airflow limitation based on the volume of forced exhalation in a one-second (FEV_1%pred) as a predictor of mortality *(Pauwels et al. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2001;163:1256-1276)*. The severity is classified based on the four stages according to the updated version of the GOLD report from 2006. Those ranks are I: mild (FEV_1%pred. $\geq$80) with FVC_1/FVC $<$0.70, II: moderate, III: severe, and IV: very severe (FEV_1%pred.: II: 50 - 79, III: 30 - 49, IV: $<$30, respectively). Normal spirometry is considered in the FEV_1%pred. range of 80% to 120% of the average value.

mMRC is a clinical tool from the Medical Research Council for the assessment of perceived dyspnea which was first published by Fletcher et al. in 1959 *(The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. BMJ. 1959;2:257-266)* and slightly modified to be as part of the BODE score. The scale contains four grades with each increment increasing levels of breathlessness: Grade 0: not troubled with breathlessness except with strenuous exercise. Grade 1: troubled by shortness of breath when hurrying on level ground or walking up a slight hill. Grade 2: Walks slower than people of the same age on level ground because of breathlessness, or has to stop for breath when walking at own pace on level ground. Grade 3: Stops for breath after walking about 100 meters or after a few minutes on level ground. Grade 4: Is too breathless to leave the house or is breathless to leave the house or is breathless when dressing or undressing.

MVPA is the abbreviation for moderate-to-vigorous physical activity. According to the definitions by the WHO *(www.who.int/dietphysicalactivity/physical_activity_intensity/en/)*, the American College of Sports Medicine, and the Center for Disease Control and Prevention, moderate PA consists of activities in the intensity range of approximately 3 to 6 metabolic equivalents (MET), whereas vigorous PA is usually defined as >6 MET. MVPA itself is defined as all PA in the intensity ranges of ≥3 MET, with light activities being defined as <3 MET according to the above stated sources. These definitions stated above are accordingly used for light, moderate, vigorous and MVPA in this thesis. Additional remark: Occasionally, PA intensities of the lower and higher septrum are divided into sedentary (<1.5 MET) and very vigorous (>9 METS) intensity levels, and due to the age-dependent nature, moderate PA has sometimes been defined as 4 to 7 MET (i.e. in children).

Chapter I

Introduction

Contents

Accelerometer-based activity monitors are increasingly used in medical and epidemiological studies as a practical tool for the assessment of physical activity (PA) in various settings. This chapter is meant to provide a brief overview in PA measurement possibilities, and the progression of physical activity research including PA recommendations, in relation to the development and application of accelerometers. Based on this summery, issues concerning the limited comparability of data acquired by objective means are outlined, and objectives for this thesis are derived.

Health benefits of PA and measurement possibilities

Regular PA and exercise is important to promote and maintain health and physical independence until the very old ages [1]. In many epidemiological longitudinal studies an active lifestyle was linked to a reduced risk in overall and disease-specific mortality and morbidity with profound evidence that physical inactivity is being a risk factor for cardiovascular disease, hypertension, type 2 diabetes mellitus, thromboembolic stroke, colon and breast cancer, osteoporosis, anxiety, obesity and mental health [2, 3]. The precise assessment and quantification of PA is therefore of great importance to different aspects of health outcomes, maintenance of physical conditions, PA interventions, the exanimation of

relationships and the development and compliance of PA recommendations [4–6]. Methods for the measurement of PA range from easy administrable but imprecise subjective self-report (i.e. questionnaires, activity diaries, and interviews), up to very sophisticated, reliable but expensive criterion measures of the metabolic rate by means of indirect- or room calorimetry, and doubly labeled water (DLW), the gold standard under free living conditions [4, 6]. Outcomes from subjective and objective methods have been translated - by means of calibration algorithms - to energy expenditure (EE) for validation purpose in order to enable a comparison with a criterion method [4, 6].
Motion sensors such as switches, pedometer, accelerometers and gyroscopes, physiological monitors (i.e. heart rate devices) and a combination of both (multi-sensor devices) are classified as objective methods [7] and provide a compromise concerning the measurement accuracy, cost and ease of assessment. Accelerometers are especially nowadays widely used in PA research.

1. The beginning of PA research and early sensor-based studies

The earliest studies on PA and cardiovascular disease started six decades ago in the 1950s. Morris and colleagues showed that coronary heart disease (CHD) mortality rates of bus conductors on London's double-decker omnibuses were approximately half of those of the sedentary bus drivers [8]. By classifying work intensity into light, doubtful, intermediate and heavy, they found men who were physically active at work such as postal service employees, civil servants and London transit workers, to be at lower CHD mortality risk and more likely to survive an attack [9].

Isochronal, for the measurement of gait function and human motion, the development of metal strain-gauge accelerometers, which deform elastically due to inertial force, started in the late 1940s and early 1950s [10, 11] and first reports of the application can be found from 1953 [12–14]. However, many manufacturing attempts at that time failed due to unsuitable transducers, the need of bulky charge-integrating amplifiers, lack of a real steady state responses, and low device-sensitivity [15]. The discovery of the piezoresistive effect of silicon and germanium by Smith in 1954, namely that the electrical resistance changes (linear) with mechanical stress applied [16], enabled the production of new transducers with strain-elements that diffused into a semiconductor cantilever substrate [17]. As these pressure sensors contained piezoresistors on or in a diaphragm, they were called piezoresistive and made commercially available from 1958 as silicon strain-gauge, metal-diaphragm accelerometers [17]. The technical advance reduced low-frequency cut-off point in the signal spectrum and enabled accelerometers to study aperiodic movements (i.e. daily PA) [15]. The stability of the first generation of this piezoresistive sensors by means of epoxies, phenolic, or eutectics bonded silicon strain gauges was poor and thermal mismatch with the metal-epoxy-silicon interface occurred, therefore very fine filaments of single crystal diaphragms with diffused piezoresistors were used instead [10, 17, 18]. First results of locomotion (i.e. walking or running) and gait analysis by means of those piezoresistive accelerometers were reported in the 1960s [19–22]. Another milestone was the development of the first integrated circuit (IC) by Jack Kilby in 1958, which was essential for the minimization of technical components [23]. At that point in time and in line with previous results from Morris et al. concerning PA and all-cause mortality, Paffenbarfer and colleagues reported findings from the Harvard Alumni Health Study in the 1960s, including 17 549 men, who entered Harvard College between 1916 and 1950. Men who remained alive were approximately 40-50% more likely to be recreationally active compared to men who died from CHD [24]. All-cause mortality from changing physical activity habits were studied in the 16-year follow-up [25, 26]: Compared to men in the "unchanged" category between 1960s and 1977, as defined by a change of EE of less than 1032 kilojoules (kJ) = 250 kilocalories (kcal) per week, an increase in EE by 5160 kJ (1250 kcal) per week was found to reduce mortality risk by 20%; a similar decrease in EE resulted in a 26% higher risk of death. Compared with death rates, gradient increases in mortality with decreased levels of activity were reported and vice versa [27]. From there on, numerous observational long-term prospective follow-up studies with consisted findings assessed physical inactivity by means of self-report and its relationship to the relative risk of (disease-specific) death [3].

While intensity and amount of PA research started to gain importance in the early 1970s, accelerometer-based studies were still focused on gait and its analysis [28–30]. Although pedometers have been used in medical studies since 1926 [31] and accelerometers from 1953 on [13], little information about the accuracy of both instruments for the assessment of daily physical activity existed [14, 32, 33]. In 1975, the Large Scale Integrated Motor Activity Monitor (LSI) was introduced for epidemiological research, based on a pedometer comparable principle of a cylinder with a mercury ball and a tilt switch mechanism [34]. The LSI became the first waist worn device, which was evaluated exhaustively in regard to technical reliability, validity and feasibility [34–36] and movement counts from the device were related to EE when attached at the waist, but not at the ankle [4, 37].

In 1977, Saris and Binkhorst assessed the reliability of a single type of pedometer and actometers (modified Swiss Tussot watches) at subjects' ankle and waist sides in the lab on a treadmill, and additionally by a mechanical setup, a rotating carriage connected by a drive shift, at different speeds [38]. The actometer (fixed to the ankle), in contrast to the pedometer (fixed to the waist), was found to be a valid indicator of daily PA in terms of EE levels at different speeds. However, a high inter-instrumental variation was reported [38, 39]. The same devices were tested for their validity in estimating free-living daily PA by means of an observation study in 4 pupils from a kindergarten using EE formulas for sitting, standing, walking and running in the same year (1977) [40]: The pedometer tended to underestimate the level of activity at higher intensities, while the accelerometers were found to give a reliable estimation of activity in children [40].

In the following year, 1978, the results from self-report based PA research led to the development of a first PA guideline for optimal body composition and cardiorespiratory fitness, issued by the American College of Sports Medicine (ACSM) and recommending to exercise 3-5 times per week, 15 to 90 minutes per session with an intensity of 60-90% of the maximal heart rate reserve [41].

2. Evolution of sensor technology

By the early 1980s, the accelerometer development has been enhanced by key technologies such as ion implantation, leading to improvements in the placement of the strain gauges in single-crystal silicon diaphragms, and the batch fabrication techniques: anisotropic chemical etching of silicon and anodic bonding [42]. By means on anodic bonding, finished silicon diaphragm wafers were bond to Pyrex glass supports reducing the thermal mismatch [17]. Anisotropic etching lead to reduced overall accelerometer-sizes and allowed for well controlled diaphragm sizes and locations by means of IC photolithography [17]. Both technologies were precursors to the micromachining period in the 1980s, which started after the first piezoresistive device, requiring three dimensional micromachining of silicon, was proposed by Roylance and Angell in 1979 [43–45]. The proposed piezoresistive sensor enabled the measurements of out-of-plane accelerations, by attaching a proof mass to silicon housing through of a flexural element with a piezoresistive material on the upper surface [42]. Two years later, in 1981, the first uniaxial motion sensor with advanced piezoelectric ceramic transducer was developed and introduced in the field [46]. This work resulted in the design of the Caltrac Personal Activity Computer accelerometer (Hemokinetics Inc.), the first commercially available device, which became widely used in research [37, 47, 48]. The focus of accelerometer based research shifted towards objectively derived Metabolic Equivalents (MET) and EE estimations in the following years and the waist worn Caltrac accelerometer was found to be superior compared to the waist or wrist worn LSI in terms of reproducibility and when related to oxygen consumption [37, 46, 47, 49–51].

Recognition of the importance of PA for health

In 1984 the problems and prospects of the assessment of habitual PA were discussed during the workshops of the Centers of Disease Control and Prevention (CDC) and the National Heart, Lung, and Blood Institute (NHLBI) [35, 52–54]. From over 30 different methods for the assessment of PA, questionnaires and surveys were still regarded as the most practical approach for large scale studies in the following years, given cost prohibitive and experimental nature of objective PA monitoring techniques [25, 35, 52]. However, only two years later in 1986, accelerometry was increasingly promoted and recommended to be used in physical therapy practice [55], as it's principle was concluded to be superior over the pedometer principle, following an extensive review on motion sensors by Saris [56, 57].

In 1985, the terminology for PA research was set by Caspersen, Powell and Christenson, who defined and distinguished the concepts "physical activity", "exercise" and "fitness" from each other [58]. Caspersen published a review on the rising PA epidemiology concepts and methods four years later [59], and the Compendium of Physical Activities (CPA) was developed for use in epidemiologic and surveillance studies to standardize the assignment of MET intensities in physical activity questionnaires [60].

PA research started to focus on the health effects of moderate intensity PA. Although not increasing cardiovascular fitness, it was presumed to have a protective effect in the development of chronic diseases and therefore, has been included in the update of the ACSM guideline issued in the year 1990 [61]. In 1993, the first version of the CPA was published [60], and one year later, physical inactivity was acknowledged as one of the major risk factors for coronary heart disease by the American Heart Association (AHA) [62]. Due to new research on health benefits of moderate-intensity PA and increasing evidence that the total amount of PA is more important than the specific form (i.e. activity bouts, duration, mode), a new recommendation was issued by the CDC and ACSM in 1995, to promote that "every U.S. adult should accumulate 30 min or more of moderate intensity physical activity on most, preferably all, days of the week" [63]. A milestone for the recognition of the association between PA and public health was reached in 1996, with the publication of the US Surgeon General's report, U.S. Department of Health and Human Services (DHHS) [64]. The report concluded that people from all ages benefit from regular PA, moderate-intensity PA levels have significant health benefits, and additional health benefits can be achieved through even greater amounts of PA. The understanding and promotion of PA has been perceived to be at an early stage.

In the same year (1996), the first textbook devoted to PA measurements and energy expenditure was published [65] and other recommendations to promote (moderate intensity) PA and to reduce sedentary behavior followed and were issued or updated by different organizations in the following years [66–68].

Establishing sensor-based PA measurement

From the 1990s research activities using objective methods for the estimation of EE and walking activities, the assessment of posture and movement, the deviation of gait parameters, the development of intensity cutpoints (device calibration), and the validation of questionnaires or recently developed sensors, started to increase tremendously due to technological progress [50, 57, 69–76]:

Accelerometer design, technology and batch fabrication possibilities advanced largely, due to the progression in micro-electromechanical system (MEMS) technology, and further enhanced anisotropic etching and bonding [17, 76]. The power consumption and cost of accelerometers in smaller form factors (i.e. diaphragm sizes were shrinking to micrometers) was strongly reduced, while their performance has been improved. Accelerometer and pedometers became small, portable and minimally intrusive to participants and new devices entered the scientific literature:

In 1994, the uniaxial Computer Science and Applications Inc. (CSA) model 7164 accelerometer, with a cantilevered piezoelectric plate mechanism, was introduced and shown to be similar accurate in predicting EE as the Caltrac monitor [49] and valid for assessing children's PA [77, 78]. Both accelerometers have been mainly positioned at the low back or hip, but ankle and wrist locations were reported as well [79–82]. PA was assumed to not be fully captured by a single instrument at one body site, however, developed accelerometers are a compromise between validity and feasibility (i.e. subject comfort) [82]. Based on three separate uniaxial piezoresistive accelerometers (ICSensors, type 3031-010), the first triaxial sensor with improved sensitivity was developed at Maastricht University by Bouten et al. in the same year (1994) [71, 83] and became later known as the Tracmore accelerometer (Philips Research) without being commercially available [84, 85]. The introduction of the triaxial TriTrac-R3D accelerometer (Professional Products Inc.) followed in 1995, and the device was shown to be valid for assessing children's PA and able to capture higher intensities compared to both uniaxial accelerometers, CSA model 7164 and Caltrac [86, 87]. CSA has changed owner and name over the years from Manufacturing

Technology Inc. to Actigraph Inc. and became the most widely used (de facto standard) device brand in epidemiological studies [88]. In order to enable a translation of acceleration signals into basic postures such as lying, sitting, standing or walking, the DynaPort activities of daily living (ADL)-monitor (McRoberts BV) was developed, the first device to use via wires connected accelerometers at two positions, namely a vertical accelerometer at the left thigh, in addition to both, a vertical and a horizontal accelerometer at the hip [89, 90]. Other uniaxial piezoelectric bender system accelerometers were released in 1996 (Bio-Trainer activity monitor, IM Systems Inc.) [91] and in 1998 (wrist-worn Mini Motionlogger Actigraph model-AWL, Ambulatory Inc.) [92] and differences in the validity of EE estimations between these aforementioned monitors were reported for both, laboratory and field conditions, due to the differences in the accuracy of the calibration equations [82, 93]. In the same year (1998), the first fall detection system was realized by means of a piezoelectric shock sensor for the impact detection, and a mercury tilt switch to monitor the orientation of the client [94] and issues and future directions in the assessment of PA where discussed at an international conference in Dallas in 1999 [95]. The next commercial biaxial piezoelectric wrist or limb worn device were introduced in the year 2000 (Actiwatch, Mini-Mitter Inc.) [96], and 2001 (Actitrac, IM Systems Inc.) [97, 98], and together with the Mini Motionlogger, extensively used in sleep research [99].

3. The dose-response challenge

Due to the epidemiologic nature of most studies and the inclusion of many patients and subjects, strong links between PA and health benefits have been found. However, the understanding of the dose-response relationship has been unsatisfactory as studies that established the associations have relayed on subjective and imprecise methods such as recalls, diaries or questionnaires for assessment of PA [100]. Using the TriTrac-R3D accelerometer, Epstein and colleagues showed that PA levels in obese children are different, depending on the assessment method, and meaningful associations are more likely to be detected by motion sensors compared to questionnaires [101]. In line with this finding, in a meta-analysis published in the year 2000 the relationship between body fatness and PA in children has been found be to strengthened when objective rather than subjective assessment methods are used [102]. These PA assessment and result issues were discussed at a dose-response symposium in the same year, and a consensus statement was published by the expert panel finding that sufficiently accurate, sensitive and reproducible field methods to determine the dose-response and multiple levels of PA were lacking [103]. Questionnaires were reported to be limited in assessing all dimensions of PA, including type, intensity, frequency, and the environment in which the PA is performed [100, 104–106]. Moreover, questionnaires were found to be subject to measurement error due to social desirability effects and recall inaccuracy [107], which accounts especially in the elderly [108, 109]. As habitual PA is likely to be underestimated by self-report, and more intense activities are easier recalled than ADL, investigators suggested to use objective devices for more accurate measurement of PA [105].

In the same year (2000), the CPA coding scheme that classifies specific self-reports based PA by rate of EE was updated [110] and until then, EE equations from accelerometers counts, developed from locomotion and/or lifestyle activities, were shown to be valid for the estimation of intensities of ambulatory activities, but limited in the accurate estimation of total EE [48, 107]. Locomotion-based equations caused a underestimation of upper body activities such as vacuuming and mopping and the time spent in sedentary and light activities; lifestyle equations resulted in an overestimation of EE during walking in comparison to metabolic equivalents [93, 111–116].

Emerging applications of PA sensors

Movement classification and fall risk detection from accelerometer counts became subject of research in the following years as well as the methodological question how to translate, adapt and interpret proprietary accelerometer signals into physiologically/biologically meaningful data [117]. Particularly, the identification of time spent in certain PA intensities (i.e. moderate to vigorous) from accelerometer counts has been considered of high importance for public health and surveillance research due to the direct relation to PA recommendations [5, 52, 107]. For this purpose, intensity cutpoints from arbitrary accelerometer data have been developed for the CSA model 7164 [114–116, 118–121] and the Mini-Mitter Actiwatch [121] based on linear regression equations, and nonlinear equation for the Tritrac-R3D accelerometer [118] around the year 2000.

Two years later, in 2002, the second textbook on physical activity assessment for health-related research was published [107], with chapters devoted to the reliability, validity and measurement issues for the PA assessment as well as measurement techniques including questionnaires, accelerometer-based motion sensors, heart rate monitors and pedometers.

With the emerge of more advanced mechanical devices for PA assessment in the following years, recommendations suggested to use pedometers and accelerometers to promote the accumulation of 10,000 steps per day [122] and hence, to overcome accuracy, validity, reliability and bias susceptibility limitations of traditionally used self-report methods in epidemiological studies [100, 104–106]. However, the goal of 10,000 steps per day is based on limited evidence and may be unrealistic for most individuals [122, 123] and translating step counts in public health PA guidelines or energy expenditure is complicated, as intensity information is lacking [61, 124].

4. Energy expenditure as driver of sensor development

The desire to objectively quantify and predict EE, ideally combined with an accurate detection and discrimination of PA types, affected remarkably the hardware development of motion sensors concerning (multi-positional) sampling location(s) and (multi-sensing) measurement capabilities, as well as the translation/calibration of counts to physiological measures by means of the device itself or it's unit-specific software: In 2003, the hip worn triaxial Research Tracker RT3 (StayHealthy Inc.) was introduced (successor of the TriTrac) [125], allowing to estimate kcal per time through a proprietary linear regression equation algorithm using the manufacturer's software [5]. In the same year, the first multi-position device was developed, containing five independent piezoelectric biaxial sensors placed at the chest (upper sternum), the midthighs of both legs, and the feet, connected by three thin flexible wires to a hip worn, mini-computer with a 32-bit microprocessor [6, 126]. The so called Intelligent Device for Energy Expenditure and Activity (IDEEA, MiniSun, LLC.)

was shown to accurately identify more than 32 types of PA, with an averaged correction rate of 98.9% for posture and limb movement type and 98.5% for gait type, while providing information about duration, frequency, and intensity [6, 126]. An uniaxial device specifically developed for sleep research (PAM-RL, SOMNOmedics GmbH) in order to count periodic leg movements (PLMs) and detect PLM-disorders at the ankle was developed in the same year, 2003, and another multi-position sensor, based on a mercury tilt switch mechanism, has been introduced in 2004 (ActiReg, PreMed AS) combining a pair of one body position and one motion sensor at the chest (sternum), and the right thigh in addition to a storage unit at the waist for EE predictions [4, 127]. Moreover, the ActiReg enables the simultaneous use of heart rate monitoring equipment [127]. The first upper-arm worn multi-sensor device, the SenseWear Pro Armband (BodyMedia Inc.), entered the market in the same year (2004), combing a biaxial accelerometer to enable reports on the total number of steps, with physiological measures such as skin temperature, heat flux and galvanic skin response, for the estimation of EE estimation in terms of METs and sleep duration [76, 128].

A step towards objective PA monitoring in large-scale studies was achieved in 2003-2004, when the National Health and Nutrition Exanimation Survey (NHANES) implemented accelerometry (CSA/MTI/Actigraph model 7164) on a nationally representative sample of $\sim$7000 participants [129]. After a scientific meeting on objective monitoring was hold in the same year in Chapel Hill, best practices and recommendations for accelerometer-based activity assessments in field-based research were published in 2005 [130–132] as well as for calibration principles [48, 119, 133].

The assessment of dose-response relationships of PA is believed to require very accurate measurement methods, and effort to improve physical activity energy expenditure (PAEE) by combining heart rate (HR) monitoring (for moderate to vigorous activities) and movement registration (for sedentary to light activities) [134, 135], fostered the development of the Actiheart (CamNTech), a chest worn multi-sensor monitor, integrating a heart rate sensor and a biaxial accelerometer at a single position [136]. Another thigh worn uniaxial device (ActiPal, Professional Research Edition) focusing on posture classification and quantification of step number and cadence was introduced in the following year [137].

Methods for PA data analysis evolve

Apart from the development of enhanced sensors, work was carried out to improve both, the recognition of the activity types (e.g. based on decision trees [138], acceleration features [139], Bayesian classifier [140], a trained hidden Markov model (HMM) [141], and artificial neuronal networks (ANN) [126, 142]), and the enhancement of EE prediction formulas for already developed devices (particularly for the Actical and the model 7164), around the year 2006 [5]. First linear EE equations from aggregated accelerometer counts were improved by including more and different intensity ranges and PA types, as well as by the development of bilinear regression models, for the separation of light intensity activities, from moderate-to-vigorous PA (MVPA). In these bilinear kcal [143] or MET [144] models, arbitrary Actical units have been directed to one of two regression formulas, either based on their "intensity" count [143, 144] with an improvement of 0.1 METs or 0.1 kcal for all activities [5], or by means of the calculated coefficient of variation (CV) [145]. The CV model was also developed for both Actigraph accelerometers, model 7164 [146, 147] and the technologically superior successor GT1M model [148], which has been introduced in 2007 [149]. However, misclassifications of EE predictions were reported to occur most frequently for vigorous, and least often for moderate intensity activities [5, 146]. Furthermore, a lack of sensitivity to accurately distinguish sedentary and light activities was noted, indicating that no above mentioned predication technique accurately classifies PA across all intensities for any monitor [5]: Prediction equations derived from the integrated signals of a single, hip positioned accelerometer have been shown to underestimate EE for both, treadmill and ADL, especially for EE associated with movements of the upper limbs, walking on different terrains (e.g. inclines, stairs) and for increased efforts when carrying loads [5]. Furthermore, the elimination of rich features of the accelerometer signal by using proprietary activity counts have been found to limit the ability of the identification of PA types, and hence, inhibit the assessment of activity pattern and intensity [5, 84].

In 2006, Dr. Janz noticed in a comment that within ten years the amount of published literature on objective monitoring methods increased by a factor of ten from 30 publication in 1994-1995 to 300 in 2004-2005 [150]. For the entire year 2011, 1634 papers can be found in PubMed using “physical activity accelerometry” as key words. This increase can be explained by the continuous development and improvement of accelerometers which are believed to be essential in gaining understanding of dose-response characteristics between PA and health and for the assessment of the activities of daily living, especially in regard to everyday tasks with short episodes of moderate intensity PA, which are likely not captured by self-report [150].

Issue of Guidelines

As an update to the recommendation from 1995 [63], separate recommendations were issued by the AHA and ACSM for adults between 18 and 65 years [151] and older adults above 65 year or adults aged 50 to 64 year with clinically significant chronic conditions and / or functional limitations in 2007 [152]: The update states that in order “To promote and maintain health, all” subjects “need moderate-intensity aerobic physical activity for a minimum of 30 min on five days each week or vigorous-intensity aerobic activity for a minimum of 20 min on three days each week”, or a combination of both in bouts of at least 10 minutes duration, in addition to muscular strength and endurance exercises which should be performed at least twice a week on two nonconsecutive days. The difference in either recommendation is the definition of aerobic fitness in absolute terms such as metabolic equivalents of task for healthy adults and, relative to fitness in the recommendation for the elderly, aiming at an intensity of 50-85% of oxygen uptake reserve to include both, moderate and vigorous intensities. This accounts for the age-dependent variation of the basal metabolic rate and the decline in VO2 in the elderly [153–155].

In the same year (2007), accelerometry has been initiated in the Canadian Health Measures Survey for PA monitoring over 7 days on a nationally representative sample of 5000 survey participants of all ages using the Actical activity monitor [52, 156].

A Physical Activity Guideline for all Americans was published for the first by the DHHS in the following year (2008), recommending to spend at least 150 minutes per week in moderate or 75 minutes in vigorous intensity PA to reduce sedentary behavior [157].

Limits of pedometers for EE prediction

In reviews published in 2007 [158] and 2008 [159] pedometers have been shown to be beneficial and motivating in intervention studies. However, the applicability of pedometers in slow moving subjects (multimorbid, elderly, obese) is limited, as speeds below 3.2 km/h are underestimated due to sensitivity thresholds [160–163]. Nevertheless, a first attempt to translate PA recommendations into a pedometer based step goal was published in 2009, by developing intensity cutpoints from a treadmill protocol [164]. Considerable error in model fit lead to the conclusion that step counts per minute is a poor proxy for METs when determining moderate-intensity walking [164].

Attempts to improve EE estimation

Apart from existing MET values of associated activities for adults, energy cost particularly for children were published by the CPA in 2008 [165] due to the higher oxygen consumption relative to body mass at rest [166]. By the year 2009, the poor results in predicting EE and detecting the type of PA from accelerometer output were attributed to the arbitrary nature of the activity counts: Different activities with comparable EE in kcal were shown to result in well different counts (e.g. raking vs. descending stairs, moving boxes vs. level walking) [5]. Therefore new approaches to detect the type of activity and to estimate METs were developed, based on the high sampled raw data output of accelerometers: Total EE estimation has been improved by applying feature extraction and ANN models to the biaxial acceleration data of a customized hip worn biaxial IDEEA sensors with extended recording positions at the hip pack, on each upper arm (uniaxial), and on the top of each hand (biaxial) in 2007 [126, 167]. The identification of PA types has been enhanced by means of decision trees (and/or ANN) with hip and wrist worn ADXL202 (Analog Devices) accelerometers in 2008 [168] and Staudenmayer and colleagues used a combination of two ANN to advance both, METs estimations and PA type recognition using the Actigraph model 7164 in 2009 [169]. In the same year, a new method was developed by Bonomi and colleagues, combing high sampled accelerometry from a modified piezocapcaitive version of the Tracmore accelerometer for the detection of the activity type based on decision trees, and EE prediction using published data on the metabolic equivalents form the CPA coding scheme for the identified tasks [84, 170, 171]. Other reported methods included statistical decision boundaries and Receiver Operating Characteristics (ROC) in comparison to direct observation, for the Actigraph GT1M accelerometer [117, 172], as well as improved algorithms for the identification of locomotive, household and sedentary activities using a triaxial sensor (Activity Style Pro HJA-350IT, Omron) [173, 174]. Apart from the development of methods, a lack of standardization in the processing of accelerometer data, also leading to differences in published cutpoints was recognized and a consensus conference on objective activity monitoring was sponsored by the NIH in 2009 [175].

5. Challenges for accelerometry

In 2010, a review on the methodologies for PA assessment, particularly suited for use in epidemiological research has been published, with particular reference to validity, primary outcome measure and considerations when using each method in the field [166]. One of the key challenges for accelerometer output was identified in the management of missing data, and the distinction of it from inactivity, as an underestimation of inaction can lead to a potential bias [166]. Due to the differences between accelerometer types, the choice of a device will influence the study design and protocol (e.g. concerning the research question) [109], and thus limit the comparability to other studies given the device dependent proprietary output. Accelerometers were found to be limited in measuring all activities equally well, but reasonably accurate for measuring locomotor movement and to have a good relationship to EE across many activities [166]. However, a variety of different cutpoints is available for different intensity levels reaching from <100 to <800 counts per minute for sedentary intensity classification, and 1900 to 8200 counts per minute for moderate intensity levels [166]. The selection of cutpoints affects the number of minutes spend in certain intensity levels, and hence, the calculation of the prevalence of meeting physical activity recommendations [166, 176]. Moreover, a uniform standard of practice for accelerometers calibration was found to be lacking [177]. Derived EE estimations from accelerometers were reported to differ to those published by the CPA [5], while a new version of the METs CPA coding scheme was published as a second update in 2011 [178].

Research focus on children and adolescence

Accelerometers that either enabled short time raw data recordings, such as the triaxial GT3X accelerometer from Actigraph, (successor of the GT1M) [179, 180], or devices with solely high sampled data output like the GENEA [181] were introduced in medical research. However, accelerometer based research for assessing PA levels, metabolic cost estimates, questionnaire and sensor validations, improvement of EE prediction formulas, and the development of intensity classification thresholds, has been carried out predominantly in children and adolescents using proprietary output. Therefore, the International children's accelerometry database (ICAD) was created in the same year (2011), as an first attempt to standardize analysis and methods in order to create comparable outcome variables across studies for data from the Actigraph accelerometers [182]. In the elderly gait performance declines [183] and spatiotemporal gait parameters might be derivable from accelerometer data [184], enabling the detection of individual falls risk by means of sensor based objective measurements in unsupervised settings [185]. However, studies exploring accelerometer based PA and PA patterns in healthy older individuals are rare [186] and the development of methods to process the data has not gained much attention in elderly subjects [187].

Where are we now?

In 2012, a global recommendation on PA for health was published by the WHO. Separate recommendations are stated for children and adolescents (5-17 years), who are advised to accumulate daily at least 60 minutes of moderate to vigorous-intensity PA, adults (18-64 years) and the elderly (65 years and above). The WHO recommendation for both, adults and the elderly is comparable to those published by the AHA & ACSM and the PA Guideline from the DHHS from 2007/2008. All organizations recommend to spend a minimum of 150 minutes of moderate intensity per week or 60 (AHA & ACSM) and 75 minutes respectively (DHHS / WHO), in vigorous intensity activities, or a combination of both, in bouts of at least 10 minutes duration (AHA & ACSM / WHO).
In light of technological advances of accelerometers, an update to the recommendation from Trost and colleagues [131] has very recently been published, including information about monitor selection and their use [188]. Epoch lengths are recommended to be set as short as possible, preferably to less than 10 seconds as densely sampled data can be converted to *1-min* epochs and processed using conventional analytic methods [188].

By the year 2012, accelerometer-based activity monitors have gained prominence in PA measurements in medical and epidemiological studies. In literature objective arbitrary PA data from a variety of different accelerometers, positioned at multiple locations can be found [189] and new devices, such as the Actigraph GT3X+ or GeneActiv are continuously under development, challenged by new multifunctional (programmable) units with streaming possibilities such as the Shimmer or the announced wireless Actigraph wGT3X+. However, many methodological questions still remain (e.g. how many axes must be measured at which sampling rate at best for how long etc.) [190].

6. Statement of the Problem

Overall it can be concluded that the comparability of accelerometer derived PA data in field research is limited due to the following factors:

(i) Variety of applied sensors and reported parameters
(ii) Variety of attachment positions of motion sensor
(iii) Variety of developed and applied cutpoints

(i) Devices currently used in PA research differ in regard to mechanical components and internal processing: The quality of accelerometry-based data depends on device-specific sampling rates and resolutions within the limitations of memory and battery capacity. The underlying measurement principles are the same for each device, however, different proprietary processes are applied when the raw accelerometer signal is filtered, processed and stored [191].

Due to a lack of standardization, device-dependent arbitrary data formats such as step or activity counts, vector magnitude units (VMU), time spent in certain intensity levels or postures, transitions or activities such as walking, METs or PAEE estimates have been reported. Unfortunately, the varying components and the manufacturer dependent arbitrary nature of each accelerometer output, limit the comparison of data acquired with monitors from different brands [6, 192].

Moreover, because of the rapid engineering process, previous generations of accelerometers are continuously replaced by successor devices with enhanced specifications or extended functionality [193]. Responses to similar movements are likely to vary between instruments from different manufacturers or different sensor generations of the same brand [149, 194].

Furthermore, only few results exist that assessed the technical reliability of different sensor, with even less reports in which different sensors have been compared for similar movements. In order to enable a between-monitors comparison it is recommended to transform counts into units of acceleration ($\mathrm{m}\times\mathrm{s}^{-2}$) [166].

(ii) Apart from the technical aspects, the attachment position of sensors is another source of variation. In medical and epidemiological studies on PA, habitual activity is predominately measured by means of a single uni- or triaxial accelerometer positioned at waist level, in order to allow for full body EE estimates near the body's center of mass [83, 195].

However, other recording positions such as ankle (step counter) [196, 197] or wrist (i.e. for sleep research) [198] are typical, as well. Accelerometers have been incorporated to clothes (i.e. electronic shirts [199, 200], shoes [201, 202]) or accessories, such as belts [203] and watches [204], or been limited to certain fixed positions on the body by their design (i.e. ear [205], upper arm [128], thigh [206, 207], etc.). Moreover, devices that can be attached at multiple sites by means of elastic snug belts for instance, are common.

Although the kinematic and gravitational components of the output of an accelerometer depend on the position of placement, the orientation on, and the posture of the subject [83], studies comparing accelerometer position are rare [6] and no agreement where a monitor should be worn exist [208].

In different diseases such as chronic obstructive pulmonary disease (COPD), PA is a considerable outcome measure for the diagnosis and therapy [209, 210], and objective PA data acquired by means of different device types at varying positions has been associated with medical outcomes such as functional capacity, airway obstruction, or disease severity scores, producing ambiguous results across a number of studies [211–221]. The reported relationships between functional capacity and objective PA data have been found to range from weak to strong, depending on the chosen device at the sampling location (i.e. ankle, upper arm and hip) [212, 216, 220, 222].

If or to which extent associations between clinical characteristics and PA are affected by a specific monitor placement has not been systematically assessed, and only few results are available regarding the comparison of sensor data acquired at different body locations [223]. However, this seems to be a key question in order to compare recordings, especially in older patients or subjects who often suffer from disorders limiting their mobility [116, 221, 223, 224].

Finally, due to the difference in counts acquired at different positions [49, 83, 225], two reports were identified in which intensity thresholds were published for different sampling locations such as ankle or wrist [116, 121]. If the estimated time spent in different intensity levels is affected by the sampling location has not been explored yet.

(iii) Research to translate arbitrary accelerometer counts into meaningful physiological data such as EE or time spend in certain different intensity levels (e.g. sedentary, light, moderate, and vigorous activities), has been carried out for multiple devices in young target groups, and to a lesser extend for adults [133]. A variety of intensity cutpoints has been developed, particularly more than 20 different thresholds have been proposed for the uniaxial Actigraph model 7164. Therefore the selection of the most appropriate regression equation and accelerometer cutpoints is difficult [191], and a consensus on the "best" PA level classification does not exist [226]. Calibration studies, and the methods applied to derive EE prediction models have yet not been standardized, and thus, vary in terms of included subjects, the selected calibration activities (ambulation/locomotion vs. lifestyle) and analysis methods (e.g. linear, bilinear, nonlinear, and mixed regression models, ANN, ROC, etc.) [176, 177]. Only few studies developed cutpoints for the elderly, however, a wide range for MVPA is already present, ranging from 574 to 2020 counts per minute [176].
Currently, is not clear, to which extend the compliance with PA guidelines will be affected by the selection of a published threshold. Only a single study assessed the variation of time spent in MVPA in the elderly, when different artificial intensity levels have been applied [176]. EE prediction formulas and cutpoints have been mostly developed for minute-by-minute aggregated accelerometer data, however, recommended epochs for PA monitoring vary dependent on the age of the target population ranging from 2-5s in children [227], 15s in adolescents [228] to 60s for elderly subjects [48, 131, 132]. The amount of variation due to the re-integration of the accelerometer epoch to 60s when determining the time spent in MVPA intensities by means of cutpoints, has not been explored thoroughly. A comparison between recently developed cutpoints and the resulting time spend in MVPA for triaxial accelerometers has not been carried out, furthermore, a comparison if thresholds for uniaxial and triaxial accelerometers will result in similar intensity classification is lacking.

7. Research Question and Objectives

The purpose of this dissertation is to improve the comparability of accelerometer-based results of medical studies. Therefore, the following main research question was formulated:

> **Are reported physical activity results in older adults affected by the selected devices and their associated proprietary outcomes, their sampling location and the applied data reduction methods, and how can the comparability of results be eased or enabled?**

This question can be addressed in many different ways, however three concrete objectives were stated for this thesis:

Objective I: *Compare the output of three widely used commercial accelerometers based on a new method concerning their performance (i.e. response to motions, technical reliability) in order to select the most reliable unit for the KORA-Age field study, and to derive conversion factors between devices;*

Objective II: *Explore the differences in activity counts acquired at different position, their location-dependent correlations to medical outcomes in COPD, as well as their positional effect on the estimated time spent in different intensity levels in the elderly, and to enable comparability by means of conversion factors between positions;*

Objective III: *Develop individualized uniaxial and triaxial cut-points in a data-driven approach for the PA classifications in the elderly and compare the acquired results with published thresholds at two different sampling intervals.*

By addressing these objectives, assistance in the selection of an accelerometer is provided, together with information on the effect of the sensor position, and how to process the PA data in order to classify the time spent in moderate-to-vigorous physical activity (MVPA) intensities in elderly subjects (see Figure I-1). The objectives are divided into different levels: At acquisition level, the direct, counts-based sensor output is compared using descriptive statistics, whereas at processing level, the activity counts have been reduced to an intensity representation. Both outputs are reported at the publication level, and presumably affected by the selected device, the chosen position and the applied data reduction methods, as indicated by the three arrows.

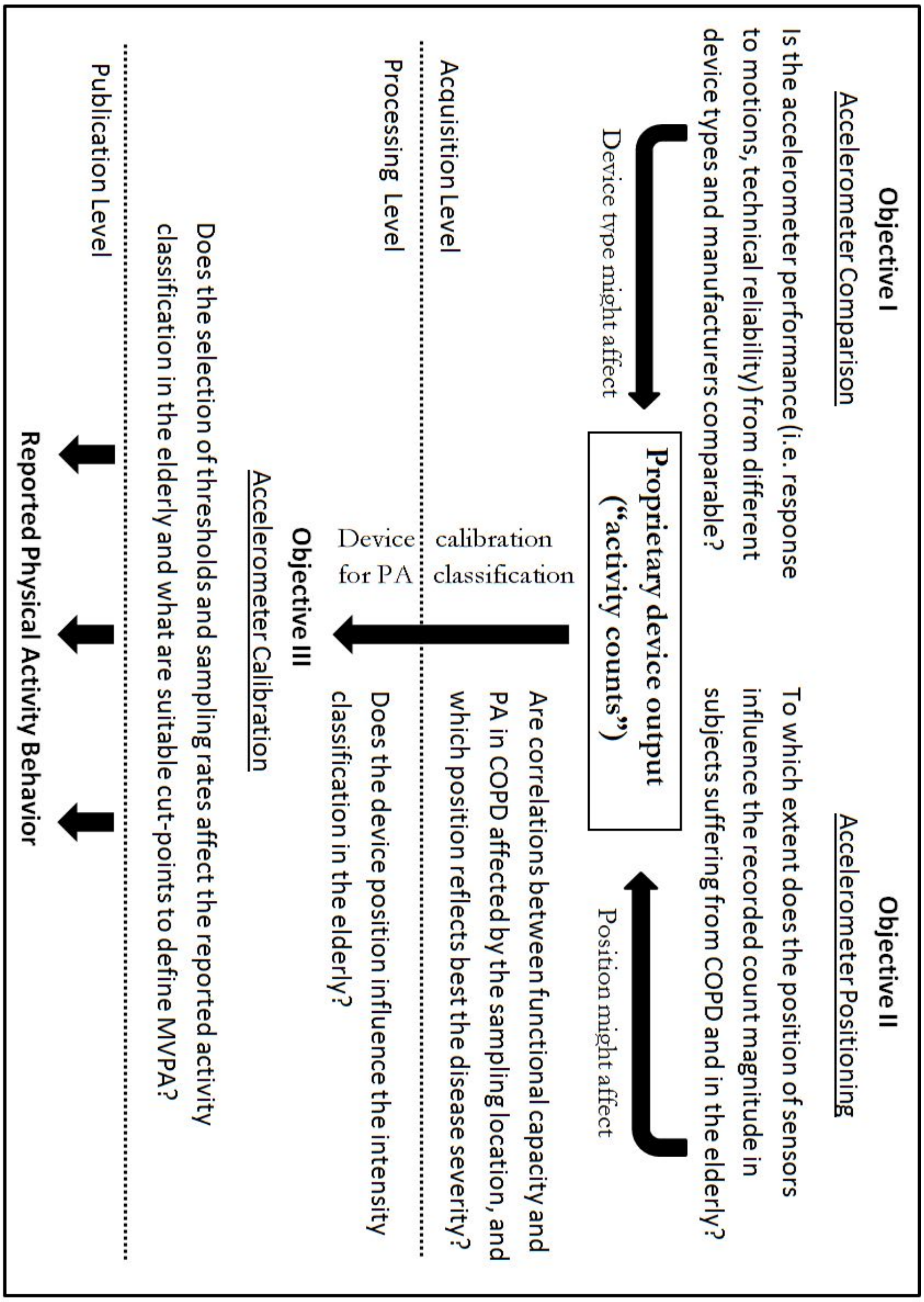


Figure I-1. Scope of the thesis

Chapter II

Materials and Methods

Contents

This chapter consists of four sections of which the first outlines the measurement methodology and hardware used in this thesis, particularly to address Objective I. The second section provides the required medical terms and definitions needed for Objective II and Objective III (e.g. the health-related dimensions of PA), as well as a description of the included study samples. The design of each study carried out to answer all stated objectives, is outlined in the third section of this chapter, followed by the statistical methods.

1. Technical Terms and Equipment

In this section, the physical principles of accelerometry are introduced, as well as its basic functionality, specifications and the different types of accelerometers. A brief technical description of each motion sensor used in the laboratory and field exanimations is provided, as well as for the robotic arm.

1.1. Definition of Physical Concepts

Human motion is subject to biomechanics, defined as the analysis of structure and function of living systems by means of knowledge and methods of mechanics, and kinesiology which address mechanical, anatomical, physiological (or psychological) mechanisms [229, 230]. Biomechanics includes both, the study of non-moving static systems, as well as dynamic systems and their kinematics (i.e. time and spatial factors acting on the system without consideration of the forces that cause it) and kinetics, the forces and torques that act upon a system to influence its movement during motion [72]. Kinematics can be referred to as the geometry of motion, as movement is described by terms such as the [229, 231]:

- *position p(t)* and *reference frame*
- *displacement* (i.e. the difference in position between two points)
- *velocity v(t)* (i.e. rate of change in *position p* with respect to *time t*)
- *speed u(t)* (i.e. the scalar absolute value (magnitude) of the *velocity v*)
- *acceleration a(t)* (i.e. the change in *velocity v* over *time t*)

The first derivate of the position of an object as a function of time $p(t)$ gives the speed *u(t)* of the object in *meters per second*, and the velocity, if a direction is specified [232]:

$$v(t) = \frac{dp(t)}{dt} \qquad u(t) = |\frac{dp(t)}{dt}| \tag{II.1}$$

With the changing speed the object, the first derivate of the speed gives the acceleration in *meters per second squared* ($m \times s^{-2}$), which is also the second derivative of the position [232]:

$$a(t) = \frac{dv(t)}{dt} \qquad = \qquad \frac{d^2p(t)}{dt^2} \tag{II.2}$$

On the other hand kinetics introduces the concept of mass and provides information on how a movement or a posture is produced or maintained, moreover it can confirm equilibrium by the absence of acceleration in static states [72, 229]. In dynamic states kinematics and kinetics are used to analyses acceleration and deceleration of the body during movement according to Newton's Second Law of Motion, which states that "the acceleration of an object is directly proportional to the net force acting on it and is inversely proportional to its mass. The direction of the acceleration is in the direction of the net force acting on the object" [72, 229]. This enables the assessment of human motion by means of accelerometry, with reflections on intensity and frequency, and translates to the formula *net force F* in *Newton meters (Nm)* is equal to the *mass M* in *kg* times acceleration *a(t)* in $m \times s^{-2}$ [76]:

$$F = M \times a(t) \tag{II.3}$$

1.2. Principle of Accelerometry

The principle of accelerometry relies on a mechanical sensing element consisting of a proof mass (referred to as seismic mass) connected to a mechanical suspension mechanism (e.g. strain induced within a flexural spring or elastic structure) in a case with respect to a frame of reference [42, 76]. An acceleration of the case with the embedded spring mass system results in a deflection of the proof mass by inertial force or gravity transmitted through the spring or elastic structure according to equation (II.3). This displacement of the spring or the mass within the case, or the (compression or stretching) force in proportion to acceleration is transmitted by the spring and can be measured in accordance with Hooke's spring equation (II.4) [72, 233]. Hooke's laws states that the extension of a spring is in direct proportion to stress applied to it [232, 233]:

$$F = -k \times x(t) \tag{II.4}$$

Equating equations (II.3) and (II.4) reduces the measurement of acceleration in a spring mass system to a measurement of the spring displacement *x(t)* in *meters per time* from its equilibrium position, by a spring constant k measured in Nm, resulting in the restoring force F, with respect to the attached proof mass [232]:

$$a(t) = -k \times x(t) \times M^{-1} \tag{II.5}$$

Reversing the acceleration in equation (II.5) results in a spring compression instead of a spring extension [232]. The acceleration for a spring mass system is ideally zero during the absence of acceleration or movement at constant velocity, in a static balanced state, for which forces causing an extension of the spring are negated and cancelled out by opposite compression forces (equilibrium) [232]. Linear acceleration itself can be measured by inertial sensors along one or several directions and is often expressed in g-force (approximately $9.81\ m \times s^{-2}$) relative to the inertial / free fall reference frame, due to the gravity at the Earth's surface [76, 232]. Therefore, a value of zero is returned by inertial sensors in gravitational free fall toward the center of the Earth. An accelerometer can record translational and rotational inertial accelerations of human movement which have a direction and a magnitude relative to the device's axis or axes of sensitivity [233] and additionally, provides information about the inclination / orientation of the inertial sensor in static situations for the sensitivity axis which is parallel to Earth's gravity [90]. However, in dynamic situations both components, the inertial acceleration of interest, and the gravitational component are combined, leading to a measurement artifact, which indistinct the desired inertial acceleration due to the transducer's mechanism of operation [90, 233]. Moreover, a constant acceleration smaller than the gravitational acceleration cannot be distinguished from a static inclination signal using a single uniaxial accelerometer [90]. As mentioned above, an acceleration signal measured by an inertial sensor contains three components, namely [90, 234, 235]:

1. Acceleration as a result of human movement
2. Acceleration as a result of gravitational force
3. Noise

As for every technical device, noise is generated by the technical components of an accelerometers (e.g. amplifying circuit), and/or can be registered as part of the measured signal due to vibrations, displacements in a vehicle, loose attachment etc. [6, 236]. Noise as a result of movement artifacts can be reduced from the acceleration signal by applying a band-pass filter on the output signal [6, 236].

1.3. Specifications and Types of Accelerometers

Commercial accelerometers for the measurement of human motion are typically characterized by their *type of physical principle*, *type of output* (proprietary vs. raw data), *number of axes* they can measure, *dimensions* and *weight* of the device, their *battery, memory* and the *measurement capacity*. Specifications concerning the accelerometer signal include [78, 232, 237]:

- *Sampling Rate* (Output data rate) in Hz states the number of measurements per second an accelerometer can perform
- *Dynamic Range* (Output, Measurement or Amplitude Range) in $\pm g$, specifies the total/maximum amplitude an accelerometer can accurately measure before distorting or clipping the output signal
- *Analog-to-Digital Converter (ADC)* in *bits*, which converts the analog voltage or current to a digital number proportional to magnitude of the input and defines the smallest detectable incremental change of input parameter in the output signal as *resolution* in *g's per bit* with respect to the maximum amplitude
- *Sensitivity* in *mV/g*, ideally a linear correlation between change in acceleration (mechanical input) and electrical output signal, valid at a single frequency
- *Thermal sensitivity* in °C or % defines the change in accelerometer output per g in relation to temperature increase, (in practice more commonly the *temperature operation range* is reported, and therefore used in this manuscript, in which an accelerometer will meet the performance specifications)
- *Frequency Response* in *Hz* specifies the sensitivity over the transducer's entire frequency range and referred to as the "amplitude response" specified with a tolerance band in % or HzdB, relative to the 100 Hz sensitivity
- *Bandwidth* defined in *dB* or Hz defines the highest frequency range that the accelerometer operates in, with signals that can be sampled without aliasing by the specified sampling rate
- *High pass* and *Low pass Filter* (Frequency Cut off Limits) gives the frequency for which the output exceeds the stated output deviation and starts to fall off below the stated accuracy
- *(Non-)Linearity* in % specifies a measure of the (maximum) deviation of the calibration curve from a perfectly constant straight line sensitivity
- *Noise* in g or Hz generated by the amplifying circuit, determines the minimum resolution of the sensors and can be lowered by restricting the bandwidth
- *Amplitude stability* dependent on aspects like *Zero g offset, Temperature Range, Bias* and *Sensitivity Drift* etc.

Although a similar spring mass operation principle is used for all available commercial accelerometers, components widely used to convert the mechanical motion into an electrical

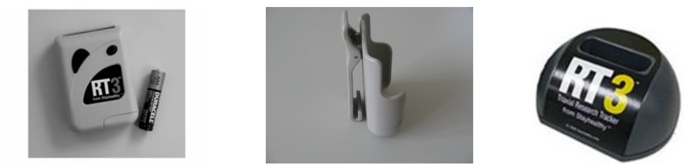
signal can be classified into piezoelectric, piezoresistive and based on change of capacitance: Piezoelectric accelerometers rely on piezoceramics or single crystals and consist of a proof mass attached to a piezoelectric sensing element. When the sensor undergoes acceleration, the sensing element is bend directly through the applied acceleration, causing a displacement of the proof mass [76] or bend as a results of the displacement of the proof mass [72]. This change causes a variable output voltage proportional to the applied acceleration [72, 76]. Piezoelectric accelerometers can support large dynamic measurement and temperature ranges as high voltage outputs are created for small strains [72], but they do not respond to constant accelerations such as gravity [76].
Piezoresistive accelerometers are formed by bulk micromachining and both, the proof mass and the attached cantilever beam contain polysilicon piezoresistors (springs) arranged in a Wheatstone bridge configuration [72, 76]. Any movement of the proof mass or the cantilever beam due to an acceleration of the sensor changes the electrical resistance of the springs and produces a proportional voltage [72, 76]. Piezoresistive accelerometers are useful for measuring vibrations at low frequencies (e.g. high shock applications), can measure gravity as a constant acceleration, and are fairly simple and low cost [72, 76]. However, output signals of piezoresistive accelerometers have a lower level and are sensitive to temperature (thermal mismatch) [17, 76].
Capacitive accelerometers are formed by bulk micromachining and consist of a differentiable capacitor with central plates attached to a freely moving proof mass, which is encapsulated between two fixed external plates (electrodes) [72, 76]. Acceleration of the device unbalances the capacitor due to a displacement of the proof mass, and the change of capacitance is proportional to the applied acceleration and can be measured [72, 76]. Capacitive accelerometers are widely used in consumer electronics due to their fast response to motions, low power consumption, large output and low noise levels and the ability to measure constant accelerations [76].

1.4. Accelerometers

One of the first triaxial accelerometers mentioned in the introduction is the Tritrac-R3D and its successor, the RT3, introduced to scientific literature in 2003, is used in this thesis for both, field and laboratory examinations. The RT3 (Stayhealthy, Monrovia, CA, Inc., firmware version 0.6) is a small and lightweight (7.1×5.6×2.8 cm^3, 65.2 g) in a holster inserted, battery powered piezoelectric accelerometer (see Figure II-1) that records motion in three orthogonal directions known as x (vertical), y (anterioposterior), and z (mediolateral) [125]. The device specifications are unpublished, although Powell and colleagues reported the dynamic range to lie between 0.05 and 2 g, with a sensitivity range of 2 to 10 Hz, calibrated at 5.3 Hz and a sampling rate from 0.017 [76] to maximally 1 Hz [125]. The temperature of operation, as stated by the manufacturer, has a range of 0 to 45°C. The acceleration signal is internally converted to a digital representation, processed and represented as an arbitrary "activity count", which is a quantification of the amplitude and frequency of the detected accelerations in customizable time intervals of 1 or 60s, summed over an "epoch" and stored in volatile memory [125]. The RT3 supports four different modes of operation: Accumulated activity counts are sampled and stored either on individual axes, or as a triaxial vector defined as

$$VMU = \sqrt{(x^2 + y^2 + z^2)} \tag{II.6}$$

at 1-s or 60-s epochs, allowing a recording between 9 hours and up to 21 days for the minute-by-minute VMU count representation, until the memory is filled and the registration is stopped [76, 125]. After the device is initialized using the RT3 software, the mode of operation is represented as a number (i.e. 1 to 4), together with a counter of days and elapsed time from the registration start, in the display. The recording is started manually, after the device has been initialized by holding the start button until a sound notification occurs. Once started, start and stop button can be used to mark specific events (e.g. entering and leaving a vehicle). The battery life allows logging up to 30 days [76, 125]. The RT3 software supports an estimation of metabolic activity units or kilocalories from the activity counts, if gender, age, height and weight are provided. In order to download registered PA data, the RT3 device is inserted into the docking station and attached by means of a serial connection. The docking station itself is connected to a PC via USB cable and the Stayhealthy software enables the data transfer and kcal and MET estimations.



(a) RT3[1] (b) Holster (c) Interface

Figure II-1. RT3 Triaxial Research Tracker Kit

The next two motion sensors that are applied in field as well as examined in laboratory settings in this thesis, are the GT1M and GT3X accelerometers from Actigraph LLC (Pensaola FL), which have been introduced to scientific literature in 2007 and 2011. The biaxial GT1M (firmware version 4.2.0) and the triaxial GT3X (firmware version 3.1.1) devices, are both small and lightweight solid state capacitive accelerometers (3.8×3.7×1.8 cm^3, 27grams) with microprocessor digital filtering, that record acceleration in a dynamic range of ±5 g [193, 239]. However, due to Actigraph-restrictions the dynamic range is limited to 0.05 and 2.5 g, sampled at 30 Hz (see Figure II-2). A 12-bit ADC is used to digitize the analog signal resulting in a resolution of 1.22 *mg/bit* [240]. The digital output is band pass filtered with a frequency range of 0.25 to 2.5 Hz and stored to non-volatile memory of 1 MB in size for the GT1M and 4 or 16 MB in the GT3X [240]. Both accelerometers can be customized to record proprietary or raw data, within memory limitations: Using an epoch of 1s enables roughly 5 days of recording time for the GT1M and almost 8 days of measurements for all 3 separate axes in the GT3X with 4 MB of memory (31 days with 16 MB, respectively). In raw data mode, only a bit more than 2 hours can be registered with the GT1M in biaxial mode, and almost 6.5 hours in the triaxial mode of the GT3X 4MB, according to the manual of the manufacturer (25 hours with 16MB, respectively). Both devices support the *VMU* representation when initialized in bi- or triaxial post-filtered mode, and are stated by the

[1]Image from Steele et al. [238]

manufacturer to have a battery life of 30 days [76]. The devices are directly connected to a PC using a USB cable. Initialization of both devices and data download is carried out with the Actigraph software (i.e. Actilife version >4.0.0). Actilife version 5.0 enables estimations of EE from 1 minute epoch activity counts based on different EE equations such as the Work Energy Theorem, Freedson equation, or a combination of both. The following measurement options are available during the initialization process: *Activity*, *Dual Axis* and *3rd Axis* only for the GT3X, *Step Count* and *Inclinometer*. Moreover, the sampling rate of raw data (12 vs. 30 Hz) or epoch period (1s - 60s) can be customized, as well as the behavior of the filter (i.e. *normal* or as *Low Frequency Extension*), the LED on both devices, and the date and time of the start of the measurements. Both devices are usually attached and fastened by means of a snug elastic belt.

(a) GT1M/GT3X[2] (b) Belt (c) Orientation[3]

Figure II-2. Actigraph GT1M and GT3X accelerometers

The successor of the GT3X and most recent MEMS accelerometer is the triaxial GT3X+ from Actigraph, which has been made commercially available by the end of 2010 and been applied in the laboratory evaluation. The GT3X+ (firmware version 2.0.0) accelerometer is the most recent MEMS device, small and lightweight ($4.6 \times 3.3 \times 1.5\ cm^3$, 19 grams) and records accelerations in a dynamic range of $\pm 6g$ sampled at 30 to 100 Hz according to the user setting. A 12-bit ADC is used to digitize the analog signal resulting in a resolution of 2.93 mg/bit. The digital output is band pass filtered with a frequency range of 0.25 to 2.5 Hz and stored to non-volatile memory of 512 MB. The GT3X+ can only be customized to record raw data, within memory limitations: The GT3X+ can record up to 40 days in raw data mode when sampled at the rate of both predecessors, namely: 30 Hz. The available measurement options are similar to those stated for the GT1M/GT3X, additionally a light measurement is supported. The device is directly connected to a PC using a USB cable. The Actilife software in version $\geq$5.0.0 enables estimations of EE from 1 minute epoch activity counts based on different EE equations such as the Work Energy Theorem, Freedson equation, a combination of both or VMU equations if measurement were carried out based on all 3 dimensions. The device is claimed to be water-resistant up to 1m for 30 minutes, and to operate at temperatures of -20 to 60°C according to the manufacturer.

1.5. Robotic Arm

To examine the technical reliability of different accelerometers (Objective I), an industrial robot TX90 (Stäubli Robotics, Pfäffikon, Switzerland) was used (see Figure II-3). The maximal height of the robot is 1428 *mm*, by aligning the articulated arm vertically, with a width

[2]Image from http://www.vividomaha.com/blog/2009/10/25/actigraph-gt3x-review, accessed: July 2012
[3]Image from ActiLife 5 - User's Manual, accessed: May 2012

of roughly 421 *mm*. The robot has a weight of 111 *kg* and a nominal load capacity of 7 *kg* up to 20 *kg* maximum. The TX90 robot is a serial manipulator robot with six rotational joints, and the articulated arm can execute movements in 6-degrees of freedom (*6-DOF*) with a repeatability precision of ± 0.03 *mm* and a reach of wrist of 1 *m* [241]. The motion range is dependent of each joint, ranging from a minimum of $+145°$ and $-115°$ for joint 5 to a maximum of $\pm 270°$ for joint 6. This applies as well to the maximum speed which falls between $400°/s$ for joints 1 and 2, and $760°/s$ for joint 6. Movements of the robotic arm can reach a maximal speed at load gravity center of up to 10.42 m/s. The working temperature of the robot lies between 5 and 40°C. The entire system consists of the robot arm, a CS8C serial controller, a SP1 manual robot control pendant and a workstation running on GNU/Linux OS with real-time extension [241, 242]. The cable connected SP1 control pendant provides an all-in-one terminal, with build-in programming, maintenance and supervision features as well as safety functions. Movement sequences can either be programmed by means of the pendant or the workstation interface. The robot is mounted on a laboratory table in the institute.

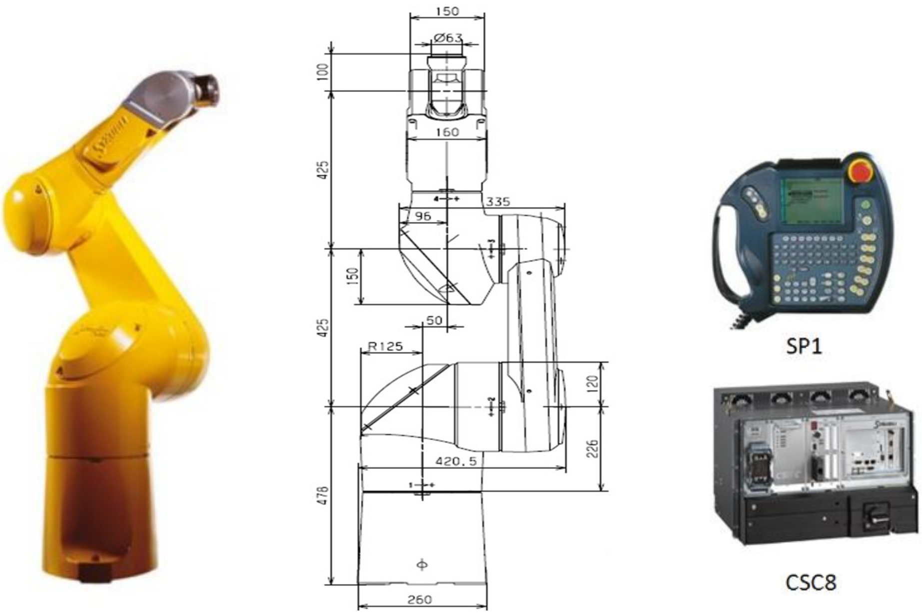


Figure II-3. Robotic arm TX90 with equipment[4]

2. Medical Terms and Study Samples

In the field assessments, human motion is measured by means of different accelerometers in subjects and patients. Accelerometers can be positioned at different body parts on a subject (Objective II) and they measure motion along one or several planes, dependent on their sensitivity axis or axes. Therefore, the anatomical body segments are introduced

[4]Images from: http://www.staubli.com/in/robotics/products/6-axis-scara-industrial-robot/medium-payload-6-axis-robot/6-axis-industrial-robot-tx90/

as well as segmental plane terms, in this section. Human motion is characterized as PA activity which results in energy expenditure, and hence, both concepts are defined in the following paragraph. Finally, the anthropometric characteristics of the included study participants are provided.

2.1. Definition of Anatomical and Segmental Plane Terms

The human body consists of main parts such as the head, neck and trunk, referred to as the "axial" portion of the body, and the lower and upper extremities (i.e. arms and legs) referred to as "appendicular" portions [229]. In total, 11 functional segments can be identified, namely: head and neck, shoulder riddle, thorax, pelvis, lumbar region, arm, forearm, hand, thigh, leg and, foot [72, 230]. Human motion generally occurs in frequencies between 0.3 and 3.5 Hz [6]. However, the frequency and the magnitude of accelerations depend on the position of registration and increases from head to ankle [130]. Accelerometers should be able to record dynamic ranges of $\pm 12g$, sampled at up to 20 Hz in order to assess all aspects of daily PA [6]. According to the Nyquist criterion, the sampling rate of an accelerometer should reach 40 Hz, twice the sampling rate of the highest frequency of movement, whereas the dynamic range of a waist worn device for the assessment of low and vigorous intensity activities from brisk walking to running and exercise is sufficient at $\pm 6g$ [6, 236]. Movement towards or close to the midline of a body is called *medial*, and the opposite motion is referred to as *lateral* [72]. A decrease in the distance to a predefined reference point (at any location on the body) is expressed as *proximal*, and *distal* for positions being further away [72]. Positions above and below a reference point on the body are called *superior* and *inferior*, respectively, while *anterior* and *posterior* define positions on the front or the back [72]. By using this three perpendicularly intersecting planes of motion at the center of mass, human movement can be described by means if these so called *cardinal planes* [72]: Left and right are separated in the *mediolateral axis (MA)* by means of the *sagittal plane (SP)*, front and back are distinguished in the *anteroposterior plane (AP)* by means of the *frontal plane (FP)*, and upper and lower in the *longitudinal axis* is divided by the *horizontal plane* [72]. Human motion is composed of both, (curvi-)linear motions in which the entire body moves the same distance in the same time period, and angular motions around an axis of rotation for which the distances travelled varies between regions of the body in respect to the time [72]. These translational and rotational inertial movements and resulting accelerations can be registered by accelerometer, along sensitive axes in the vertical, anteroposterior, and mediolateral planes [233]. Accelerometers register both, the frequency and intensity of movement and have been widely used to assess PA and EE.

2.2. Definition of Physical Activity and Energy Expenditure

In 1985, Capersen et al. distinguished "physical exercise", as a planned, structured and repetitive subcategory of PA, done to maintain or improve aspects of one or more components of fitness, and "physical fitness", as a set of health-related fitness attributes such as cardiorespiratory or muscular endurance, body composition, flexibility and skill-related fitness attributes (i.e. agility, balance, coordination, power, speed, reaction time) that people have or achieve in order to perform PA, from the concept PA [58]. PA was defined as "any bodily movement produced by skeletal muscles that result in energy expenditure"

(EE) [58]. The amount of energy needed to carry out a movement is measured in physics in kJ but in energy calorism as kcal per time [58] and can be therefore expressed as physical activity associated energy expenditure: (PAEE) = kcal $\times$ min^{-1}. The minute-wise body oxygen consumption at rest (VO_{2rest}) in a healthy normal-weight individual is approximately

$$VO_{2rest} = 3.5mlO2 \times kg^{-1} \times min^{-1} \tag{II.7}$$

and this equates to about 1 kcal/kg/h, as 1 liter of oxygen has an energy cost of circa 5 kcal, defined as 1 MET [166]. PA in the range of 1.8 - 2.9 MET is considered to have a low intensity, MVPA is defined as 3.0 - 5.9 MET and vigorous as $\geq$ 6.0 MET, however, the basal metabolic rate is lower in elderly [153–155], and higher for children [166]. PAEE compromises posture, spontaneous and voluntary PA and accounts for 15-30% of the daily total energy expenditure (TEE) in humans but can constitute up to 70% in extremely active subjects [243]. In addition, TEE is comprised roughly to 10% by diet-induced thermogenesis (DIT), the amount of energy utilized in the digestion, absorption and transportation of nutrients, and to 60-75% of the resting metabolic rate (RMR), an individual's body metabolism which is dependent on the gender, age, body height and size, muscular mass, thermal isolation and state of health, determined at absolute rest but not sleep [166, 243]. TEE can be summarized as the sum of internal heat produced (RMR + DIT) and external work (PAEE). External work is the most variable component of TEE as many occupational and leisure-time activities such as household chores, gardening, sports, transportation, shopping and so forth, contribute, while there are only little differences within and between individuals for internal heat production [7, 244]. PA is a complex behavior and can be described by different dimensions including [58, 245]:

- the type of an activity (e.g. walking, running)
- the intensity, or physiological effort which is associated with participating in this activity type (i.e. running on ground level vs. uphill while carrying loads)
- the duration, as the amount of time during which the activity is performed (i.e. jogging vs. marathon), and
- the frequency which states the number of PA events during a specific time period

Other dimensions include environmental surroundings of PA and the social conditions PA and PAEE are not synonymous, but measurements from PA can be extrapolated to units of EE, namely by using the product of the PA dimensions intensity, frequency and duration [243]. PAEE can be as well calculated by subtracting RMR from TEE [166].

2.3. Characteristics of Patients and Subjects

In order to address both, Objective II and Objective III, PA was measured by means of accelerometry in two different sedentary target groups in the field. Both samples fall into the "Physical Activity and Public Health in Older Adults" guideline from the AHA & ACSM published by Nelson and colleagues [152], as patients with clinically significant chronic conditions were included, as well as healthy older adults. A brief description of both study samples and the accelerometer distribution is provided in the following paragraph.

2.3.a. Patients with severe chronic disease

This paragraph is copied from the publication by Gorzelniak et al., "Comparison of Recording Positions of Physical Activity in Patients with Severe COPD Undergoing LTOT" [223]:

A sample of one hundred patients suffering from COPD and undergoing long-term oxygen therapy (LTOT), with or without walking aids (rollator), who had been admitted for a 3-week in-patient PR program at the clinic Bad Reichenhall, was approached. 58 patients (23 females) agreed to participate in the study. Reasons for refusal were the complex protocol involving the burden to attach, and detach the set of motion sensors at ankle, hip and wrist on a daily basis, exposure due to wearing the sensors, the lack of perceiving subjective benefit, severe medical condition, technical complexity, unwillingness to sign the required consent and difficulty in understanding the goal of the study. All patients had the diagnosis of smoking-related COPD of stage IV according to the global initiative for chronic obstructive lung disease (GOLD) classification with a demand of at least 1 liter of oxygen per minute at rest. All patients were instructed to increase O2 supply during training sessions, if a desaturation was discovered during walking or ergometer test by means of blood gas analysis or pulse oximetry. PaO2 should remain above 60mmHg or 90% sO2 during exercise according to the guideline of the German Society for Pneumology [246]; O2 was prescribed accordingly. Patients with type 2 respiratory failures were excluded, as well as those who had not been mobile due to medical conditions. Furthermore, subjects with less than four valid days of accelerometer recording from at least two measurement positions were excluded which occurred in five patients who did not wear the sensors regularly and in one patient in whom all three sensors failed. Therefore, a total of 52 patients (22 females) was available for final analysis. The accelerometers were distributed face-to-face and proper placement on the participant's body was demonstrated, questions about the wearing procedure were answered, and all patients received a manual with clear instructions and illustrative figures. After the measurement period, the device set was returned to the physicians or the nurses, before discharge. Patients were grouped into those using a walker (Group A) and those without (Group B) (see Table II.1). The study was approved by ethics commission of the Bavarian State Board of Physicians, all procedures were performed according to the ethics guidelines of the Declaration of Helsinki and all individuals gave informed consent.

	All Patients (N=52)	**With Walker (N=21)**	**Without Walker (N=31)**	**p-value**
Age (y)	62.2 ± 9.6	66.9 ± 6.6	59.0 ± 9.5	<0.01
Sex (F/M)	22 / 30	10 / 11	12 / 19	
BMI	25.5 ± 7.0	23.4 ± 3.4	26.9 ± 8.3	Ns

Table II.1. Characteristics of patients with COPD

2.3.b. Healthy older adults from the KORA-Age sub-cohort

A sample of two hundred and one elderly subjects >65 years, without diagnosis of bronchitis, asthma, emphysema, COPD or a combination of these diseases, was selected based on assessed spirometry values, from the KORA-Age cohort [247]. Ten subjects denied the participations, due to reasons regarding personal privacy, absence or denial of the sensors. One subject met the exclusion criteria (see Figure IV-5). Anthropometric characteristics of the subjects can be found in Table II.2. PA data from the day at the study center (first recorded day) was discarded, and in line with recommendation for objective devices [131, 132, 188], any other day with a wear time of <10 hours was excluded, as well as subject for whom a minimum of four valid days was not recorded. In adults, "3-4 days of monitoring (...) is sufficient to achieve 80% reliability for moderate or higher intensity physical activity" [108]. Wearing time did not have to be continuous. Additionally, in order to enable a comparison of hip and ankle mounted accelerometers, the above stated requirement had to be met for both sensors. The need to have at least a single registered weekend day (among the four or more valid days) as stated by the aforementioned recommendations, was neglected as PA in the elderly is assumed to not vary tremendously between days of the week and the weekend. According to the stated criteria, 162 subjects were found to be eligible for analysis (85%), providing 1388 valid ankle (8.57 $\pm$ 3.12 days), and 1333 valid registered hip days (8.23 $\pm$ 3.10 days). In total 24 subjects were excluded, 3 due to insufficient days of ankle recordings, 2 due to lacking hip measurements, and 19 in which both, registered hip and ankle registrations, were not enough. The KORA-Age study was approved by the ethics committee of the State Board of Physicians, written informed consent has been obtained from the participants and all investigations have been conducted according to the principles expressed in the Declaration of Helsinki.

Table II.2. Characteristics of healthy elderly subjects from the KORA-Age cohort

	All Subjects (N=190)	**Male Subjects (N=92)**	**Female Subjects (N=98)**
Age (y)	75.1 $\pm$ 6.6	75.3 $\pm$ 6.4	74.9 $\pm$ 6.8
Height (cm)	164.1 $\pm$ 9.0	170.3 $\pm$ 6.6	158.3 $\pm$ 6.8
Weight (kg)	75.2 $\pm$ 11.7	79.4 $\pm$ 10.2	71.3 $\pm$ 11.7
BMI	28.0 $\pm$ 4.0	27.4 $\pm$ 3.3	28.5 $\pm$ 4.5
Waist circumference (cm)	96.8 $\pm$ 11.4	100.6 $\pm$ 9.4	93.3 $\pm$ 12.0
Hip size (cm)	106.5 $\pm$ 8.5	104.7 $\pm$ 6.1	108.3 $\pm$ 10.0
Waist-Hip-Ratio	0.9 $\pm$ 0.1	1.0 $\pm$ 0.1	0.9 $\pm$ 0.1
Body fat (%) (N=178)	33.8 $\pm$ 7.3	27.8 $\pm$ 4.6	39.4 $\pm$ 4.4
6MWD (m)	453.0 $\pm$ 104.7	475.8 $\pm$ 103.5	431.6 $\pm$ 101.8
Tiffeneau Index	74.3 $\pm$ 8.0	73.1 $\pm$ 7.7	75.4 $\pm$ 8.1

3. Design of Studies

In order to address Objective I, an experimental laboratory study was conducted. In this study, the feasibility of using a robotic arm to assess the variability of proprietary accelerometer output was explored (Section 3.1): For a comparison of widely used accelerometers, motion sequences were defined, implemented and carried out by the robotic arm, after single accelerometers have been consecutively mounted on the robot. A similar motion sequences was repeated for every device and the sensor output was compared.

In order to answer the field-related Objective II and Objective III, a clinical observation and an epidemiological cross-sectional study were conducted. The medical study included a group of 58 chronic patients suffering from COPD in a controlled setting, during pulmonary in-patient rehabilitation (Section 3.2), while the epidemiological study consisted of 190 healthy elderly subject of the KORA-Age cohort in daily free-living (section 3.3). In both groups, PA has been measured by means of accelerometers placed at multiple body positions, for up to ten days. All accelerometers used in both field examinations have been previously examined in the accelerometer variability study (Section 3.1)

The resulting PA data from the different body locations was used to compare the accelerometer recordings in both samples, to explore relationships to clinical outcomes, such as functional capacity and the disease severity score in COPD (Section 3.4). In the healthy elderly, ankle and hip PA measurements were used to classify the time spent in different intensity levels (Section 3.5).

Furthermore, the time spent in MVPA was compared according to published literature by adapting the proposed intensity cutpoints. The performance of the PA classification based on the data-derived performance levels were discussed in comparison, as well as the effect of a chosen sampling interval on these PA classifications (Section 3.6). The results from this analysis were used to assess the amount of KORA-Age cohort members, who were compliant with the recommendations from a recently published PA guideline. Based on the criteria specified in the PA guideline, the amount of subjects meeting the recommendation has been calculated (Section 3.7). Only subjects with 7 full days of recorded accelerometer data have been included in the analysis.

Table II.3. Overview of laboratory and field studies

Study Title	Objective of the Study	Setting	Devices	Section, Obj.
Accelerometer Variability Study	Comparison of the variability of accelerometers	Laboratory setup: Single accelerometers attached to a robot	11 RT3 5 GT1M 5 GT3X	3.1, I
Comparison of recording positions of PA in patients with severe COPD	Position-dependent comparison of the PA output in COPD	Field exanimation: 52 patients (62.2 ± 9.6 years old) with very severe COPD undergoing LTOT in an in-patient rehabilitation setting	RT3 (hip) GT1M (ankle and wrist)	3.2, II
	Comparison of relations between position-dependent PA data and clinical outcomes			3.4, II
Individualized physical activity cutpoints for the elderly - A data-driven approach in comparison to published fixed thresholds	Position-dependent comparison of the PA output in the elderly	Field exanimation: 190 healthy elderly subjects >65 years in free daily living	GT3X (ankle and hip)	3.3, II
	Comparison of ankle and hip-based PA classification			3.5, II
	Comparison of uni- and triaxial intensity cutpoints and epoch effects for the time spent in MVPA			3.6, III
	Determining the amount of subjects meeting the AHA & ACSM PA guideline			3.7, III

3.1. Comparison of the variability of accelerometers

In order to address Objective I, the feasibility of using a robotic arm for the assessment of the variability of widely used RT3 (Stayhealthy), GT1M and GT3X (Actigraph) accelerometers was examined. The goal of this study is to compare the variability in proprietary (i.e. post-processed) accelerometer response of different manufacturers to reproducible movements, therefore, the SP1 control pendant of the TX90 robot (see Figure II-3) was used to program a motion sequence at two randomly selected speeds of the robot (namely: 10 and 25% of the maximal speed): The first motion sequence consisted of simple movements along each axis, beginning and ending at the resting position of the robot, followed by a break used for a manual change of the robot speed, before the second "random" movement sequence with components along all axes was iterated two times, with short stops in-between the repetitions [180]. The sequences were chosen to assess each axis first individually, and later combined [180]. The break without motion after the slow movement period was used to calculate the SNR, as especially the RT3 appeared to have an implemented noise reduction filter mechanism, which seems to reduce noise to zero, after passing a certain time-distance from the last movement(s). Recorded time information concerning the end of the slow, and the beginning of the faster sequence were used to identify the break period. For a rigid attachment of the sensors, a single RT3 holder was used in which the RT3 and the GT1M / GT3X accelerometer consecutively could be inserted (see Figure II-1 (b)). To enable a fixed position for both Actigraph devices, Velcro strips were bonded on the top layer to the holster using sticky tape. Additionally, strengthened by duct tape after the Actigraph devices were inserted (see Figure II-4).

(a) GT3X fixed to the RT3 holsters by means of sticky tape and Velcro

(b) Position of holster attachment at the robotic arm

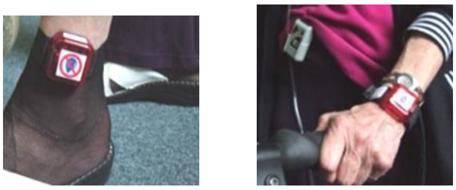
(c) RT3 inserted in the robot attached holster

Figure II-4. Final experimental setup for the Accelerometer Variability Study

The fastener-elements was removed from the RT3 holster and the remaining structure was screwed on the robotic arm. Single accelerometer units were consecutively mounted on the robotic arm at exactly the same position before the programmed motion was executed [180]. For this exploratory study, 11 piezoelectric triaxial RT3, 5 biaxial GT1M and 5 triaxial GT3X accelerometers were used [180]. All devices were initialized to record motion second wise (*1-s epoch*) in VMU representation. The GT1M was recording in biaxial, the GT3X in triaxial mode and response to the movement of the robot were compared among the accelerometers.

3.2. Position-dependent comparison of the PA output in COPD

In order compare uni- and triaxial accelerometer output and to explore if the sampling location is of relevance, as part of Objective II, PA has been measured at different body sites in patients suffering from severe COPD (see Tables II.1 and II.4 for characteristics of the patients). PA levels of the upper (wrist) and lower extremities (ankle) were assessed using the biaxial GT1M accelerometer, attached by means of labeled elastic snug belts (see Figure II-2 (b)) and worn at the dominant side of the extremities over a period of 8.5 ± 3.1 days. The sensors were initialized to recorded PA in proprietary uniaxial *activity counts* mode, which is a post filtered quantification of the amplitude and frequency of the detected accelerations in time intervals of *1-minute epoch* [191]. Additionally, trunk movements were assessed by the piezoelectric triaxial RT3 accelerometer, worn in a holster at the non-dominant side of the waist, initialized for recordings in VMU mode, at similar epoch time (see Figure II-5). PA data from the first day and of any other day with a wearing time of the sensor set of <10 h was discarded. Only the interval from 6am to 10pm was included in the analysis.



(a) Ankle (GT1M) (b) Wrist (GT1M) & Hip (RT3)

Figure II-5. Accelerometer measurement positions in patients suffering from COPD

3.3. Position-dependent comparison of the PA output in the elderly

In order to explore if the sampling location is relevant, in another sedentary but healthy target group, two triaxial accelerometer outputs are compared as part of Objective II. PA levels from the body center (non-dominant side of the hip) and the lower limbs (ankle) were assessed by means of two GT3X accelerometers, in 190 elderly healthy subjects from the KORA-Age cohort during free daily living (see Table II.2 for the characteristics of subjects). PA was recorded up to 10 days, starting from the day at the study center at which the accelerometers were handed out to the cohort members, until the eleventh day, at which the subjects were instructed to return the devices (via reminder call). For this, a pre-stamped and pre-addressed enveloped was handed out to each participant during the study center visit, providing device specific information, contact data and the issued device return date. The ankle worn GT3X device was attached via elastic snug belts, similar to those used in the previous study (see Section 3.2). To ease the attachment of the hip worn GT3X accelerometer, and in order to provide a stable positioning, the device was embedded in the previously used RT3 holster (see Figure II-4 (a)), by attaching double-sided sticky tape on both, the back of the GT3X device and the front of the RT3 holster. To enable an easy replacement of holster or sensors, Velcro strips were bonded on top of the sticky tape, and after the device was initialized and embedded in the holster, another duct tape layer was applied to fasten the inserted GT3X accelerometer. All subjects were carefully instructed about how to position the devices, and they received a manual with clear instructions and illustrative figures. Both devices were initialized to register *Activity, Dual Axis, Three Axis*, and *Step Count*, at a *2-s* epoch time, in order to enable a recording of at least 11 days. By initializing more than a single axis, the VMU representation is automatically stored as well. In order to calculate the wear time an adjusted algorithm from Hecht and colleagues [248] has been applied on the cohort data, based on the triaxial VMU representation. By means of triaxial PA data, sedentary and non-worn periods are assumed to be better distinguishable compared to uniaxial recordings [249]. Calculations of PA variables were only carried for the identified wear time.

3.4. Comparison of relations between position-dependent PA data and clinical outcomes

Another aspect of Objective II, that address the question if the sampling location is of relevance, is examined based on a comparison of position depended correlations of PA data to medical outcomes. In order to explore if the accelerometer position had an effect on the relationship to clinical outcomes, associations between PA, functional capacity and a multivariate diseases staging score have been examined, based on the PA data introduced in section 3.2. Medical characteristics assessed at the start of the rehabilitation program include the airway obstruction expressed as forced expiratory volume in 1s in % predicted (FEV_1%pred.), lung function capacity as forced vital capacity in % predicted (FEV_1 %VC), self-rated breathlessness by the modified Medical Research Council dyspnea score (mMRC), the functional capacity as 6-Minute walk distance in meter (6MWD) and the multidimensional disease grading index called BODE (BMI, FEV_1%pred., mMRC, 6MWD) and can be found in Table II.4:

	All Patients (N=52)	**With Walker (N=21)**	**Without Walker (N=31)**	**p-value**
FEV_1%pred.	38.0 ± 11.8	38.5 ± 11.2	37.7 ± 12.4	Ns
FEV_1 %VC	44.9 ± 13.0	49.1 ± 16.2	41.9 ± 9.8	Ns
6MWD (m)	265.4 ± 93.7 (N = 37)	218.6 ± 85.2 (N = 19)	314.8 ± 76.6 (N = 18)	<0.01
Borg CR 10	5.2 ± 2.1 (N = 36)	5.8 ± 2.2 (N = 18)	4.6 ± 1.9 (N = 18)	Ns
MMRC	3.0 ± 1.0 (N = 40)	3.4 ± 0.8 (N = 20)	2.6 ± 1.1 (N = 20)	<0.05
BODE Score	6.2 ± 1.9 (N = 37)	6.7 ± 1.7 (N = 19)	5.6 ± 1.9 (N = 18)	Ns

Table II.4. Clinical outcomes of patients with COPD

3.5. Comparison of ankle and hip-based PA classification

In literature, the validity of the proprietary output of accelerometers has been explored in calibration studies against criterion measures of EE or oxygen consumption, in order to derive device specific count cutpoints, corresponding to light, moderate, and vigorous intensities [226]. Although these cutpoints were deduced in calibration studies predominantly for hip-worn accelerometers, few reports exist in which thresholds were defined for the wrist [116, 181, 204, 250] or the ankle [121]. As PA was measured in the KORA-Age cohort at ankle and hip sites, the time spent in different intensity levels was calculated for each position separately, using the thresholds proposed by Puyau and colleagues [121]. Furthermore, individualized thresholds were calculated by using quartiles, in order to classify the PA data "performance-based". The classification results between both positions and both methods were compared.

3.6. Comparison of uni- and triaxial intensity cutpoints and epoch effects for the time spent in MVPA

The lack of standardization in calibration studies lead to a considerable variability in the definition of cutpoints in younger populations, limiting the comparability between studies [117, 133, 226]. Older adults have been rarely included and elderly-specific cutpoints are widely lacking [108]. Using MVPA cutpoints similar to the one proposed by Freedson et al. [114] (i.e. $\geq$1952), only very little time was found to be spent in moderate and vigorous intensity levels in the aged [129, 251, 252], in contrary to the time spent sedentary [186, 253–256]. Therefore, this study explored if the MVPA threshold selection is meaningful in older adults. For this, the selection-effect of specific MVPA cutpoints was compared, based on KORA-Age cohort data acquired in the elderly. cutpoints from different Actigraph generations (i.e. uniaxial to triaxial) were included in the analysis as well as the MVPA classification according to the "performance-based" activity quartiles. As the PA data was acquired in 2s-epochs, while most cutpoints were developed based on 60s sampling intervals, the effect of the epoch on the estimated time in MVPA was investigated in addition.

3.7. Compliance with PA Guidelines

The implications of the selection of a cut-point are presented in this study. This is done by calculating the amount of KORA-Age individuals meeting the PA recommendations published by the AHA & ACSM for elderly subjects in 2007 [152]. For this analysis, the time spent in MVPA and vigorous PA levels is estimated and compared based on three selected cutpoints. As the PA guideline defines certain PA goals within the time frame of a week (i.e. the accumulation of 150 minutes of moderate activity or 75 minutes of vigorous intensity or a combination of both), only 101 of the 190 subjects with 7 consecutive, valid days have been included in the analysis. From this sample of 101 subjects, those meeting the PA guideline are compared to those who are not, in terms of their medical outcomes such as lung function and functional capacity.

4. Statistical Methods

In order to assess and compare the variability of different devices as part of Objective I (see Sections 3.1), descriptive statistics is used, including mean (μ), range, and standard deviation (SD [σ]). The reliability is assessed by means of the intraclass correlation coefficient (ICC) with a two-way random-effects model for absolute agreement, and the intra- and inter-instrument coefficient of variation *(CV)* in % [194]:

$$CV = (\frac{\sigma}{\mu}) \times 100 \tag{II.8}$$

or its inverse, the signal-to-noise ratio (SNR). As the amount of accelerometers to be tested is limited by financial means, an amount of five to ten devices per type is assumed to deliver reliable estimates for the assessment of the technical reliability. This number of sensors is in line with previous studies ranging from 6 Actigraph 7164 models [257], over 11 GT1M, 12 model 71256, and 13 model 7164 Actigraph accelerometers [194], to 15 RT3, Actical and Actigraph 7164 devices, which all have been tested by means of mechanical setups (i.e. mechanical shakers and rotating wheels) [258]. Half of the sensors were assumed to be sufficient to estimate the variability in the response to similar motions.

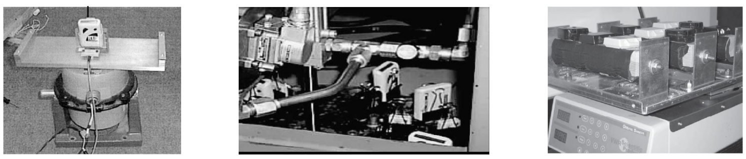
The distribution of all data from both field studies (see Sections 3.2, 3.3, Objective II) was assessed by descriptive statistics using histograms and by means of the Shapiro-Wilk test [259]. As the PA data was found to violate the assumption of a normal distribution, two-sided non-parametric tests were chosen to compare the PA data at a significance level of 0.05 in both studies. These tests include the Mann-Whitney-U-Test for comparisons of baseline characteristics between groups [260], and the Wilcoxon signed-rank test [261] for comparison of PA and PA patterns from different positions. For the description of quantitative data, descriptive statistics including median and IQR were used, and visually summarized by means of Box-Whisker-Plots [262]. Agreement between the different recording position was assessed with Bland-Altman plots [263], while associations between PA from different positions was examined using Spearman's rank correlation coefficient [264]. Associations between position-dependent PA data and medical outcomes (see Sections 3.4) were measured similarly, including 95% confidence interval (CI) based on 100.000 replicates, in a bootstrap approach [265]. To determine the relationship between PA measures at ankle, wrist and hip and the disease severity score (i.e. BODE) in the COPD patient sample, linear regression analysis was used including gender, and walker-use as variable. Due to the explorative nature of the COPD study, post-hoc power analysis was conducted, finding that 70 patients were needed to detect statistical significant association for weak correlations at a power of 80%. The PA data in the KORA-Age cohort was assessed for outliers using the outlier labeling rule with a selected *g*-parameter of 2.2 [266], and data from five identified subjects was trimmed. All analysis was carried out using PASW Statistics 18.0 and R software version $2.9.2$ [267].

Chapter III

Objective 1: Accelerometer Comparison

Contents

As reliability sets the limits on validity [258], an accurate objective measure of PA is required to quantify relationships with medical conditions (see Chapter II, Sections: 3.4), and to determine whether a population meets certain PA guidelines (see Section 3.7) [95, 125, 268, 269]. Variation in PA can be attributed to the recording device itself or the subject under monitoring. By reducing the device dependent measurement error, focus can shift to other sources of variation, namely the sampling location (see Sections 3.2, 3.3) or differences in PA over time by means of longitudinal studies [258, 269]. As the quality of information acquired is only as good as the devices recording it, quantification of accelerometer accuracy has been carried out using mechanical apparatus (see Figure III-1), or by means of subject-mounted setups during laboratory (e.g. treadmill protocols), or less controlled free-living assessments [194, 258]. In order to measure the intrinsic device variability, laboratory exanimations by means of a robotic arm were conducted in this thesis. Results concerning the reliability of different sensors with proprietary data output used in the field studies (see Section 3.1) were compared, and are presented in the following sections.



(a) Vibration table[1]   (b) Hydraulic shaker[2]   (c) Orbital shaker[3]

Figure III-1. Examples of mechanical apparatus for accelerometer reliability testing

1. Accelerometer Variability

The following results have been previously published in the proceedings of the XXIII International Conference of the European Federation for Medical Informatics [180].

Proprietary acceleration data was acquired from the RT3, GT1M and GT3X devices using a similar motion sequence at two different speeds (i.e. 10 and 25% of the maximal robot speed) with two iterations of the faster sequence and brief stops in-between. The motion sequences were programmed by means of the SP1 control pendant and executed via the TX90 robotic arm, which allows controlling the magnitude of the acceleration and the frequency of the movement. All accelerometers were initialized and started program-wise (Actigraph) or manually (Stayhealthy) before the motion sequences were executed (see Figure III-2).

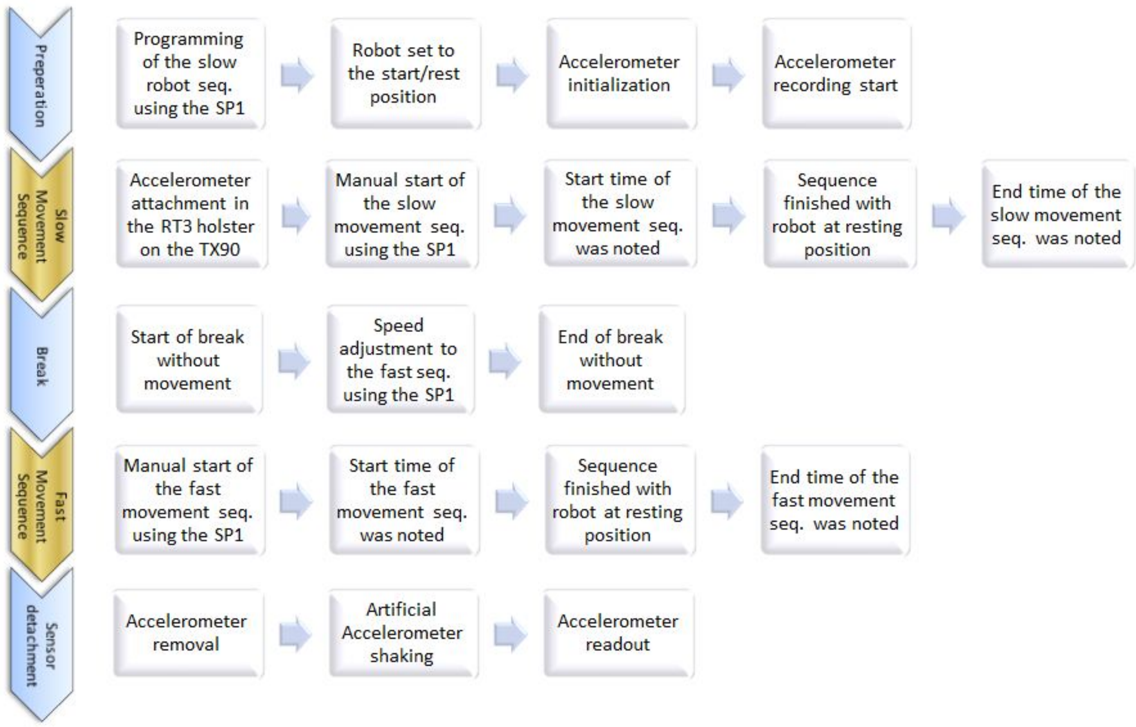


Figure III-2. Schematical measurement sequence

Acceleration data recorded prior to the data acquired during the robot movement sequences was discarded based on notes taken by two researchers, containing the measurement start information. Upon completion of the robot motion sequences, the stop time of the experiment was noted and sensors were shaken, to enable an identification of the measurement stop. During the post-processing steps, the first appearance of a non-zero value from the registered accelerometer data served as the beginning of the movement sequence.

[1]Image from Powell et al. [125]
[2]Image from Eslinger et al. [258]
[3]Image from Rothney et al. [194]

The last non zero value, recorded before reaching the high peaks created by detachment and artificial shaking process was used as the measurement stop.
However, both the manual adjustment of the robot speed and the manual start of the faster movement sequence caused a measurement break. The duration of this break varies in length for sensors. The break was used in a shortened form (i.e. the first and last second from the break time were cut away) for the assessment of the SNR, and elsewise discarded from the motion analysis (see Figure III-3).

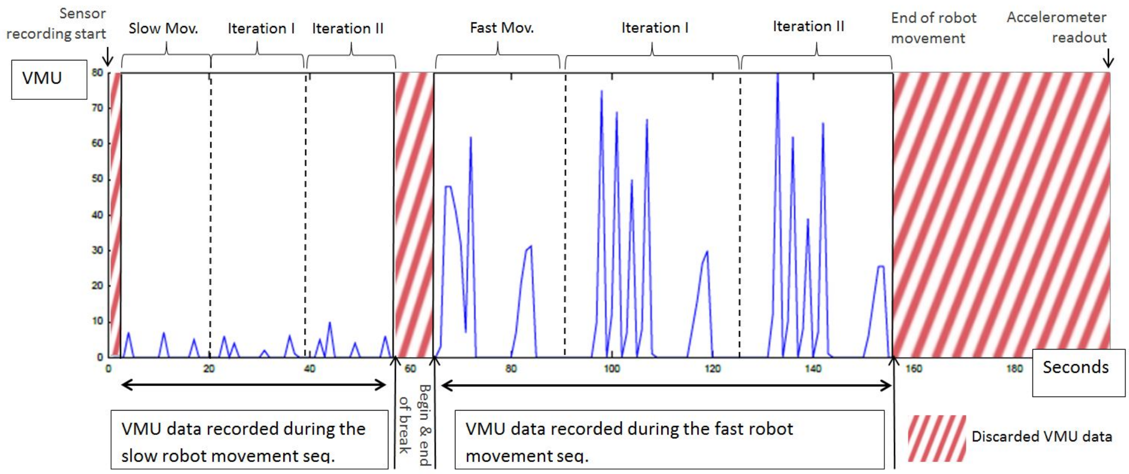


Figure III-3. Post-processing example based on data of a GT3X accelerometer

1.1. Results from descriptive statistics

After post-processing, an average of 132 VMU values (range 118 - 140) for the RT3, 134 for the GT1M and GT3X recordings (range 133 - 136) were available for analysis (see Table III.1) [180]. The RT3 accelerometers showed the lowest mean VMU counts (5.3 ± 6.8) and mean maximum (31.9 ± 6.3) compared to the GT1M (mean VMU: 7.1 ± 15.1, mean maximum 66.5 ± 8.9) and the GT3X (mean VMU 10.8 ± 18.7, mean maximum 71.8 ± 15.8) [180]. However, when the slow and faster movement sequences were analyzed separately, the RT3 VMU values (4.1 ± 0.9) were greater for the slow movement sequence compared to the GT1M (1.3 ± 0.2) and GT3X (2.8 ± 0.2), while still being smaller for the faster movement sequence (RT3: 6.0 ± 1.2; GT1M: 10.6 ± 0.3; GT3X: 15.5 ± 0.4). The range of the inter-device mean was greater for the RT3 VMU (4.1 - 6.8, difference: 2.7) than GT1M (6.9 - 7.4, difference: 0.5) and GT3X (10.3 - 12.0, difference: 1.7) for both the combined sequences [180] and when separated for the slow (RT3: 2.6 - 5.6, difference: 3.0; GT1M: 1.1 - 1.6, difference: 0.5; GT3X: 2.6 - 3.0, difference: 0.4) and faster movement sequences (RT3: 4.6 - 8.4, difference: 3.8; GT1M: 10.4 - 11.0, difference: 0.6; GT3X: 14.8 - 15.9, difference: 1.1, respectively).

Considerably difference in magnitude and codomains even remained between all three device types, when the VMU was calculted based two instead of three axes. For this comparison, the VMU from the vertical and the anteroposterior planes were analyzed. In a single-axis comparison, a very high agreement was found for the vertical axis of both Actigraph device types, but not for the anteroposterior plane.

Table III.1. Results from the Accelerometer Variability Experiments

Sensor type	Number of values during motion	Mean VMU ± SD during motion	Max. VMU during motion	Noise ± SD during seq. without motion (break)
I RT3	124	6.35 ± 6.95	27.39	2.88 ± 2.20
II RT3	140	6.81 ± 7.09	32.50	1.48 ± 4.61
III RT3	138	5.36 ± 6.59	31.40	2.68 ± 2.00
IV RT3	118	4.46 ± 6.78	37.00	SD <0.01
V RT3	136	5.93 ± 7.83	46.17	1.85 ± 3.20
VI RT3	137	4.73 ± 5.93	31.13	3.53 ± 1.34
VII RT3	129	4.12 ± 6.96	43.46	0.86 ± 4.80
VIII RT3	138	5.65 ± 7.61	29.77	1.90 ± 2.98
IX RT3	119	4.44 ± 6.39	29.00	1.91 ± 2.32
X RT3	139	4.87 ± 6.57	41.23	1.31 ± 3.71
XI RT3	130	5.65 ± 6.56	35.00	1.62 ± 3.48
I GT1M	135	7.14 ± 14.56	58.00	SD <0.01
II GT1M	134	7.13 ± 16.88	82.00	SD <0.01
III GT1M	133	6.85 ± 14.35	62.00	SD <0.01
IV GT1M	133	7.08 ± 14.71	73.00	SD <0.01
V GT1M	136	7.43 ± 14.95	57.58	SD <0.01
I GT3X	134	11.91 ± 18.76	75.00	SD <0.01
II GT3X	134	10.34 ± 17.47	67.00	SD <0.01
III GT3X	134	10.60 ± 18.86	78.00	SD <0.01
IV GT3X	134	10.91 ± 19.68	69.00	SD <0.01
V GT3X	134	10.97 ± 18.55	70.00	SD <0.01

The variation in the codomains and measured magnitude (i.e. counts or maxima / peaks) of accelerometers can be explained by the different technical components and the manufacturer dependent proprietary units. Therefore, comparison is carried out based on relative, and not absolute values. For this purpose, the dimensionless CV was used to compare the inter-device-variation as a percentage of the mean (i.e. the relative SD) for each device type: The RT3 devices had the lowest codomain, and its inter-device dispersion of the mean VMU was approximately six fold greater (15.4%) compared to the GT1M and GT3X accelerometers (2.6% and 2.4%, respectively). The speed separated inter-device CV of the RT3 devices was considerably greater for slow (22.0%) and faster movement sequences (19.1%) in comparison to the GT1M (12.0%, 2.8%) and the GT3X (5.7%, 2.5%, respectively). Moreover, the RT3 device showed the highest variability in their mean maxima values (18.0%), closely followed by the GT1M devices (16.0%) and the GT3X (6.3%). Similar results were acquired for the ICC, with the GT3X devices performing better than

GT1M and RT3.

Both Actigraph accelerometers types identified brief stops in-between motion sessions very precisely, so that the measured noise SD during the break was close to zero, leading to a very high SNR. 10 of 11 RT3 devices had a non-zero value for the noise standard deviation (± 2.8) and a very low average SNR was computed [180].

1.2. Results from visual comparison

In order to compare the variability of each device type, all acquired VMU data was plotted for visual comparison. In the ideal case, in which no noise is affecting the VMU output signal, data from all accelerometers, without (remarkable) inter-device-variability, would result in only a single plotted line of measured acceleration. However, for the given data, a certain spatial displacement is expected as the movement start, stop and break sequences had to be aligned manually among the different sensor datasets (see Figure III-3) [180]. Taking this into account, the shape and magnitude of peaks, although presumably not perfectly overlapping, should be recognizably similar. The plot is expected to contain high acceleration peaks as a result of the rotation or translation of the robotic arm, and gaps of acceleration values close to zero, during robot movements at an almost constant speed or periods with no movement between interactions for instance.

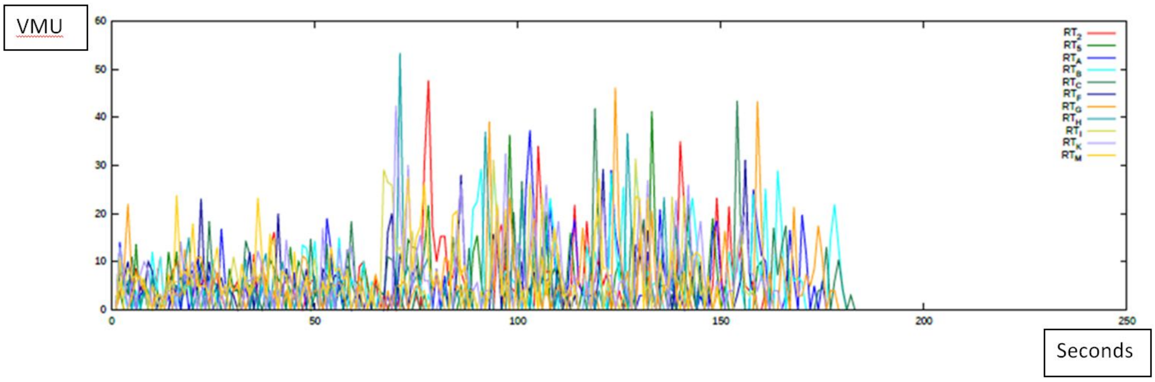
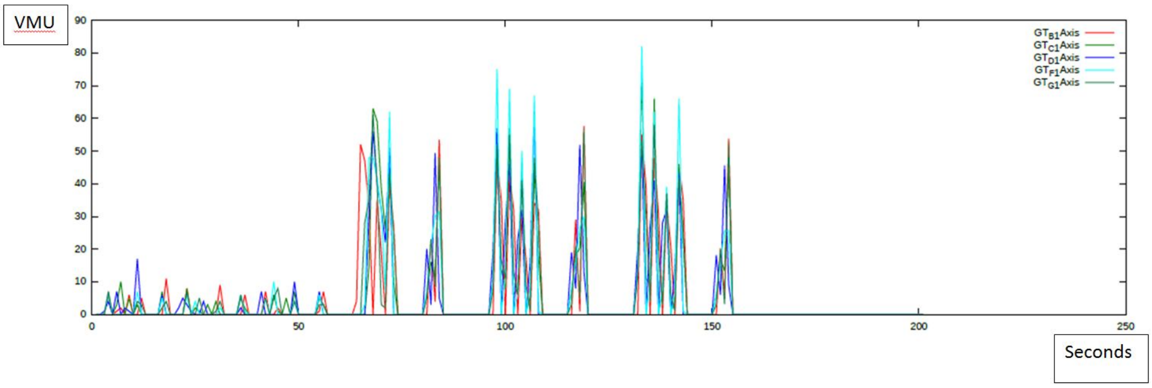


Figure III-4. Plot of all RT3 accelerometers with triaxial VMU data

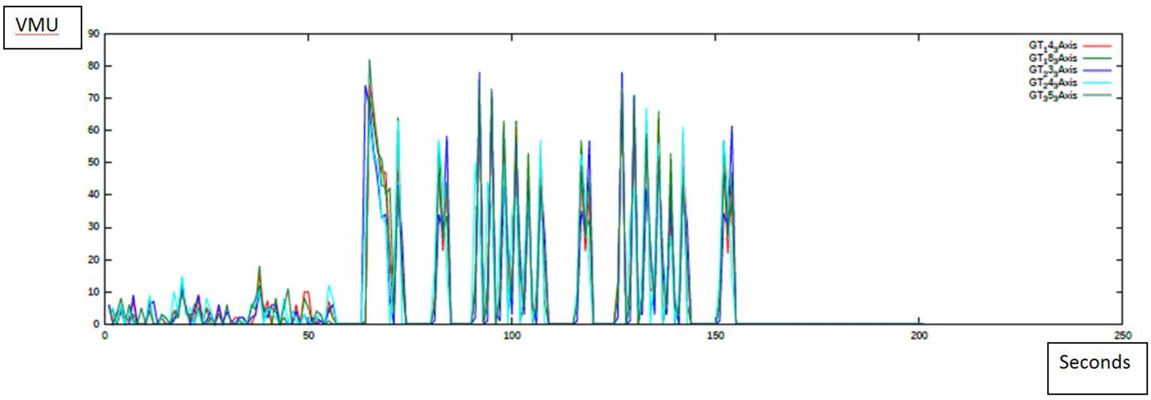
However, due to the very low SNR in all RT3 sensors, we expected a high variation between devices, as all except one device continuously recorded (at least) low accelerations during breaks and short episodes of no activity, which can be (partly) attributed as noise. Therefore, we did not expect to identify these breaks in the plot (see Figure III-4) [180]: No clear measurement line can be observed between all RT3 devices due to a high variation of the peak magnitudes and differences in the VMU values.

Unlike the RT3 devices, both Actigraph accelerometers types identified brief stops in-between motion sessions very precisely. As outlined by the descriptive statistics (CV), the inter-device variation was found to be lower, and the VMU data overlap to a higher extent. Peaks and gaps without movement can be identified more clearly in both, the GT1M and GT3X, especially for the faster movement sequence (see Figure III-5) [180]. As the GT1M devices measured movement in biaxial mode, triaxial VMU data from the GT3X is plotted separately.

Based on descriptive statistics and visual comparison, our results indicate that the RT3 accelerometers are less reliable compared to Actigraph devices, namely the GT1M and the GT3X, which was shown to have the best reliability [180]. Signals from the RT3 accelerometers appeared to be (stronger) affected by noise with higher inter-device variations. Although the RT3 devices had the smallest codomain, the average RT3 VMU values exceeded those of both Actigraph device types during slow motions. The variation for all device types was higher during the slower movement sequence.



(a) GT1M accelerometers with biaxial VMU data



(b) GT3X accelerometers with triaxial VMU data

Figure III-5. Plot of all the biaxial and triaxial Actigraph accelerometer

1.3. Discussion

In order to examine if the selection of a device type affects the reported results (see Research Question and Objective I in Section 7 of Chapter I), the proprietary acceleration output of three widely used device types was compared for similar motion sequences in this study (see Chapter II, Section 3.1).

Despite having used a similar output format (i.e. VMU), considerable differences were observed between count magnitudes and codomains of all device types in the mechanical setup, when data from $\geq$2 axes was compared. Moreover, output differences were present between both Actigraph generations. This result confirms that the reported VMU levels are affected by the chosen accelerometer type. The accelerometer responses to similar movements were found to be dependent on the in-build signal post-processing methods. Differences in the output between proprietary activity counts and pre- or post-filtered raw data, have very recently been reported by Chen and colleagues [270]. Therefore, knowledge of the applied device dependent internal algorithms is needed to enable a straight forward conversion between activity counts from different device types. However, this was outside the scope of this study. Whether the count output differences effect the derived intensity thresholds and the PA classifications [249], needs still to be examined.

In order to select the most reliable device type for the KORA-Age cohort study as part of Objective 1, the results from this accelerometer comparison study were analyzed and compared to published literature, concerning reports on the reliability of each tested device type (i.e. the RT3, the GT1M, and the GT3X accelerometers) in the next paragraphs.

RT3 reliability assessment using mechanical setups

The inter-device variability was measured by means of sinusoidal movements using mechanical setups in literature. As non-sinusoidal movements were used in this thesis, the comparability is limited. However, in line with previous publications, we found a high inter-monitor variability in the RT3 devices in general, and especially during the slower movement sequence.

Powell and colleagues assessed the inter-device CV in 23 RT3 devices unit-wise by means of a motorized vibration table (MVT) and sinusoidal vibrations along each sensitive axis in isolation at frequencies of 2.1, 5.1 and 10.2 Hz during test sessions of 8 minutes in length [125]. In agreement with our axis-combined VMU data, they found, based on 6 epoch values, that the inter-device CV for each separate axis decreased as frequency increased (2.1 Hz: 21.9 - 26.7%, 5.1 Hz: 6.3 - 9.0%, and 10.2 Hz: 4.2 - 7.2%). They observed similar results for the intra-instrument CV (2.1 - 56.2%, 0.3 - 2.5%, and 0.2 - 2.9% at 2.1, 5.1, and 10.2 Hz, respectively) [125]. Increasing the speed of the robot by 2.5% in our study reduced the triaxial inter-instrument CV in the 11 RT3 devices from 22.0% to 19.1%.

Krasnoff et al. assessed the reliability of 22 RT3 accelerometers using a shaker (i.e. laboratory agitator) in the antero-posterior and medio-lateral directions at speeds of 150 and 275 rounds per minute (rpm), which translates to approximately 2.5 and 4.6 Hz, during three 24-hour periods [271]. In agreement to results from Powell et al. and our study, Krasnoff and colleagues reported an inter-instrument CV range of 9.5% to 34.5% and an intra-device CV of <1.81% [271]. This data can be compared to the range assessed by means of the vibration table at 2.1 Hz ($\approx$ 126 rpm) and 5.1 Hz ($\approx$ 306 *rpm*) [125] (see Table III.2). Eslinger and colleagues were the first to simultaneously assess the reliability of 15 accelerometers of three different models (including the RT3 and the GT1M predecessor model 7164) using a hydraulic shaker table (HST) [258]: 6 different condition at accelerations of 0.5, 1 and 1.25 g including frequencies of 1.5, 2 and 2.5 Hz per test period of 7 minutes length were chosen. Accelerometer activity counts (VMU in case of the RT3 devices) were generated at *1-min* epoch length and 5 out of 7 values have been included in the analysis. Both, inter- and intra-device CV were reported to be remarkably greater for the RT3 (42.9% and 46.4%) than for the model 7164 (4.9% and 4.1%) [258]. By including smaller frequencies compared to the studies by Powell and Krasnoff et al., a greater CV resulted as expected. These results are in agreement to the speed-dependent inter-device variability we found in our study.

Table III.2. Overview of publications using mechanical setups for the assessment of the variability of the RT3 devices

Study	Protocol (Setup)	# Devices (Output)	Frequency (rpm)	Inter-unit CV	Intra-unit CV
Eslinger [258]	HST (multiple)	15 (VMU)	1.5 Hz (90) at 0.5 g	12.7%	13.2%
Eslinger [258]	HST (multiple)	15 (VMU)	2.0 Hz (120) at 0.5 g	94.8%	106.9%
Eslinger [258]	HST (multiple)	15 (VMU)	2.0 Hz (120) at 1 g	35.5%	38.9%
Powell [125]	MVT (unit-by-unit)	23 (x, y, z)	2.1 Hz (126)	27.7% - 21.9%	56.2% - 2.1%
Eslinger [258]	HST (multiple)	15 (VMU)	2.5 Hz (150) at 0.5 g	42.4%	43.2%
Eslinger [258]	HST (multiple)	15 (VMU)	2.5 Hz (150) at 1 g	35.3%	40.0%
Eslinger [258]	HST (multiple)	15 (VMU)	2.5 Hz (150) at 1.25 g	36.9%	36.2%
Krasnoff [271]	MVT	22 (VMU)	2.5 Hz (150)	34.5%	<1.81%
Krasnoff [271]	MVT	22 (VMU)	4.6 Hz (276)	9.5%	<1.81%
Powell [125]	MVT (unit-by-unit)	23 (x, y, z)	5.1 Hz (306)	9.0% - 6.3%	2.5% - 0.3%
Powell [125]	MVT (unit-by-unit)	23 (x, y, z)	10.2 Hz (606)	7.2% - 4.2%	2.9% - 0.2%

Results concerning the reliability of the model 7164 accelerometer using mechanical setups [93, 149, 194, 257, 269, 272, 273], subject-mounted examinations using laboratory treadmill and/or structured activity protocols [116, 120, 274–276], or direct uncontrolled field assessments [149, 239, 277], can be found elsewhere.

An excursion on the RT3 reliability based on subject-mounted setups using structured laboratory protocols and daily free-living assessments can be found in the Appendix (see Chapter A.1).

GT1M reliability assessment using mechanical setups

In line with reports in literature, a significant difference in the inter-monitor variability of the GT1M device was found between the slow and the faster movement sequence in this thesis:

Rothney and colleagues used a modified orbital shaker with a frequency range of 25 - 500 ($\pm$2) rpm ($\approx$ 0.4 - 8.3 Hz) and an adjustable radius ranging from 10.2 to 66.8 mm, for the comparison of three different Actigraph generations (13 model 7164, 12 model 71256, and 11 GT1M) [194]: They selected radii of 22.1, 35.1, 41.6, 46.6, and 60.4 mm at a constant frequency of 2.5 Hz (150 rpm) to produce sinusoidal accelerations at an epoch of *1-min* in length, during 6 minutes per radius setting and more than 3 minutes of breaks in-between.

For frequencies greater 40 rpm ($\approx$ 0.7 Hz) the inter-device CV of the GT1M accelerometers (<1%) was reported by the authors to be consistently lower as compared to both predecessors, but high for all generations at low frequencies (CV >20%). In line with their results, the mean CV of the GT1M units in this thesis, lies within the specified CV range, with an inter-device variability of 2.8% for the faster and 12.0% for the slower movement sequence.

In order to determine the dynamic range of all accelerometers, oscillations at 21 different frequencies, ranging from 25 to 250 *rpm* ($\approx$ 0.4 - 4.1 Hz) at a fixed radius of 46.6 mm were carried out by Rothney and colleagues. Although a similar curve shape was observed, which indicates that the weighting function did not change over device generations, the GT1M devices varied from the 7164 models at all frequencies except at 120 *rpm* (2 Hz), and by exceeding 160 rpm ($\approx$ 2.6 Hz), all Actigraph generations were significantly different from each other in their count response [194].

Rothney et al. found that the GT1M has a more rapidly increasing count response while requiring a larger acceleration to register nonzero activity resulting in a cross-over effect [194]. Compared to the combined predecessors, a statistical significant slope difference was detected for the GT1M [194].

Intra-monitor variability among all device generations was small (around 0.55%) for frequencies above >40 rpm) [194]. In agreement to our data, a smaller inter-device CV (2.8%) was measured during the faster movement, compared to the slower movement sequence (12.0%) [180]. The greater inter-device CV magnitude in our GT1M data can be explained by the inclusion of sinusoidal and non-sinusoidal movements (e.g. torsions), which likely increased the variation effects. Moreover, the assessment of biaxial accelerations represented in the VMU output, has likely contributed to a higher variation as well. Rothney and colleagues found an increase of device reliability with every new Actigraph generation, and this appears consistent regarding the GT3X. In our data, the GT3X had a twofold lower inter-device variability at slow and a three-fold lower CV at fast movements.

In another report, Corder and colleagues tested 25 model 7164 and 25 GT1M devices by means of a mechanical spinning apparatus before field application, in order to assess the accelerometer response for sinusoidal accelerations between $\pm$ 1 *g* at a frequency of 3 Hz [149]. They found significant differences regarding the mean *counts per minute (cpm)* between both device types. The GT1M was reported to have an 11% lower activity count (1138 $\pm$ 45 vs. 1281 $\pm$ 131 *cpm*) and a lower inter-device CV of 0.04, compared to the model 7164 (CV: 0.1, respectively) [149]. In our experiment, mean count output from the predecessors GT1M accelerometers was 34% lower compared to the GT3X devices, however, this difference can certainly be attributed to the assessment of the additional third axis in the GT3X [180].

An excursion on the GT1M reliability based on subject-mounted setups using structured laboratory protocols and daily free-living assessments can be found in the Appendix (see Chapter A.2)

GT3X reliability assessment using mechanical setups

In this thesis, the VMU output of the GT3X accelerometers showed a low mean variability between units for both motion sequences. In line with our results, Santos-Lozano and colleagues reported a low inter-unit CV for frequencies of 2.1 to 4.1 Hz (Y: 2.2 - 3.7%, X: 1.2 - 9.9%, Z: 1.5 - 9.2%) from 5 minute-by-minute count comparisons using a vertical shaker (vibration table) to generate axis dependent accelerations in 10 GT3X devices at an amplitude of 0.04 m [278]. Frequencies of 1.1 and 10.2 Hz were included to allow a reasonable simulation of repetitive human movements such as gait. In contrast to the low mean inter-device CV values at frequencies of 2.1 to 4.1 Hz, an extraordinary high mean between-unit variability was reported for the smallest and highest frequency for Y (201.8%, 67.3%), X (287.0%, 99.5%) and Z (149.4%, 52.6%, respectively) [278]. Similarly results were reported for the intra-device variability, with a high intra-unit CV at 10.2 Hz for the X axis (22.5%), and for the smallest and highest frequencies at Y (18.5%, 27.3%) and Z (11.5%, 8.6%) axes, and low intra-unit CV at frequencies of 2.1, 3.1 and 4.1 for Y (0.5 - 2.3%), X (0.2 - 4.9%), and Z (0.3 - 4.9%) axes [278].

As the mean inter-device variability of the GT3X was found to be twice as high for the slower movement in our study, we assume that a decrease of the robot speed would have resulted in even higher variations between GT3X units.

The authors discussed the slightly higher inter-unit CV observed in the GT3X at frequencies of 2.1 - 4.1 Hz compared to previously reported lower values for the model 7164 [257, 269, 273] and GT1M [194]. However, such a comparison is limited by different mechanical setups, measurement protocols (i.e. included amplitude and frequency ranges) and accelerometers. In a direct comparison of both device generations, as conducted in our study, the triaxial GT3X had a lower inter-unit variability, especially evident for the slower motion sequence (GT3X: 5.7%, GT1M 12.0%).

An excursion on the GT3X reliability based on subject-mounted setups using structured laboratory protocols can be found in the Appendix (see Chapter A.3)

In the following paragraphs, reports comparing the reliability of different device types using structured laboratory protocols and/or free-living assessments are discussed, as publications comparing differences in the reliability or the device output between accelerometer types using mechanical setups are widely lacking. Publications that compared different device types using structured laboratory protocols and/or free-living assessments were included in the discussion, given that all examined devices were used in the field studies to address Objective II and Objective III.

Comparison of the reliability of the RT3 and GT1M accelerometers in free-living

Very recently, Vanhelst et al. assessed the inter- and intra-device reliability in 15 healthy adults during free-living conditions by attaching 5 RT3 and 8 GT1M devices per person to their back, using an elastic belt [279]: They found the inter-monitor CV for the RT3 (12.6 - 35.5%) and the GT1M (3.0 - 10.5%) to decrease with increasing PA, while the variability was statistically lower for the GT1M devices. This agrees to our data from the mechanical setup: The CV decreased in all devices for the faster movement sequence. However, all RT3 devices showed a higher inter-unit CV compared to the GT1M accelerometers in both, the slow and faster movement sequences.

Comparison of the reliability of the GT1M and GT3X accelerometers from structured laboratory protocols

Sasaki and colleagues compared the axis-dependent inter-monitor variability by means of two different treadmill speeds for walking and two for running, in 32 subjects at 4.8, 6.4, 9.7 km/h and in 21 subjects at 12 km/h [240]. They reported a high agreement between the vertical axis counts from the GT1M and GT3X in agreement to previous reports [239, 274] and no significant differences at any of the 4 speeds were noted, in contrast to the antero-posterior axis counts, which had a poor agreement and significantly higher count output in the GT1M at 4.8, 9.7 and 12 km/h resulting in a count difference compared to the GT3X of 21%, 38% and 45%, respectively. The biaxial VMU counts of the GT1M from the experiment at 4.9, 9.7 and 12 km/h were significantly higher than those of the GT3X and due to the difference in the antero-posterior axis, only a moderate agreement was found [240]. Moreover, the triaxial VMU counts of the GT3X were reported to show the same trend than the biaxial [240].

Comparison of GT1M and GT3X accelerometers in free-living

The uniaxial vertical output of the GT1M and the GT3X was compared in 25 adults by Vanhelst and colleagues during a single day of free-living [280]. The authors suggested that both devices assess PA similarly, therefore, data from the GT1M and GT3X (in GT1M mode) is comparable in studies of PA patterns, and thus, is equal in the identification of time spent in MVPA [280].

Conclusion

In conclusion, the resulting proprietary count magnitudes and codomains were shown to be affected by the chosen device type in this accelerometer variability study. Therefore, the difference in accelerometer responses to similar motions might affect the reported PA levels in the field and presumably lead to differently derived cutpoints in calibration studies [249], and thus, to different estimates on subjects meeting the recommended levels of PA according to PA guidelines. Furthermore, the comparability of results acquired with different commercial sensors is limited, especially, when proprietary data representations are used. Comparability of results can be enabled through conversion factor between different device types. However, a translation of counts between different devices requires knowledge of the in-build signal processing algorithms, or extended study protocols with a wide range of different amplitude and frequency settings for an approximation. To ease the development of conversion factors, raw data measurement should be used in future studies.

Concerning the device reliability: Both Actigraph devices had a lower inter-unit CV with the GT3X performing best, compared to the GT1M and the RT3. All tested accelerometers were found to have a higher inter-unit variability at the slower motion sequence. This finding is in agreement with current literature in which a poor reliability for frequencies below approximately <1 *Hz (60 rpm)* was stated. However, in multiple studies, the Actigraph devices were shown to have a high reliability in the range of human motions, at intensities of light to vigorous PA. This is important as accelerometers are more often used for the quantification of the time spent in MVPA, and to estimate the compliance with PA guidelines.

Due to the high between-unit variability in certain device types such as the RT3, or during slow motions, each subject should use the same device in longitudinal studies at each assessment [271] and instruments should be tested for their technical reliability before use in order to identify and exclude outlying devices [125].

1.4. Innovation and limitations

This is the first study to assess the variability of motion sensor by means of a robotic arm. Previous studies have either used mechanical shaker devices, which applied vibrations in different directions to accelerometers, (rotating) tables or wheel-chair setups, in order to generate sinusoidal movements. However, no previously used system allowed freely programmable movements in six degrees of freedom at a wide range of different speeds at a very high movement repeatability. Using the robotic arm, it was feasible to assess the variability of different accelerometers. Moreover, this is the first technical study to examine the reliability of the GT3X accelerometer and compare its performance to the predecessor, the GT1M, and the widely used RT3. To the knowledge of the author, only a single other study [258] compared the reliability of accelerometers from different manufacturers using a mechanical setup. Except for the comparison of different accelerometer generations, the comparison of different accelerometer types from different manufacturers is widely lacking. Results from such studies are essential in the development of translation equations between different sensor types. This is important to enable a comparison between studies using different devices. Currently, the comparison of PA data acquired by means of different accelerometers is limited, e.g. in two large national cohorts (NHANES (7164) and the Canadian Health Measurement Survey (Actical)). A recently published study by Straker et al. attempted to enable a translation and comparison of recorded minute by minute ActiGraph GT3X and Actical accelerometer outputs based on field data [281]. Another novel aspect of the works in this thesis is the high resolution of 1 second epoch length in VMU mode. Previous publications have mostly used the more common 60 seconds epoch to compare the reliability of the sensor output.

The presented study has a couple of limitations. The robot arm was mounted on a steel table and thus, especially during the faster motion sequence, movements of the robot arm are likely to have caused vibrations of the table, which have not been assessed and might have decreased the accelerometer accuracy [180]. As the robot defines its maximal speed joint dependent, the corresponding frequency of the movements was not stated, limiting the comparison of our results to published literature. Another limitation is the small number of devices added in the study and the small amount of different measurement conditions (i.e. 2 movement types, 2 speeds only), due to which no results concerning the intra-device variability have been reported. Although we were cautious to firmly attach all accelerometers in the holster, potential movements of (especially the Actigraph) devices cannot be fully excluded. Acquired results might be affected by the unit-by-unit examinations, as the devices were not tested simultaneously. Unfortunately, in this initial experiment we missed to real-time record the movement sequences from the robot data interface, which, together with the measurement of table vibrations, could have served as gold standard [180]. The RT3 devices were started manually, and the break in-between the slow and the fast movement sequence varied in length in all devices, requiring a synchronization and data cutting in the post-processing step, which might not have been absolutely exact. Last not least, the signal-noise-ratio was computed from no-motion intervals with varying length and based on very small data set.

Chapter IV

Objective 2: Accelerometer Positioning

Contents

After having providing guidance on the sensor selection by comparing the device reliability with focus on slow motions in the previous chapter, this chapter explores differences in objective PA data simultaneously measured at different recording positions in two study groups: patients suffering from COPD (see Chapter II, Section 3.2) and healthy elderly subjects (see Chapter II, Section 3.3). Apart from the direct comparison of the position-based activity counts in both study samples, in COPD, the position dependent correlations with a measure of functional capacity are explored as well as the "best" sampling location to reflect the disease severity; while in the healthy elderly subjects, results of the intensity-based PA classification from ankle and hip recordings are compared.

1. Recording position comparison (COPD)

The following results, figures, descriptions, and discussions (with the exception of "Agreement between recordings" (including Figures IV-2, IV-3, B-1 and B-2) and the paragrah outlining the strengths of this COPD study) have been previously published as a journal article by Gorzelniak et al., "Comparison of Recording Positions of Physical Activity in Patients with Severe COPD Undergoing LTOT" [223].

This section is divided into results regarding the usability of the applied sensors, results concerning the quantification, classification and comparison of the acquired PA data, and the relationship between PA assessments and functional capacity, and the discussion and conclusion.

Results on the usability and reliability

Four patients stopped wearing the devices at the first day of assessment, three did not wear all sensors. Twelve of the GT1M devices failed due to unexplained technical problems, accounting for a total of 57 days of data loss (6%). The RT3 device failed twice, 16 days of data were lost (1%).

The PA data was normally distributed except for the ankle and hip data of the walker patients. Patients with and without walker were comparable regarding their lung function, sex, BMI and Borg score assessed at the beginning and end of the PR program, and their BODE score. There were statistically significant differences regarding age, MMRC score and 6MWD at both assessments. COPD patients with walking aid were older compared to those without a walker. They rated their dyspnea as more severe in terms of MMRC and achieved a lower 6MWD (see Tables II.1, II.4).

1.1. Results from position-dependent PA comparisons

Data from 52 patients with COPD were evaluated including activity monitoring at ankle, wrist and hip over a period of 8.5 ± 3.1 days. Median data for activity and attachment position are shown in Table IV.1. The mean PA values recorded simultaneously were lower in COPD patients with walkers who had a higher BODE score.

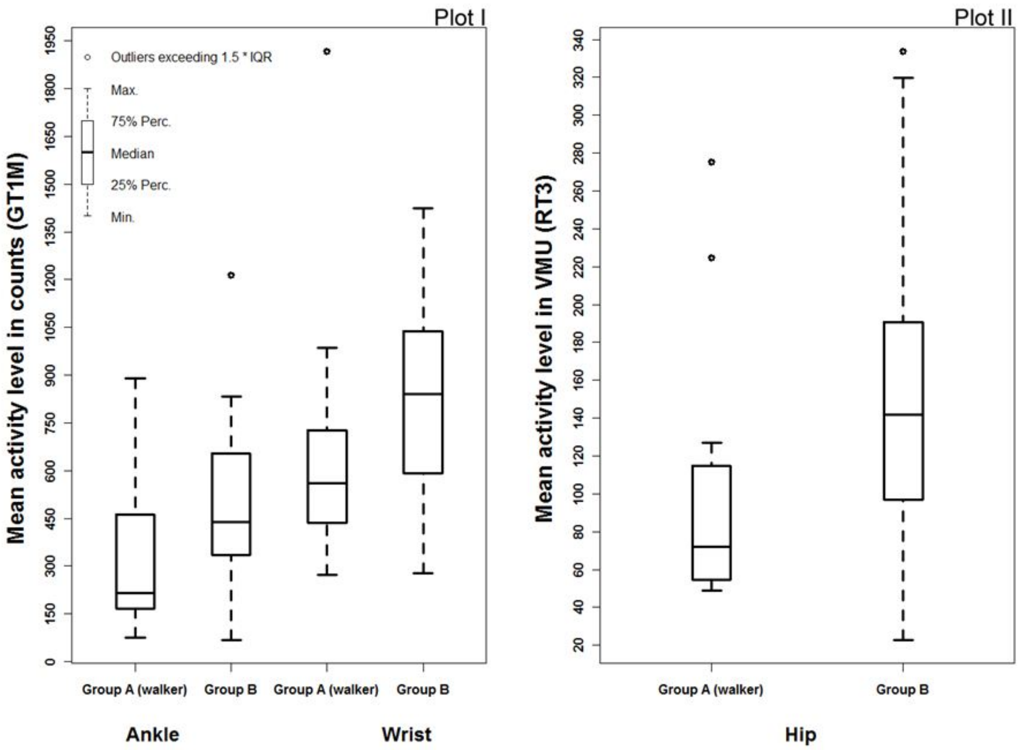


Figure IV-1. Box plots of the mean physical activity for the entire measurement period assessed at ankle and wrist (I) and hip (II) in patients with (group A) and without (group B) walkers

Among both groups, the amount of activity measured by the accelerometers was largest for the wrist and lowest for the hip recording (see Figure IV-1). Compared to the ankle, the wrist recordings were on average 2.6-fold greater in walker patients, and 1.9-fold in subjects without walker, respectively.

Table IV.1. Measurements of activity obtained by the GT1M (wrist, ankle) and the RT3 (hip) in patients with and without walker

	Group A: (Walker) **Median (N)** **Interquartile range**	**Group B: (Non-Walker)** **Median (N)** **Interquartile range**
Ankle activity counts	215.6 (19) 145.7 to 523.0	438.1 (31) 333.1 to 655.3
Wrist activity counts	561.4 (20) 431.2 to 733.8	834.0 (31) 588.9 to 1062.9
Hip activity VMU	72.0 (20) 53.9 to 116.9	141.9 (28) 96.2 to 192.6

We observed statistically significant moderate associations between wrist and ankle and wrist and hip PA data in walker-free patients (see Table IV.2). There was a moderate to strong correlation between the hip VMU score recorded by the RT3 and the ankle activity score from the GT1M in both patient groups.

Table IV.2. Correlations between activity data from different monitor positions in patients with and without walker

	Group A: (Walker) **Spearman's rank coefficient r (N)** **95% CI (P-value)**	**Group B: (Non-Walker)** **Spearman's rank coefficient r (N)** **95% CI (P-value)**
Ankle/Wrist activity	r = 0.13 (18) CI -0.42 to 0.60 (p=0.63)	r = 0.49 (31) CI 0.13 to 0.76 (p<0.01)
Ankle/Hip activity	r = 0.73 (19) CI 0.32 to 0.92 (p<0.01)	r = 0.65 (28) CI 0.38 to 0.81 (p<0.01)
Wrist/Hip activity	r = 0.33 (19) CI -0.22 to 0.73 (p=0.17)	r = 0.44 (28) CI 0.03 to 0.75 (p<0.05)

Agreement between recordings

The agreement between different recording positions was assessed by means of Bland-Altman plots, in which two different recording positions are compared in a pairwise manner, using the average of the PA data acquired at both locations on the x-scale, and their difference on the y-scale [263]: In each plot, the mean difference (*bias*) is displayed together with the 95% limits of agreement, an integral, in which 95% of the differences are expected to lie, estimated by the bias $\pm$ 1.96 $\times$ SD. If the acquired objective PA data from both positions is similar, all point would lie on the line of equality (zero-line), with a bias of 0 [263].

Additionally, the 95% CI of mean of differences is stated.

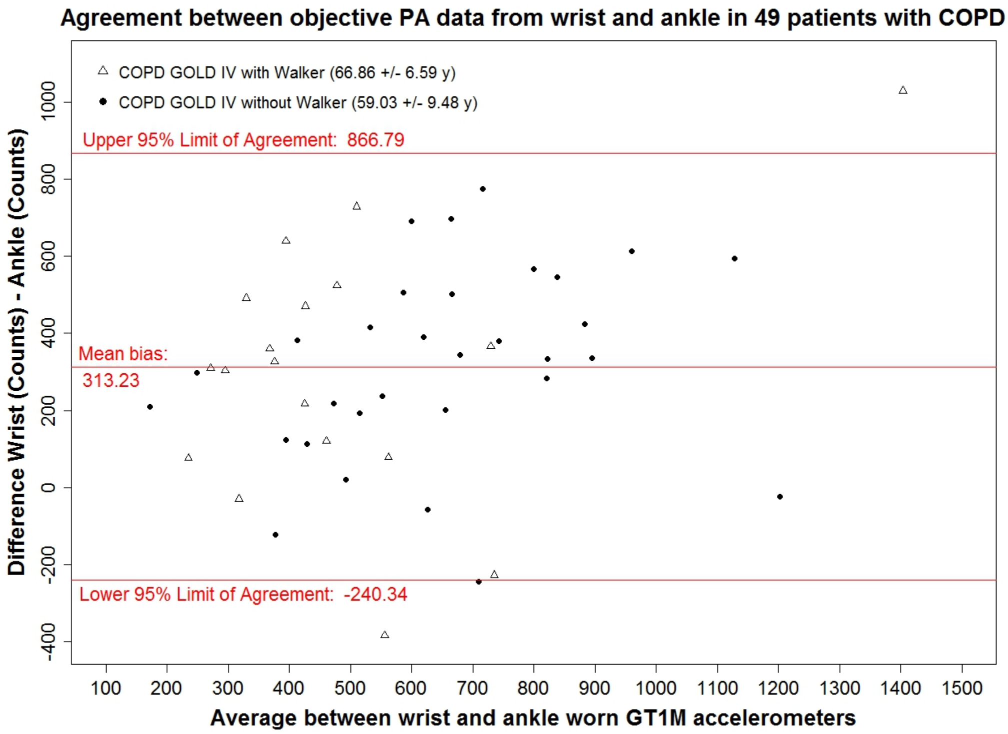


Figure IV-2. Bland-Altman plot comparing uniaxial mean wrist and ankle measurements

In total, data from 49 subjects was included in the comparison between objective mean PA data from the GT1M accelerometer, measured at ankle and wrist, except for three subjects, in whom one of both recordings was lacking. The calculated average discrepancy of methods was 313.23 counts (i.e. the bias), with the following limits of agreement: -240.34 and 866.79 counts. This result indicates that in 95% of the cases, the mean difference lies within these limits, with wrist activity being on average, but not always, higher compared to the ankle. The required count difference to reach clinical significance has not been established yet. However, the discrepancy between both measure of above 300 counts seems rather large and thus, the methods tend to produce different results, given the bias and the calculated 95% CI of mean of differences from 234.15 to 392.31, which is clearly above the line of equality. The distribution of data points shows no trend with increasing averages and a constant variability across the graph can be observed (see Figure IV-2).

For the comparison of the mean wrist uniaxial activity counts and the hip triaxial VMU data, 47 subjects were included in whom both measurements were available. The resulting discrepancy between those two device positions was 607.95 units, with limits of agreement of 54.73 to 1161.17 and a 95% confidence interval of the mean of difference from 527.25 to 688.64 units. This shows a significant systematic difference, as the line of equality is not in the 95% CI and all plotted values are clearly above the line of equality (see Figure IV-3). The difference between both methods tends to get larger as the averages increase.

Wrist activity rises proportionally higher compared to the hip recordings (i.e. proportional error), while the variability seems to remains constant. However, heteroscedasticity was identified by positive correlations between the absolute difference and the average of the two measures (r= 0.90, p<0.01). Therefore, the natural logarithm was applied on the wrist and hip PA (see Appendix B-1). To which extend the higher bias can be attributed to the triaxial recording of the hip remains questionable.

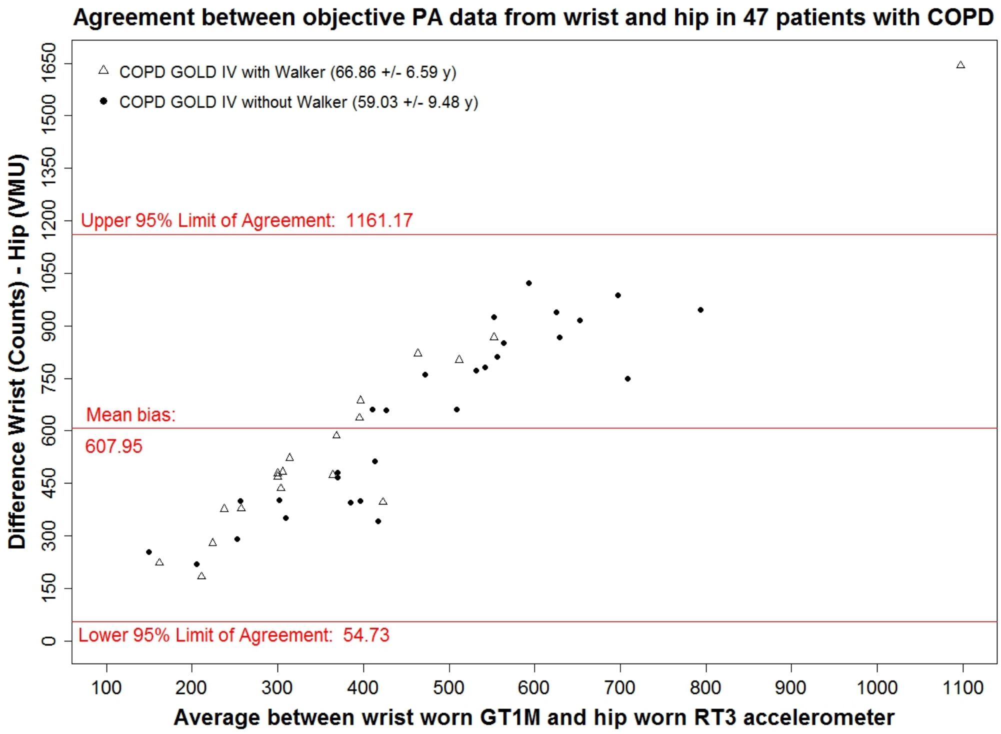


Figure IV-3. Bland-Altman plot comparing uniaxial mean wrist and triaxial mean hip measurements

In the last agreement of recordings the uniaxial ankle and triaxial VMU hip data was compared in 47 subjects. From this analysis an average bias of 302.89 units was calculated between both methods, with 95% limits of agreement ranging from -103.06 to 708.85, and the 95% confidence interval of the mean of difference spanning from 243.48 to 362.11 units. Comparable to the aforementioned difference between wrist and hip recordings, a proportional error was observed as the difference between both methods increased with a higher average. However, the bias in this comparison is only approximately about half as large.

1.2. Results from position-dependent associations between PA and medical outcomes

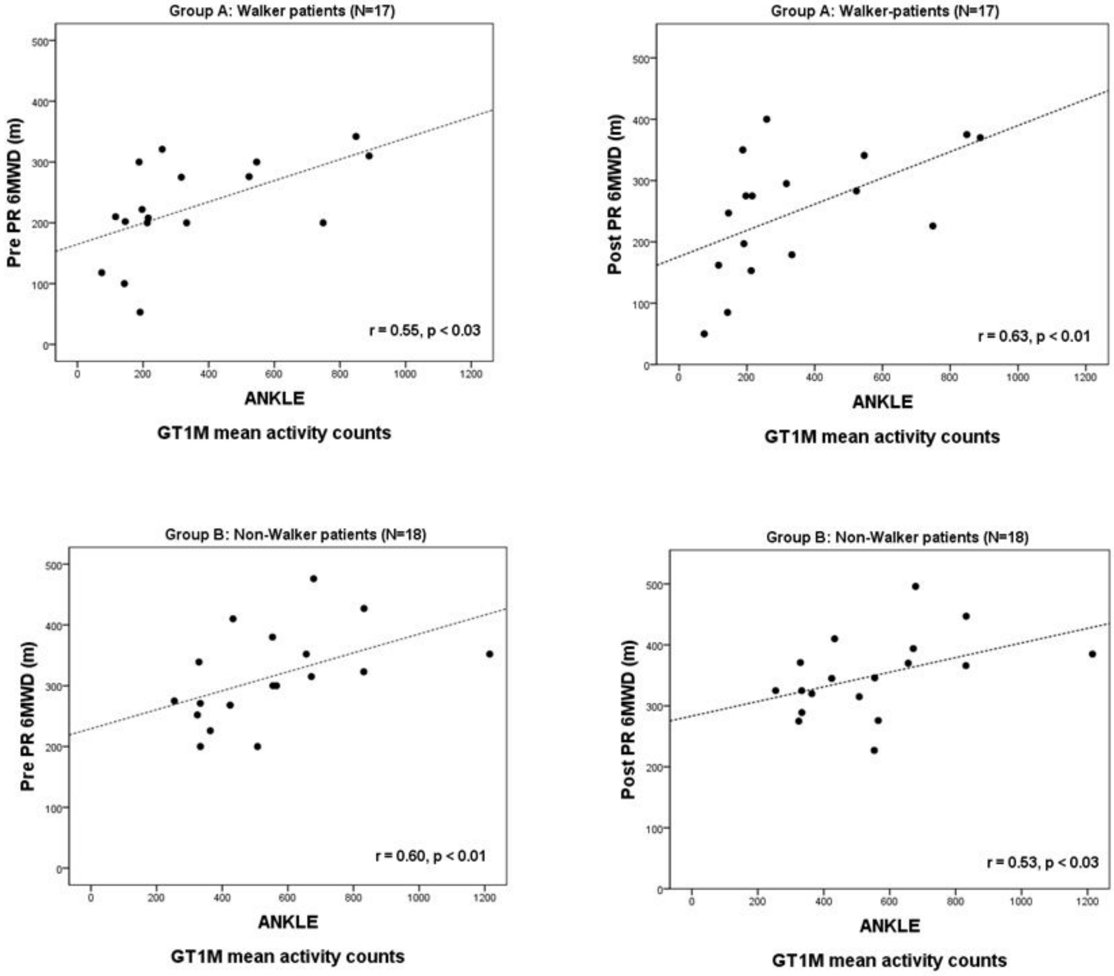


Figure IV-4. Relationship between the mean PA values assessed at the ankle and the 6MWD assessed at the beginning and end of the PR program in both patient groups

The relationships between daily mean physical activity data from hip, ankle and wrist and the 6MWD at the start and at the end of the PR were examined in both groups separately (Figure IV-4). In this analysis, statistically significant positive associations were observed only for mean ankle activity counts and both 6MWD examinations. Mean ankle PA data was moderately related to the 6MWD assessed at the start of PR in COPD patients with ($r = 0.55$, $p<0.05$) and without walkers ($r = 0.60$, $p<0.01$) and to the 6MWD assessed at the end of PR ($r = 0.63$, $p<0.01$; $r = 0.53$, $p<0.05$, respectively). Wrist and hip activity measurements were not significantly associated with the 6MWD. In order to assess the individual contribution of ankle, wrist and hip recordings on disease severity as the dependent variable, a multivariate regression model was used including group (walker vs. non-walker) and gender information as independent variables (adjusted R^2 = 0.406, p<0.01; Table IV.3).

	Unstand.Coeff.		Stand. Coeff.	t	Sig.	Correlations			Explained Variance
	B	Std. Error	Beta			Zero-order	Partial	Part	
Bode	9.24	0.97		9.51	<0.01				
Hip	0.01	0.01	0.30	1.24	=0.28	-0.46	0.24	0.17	3%
Ankle	-0.01	0.00	-0.65	-2.88	<0.01	-0.64	-0.50	-0.41	16%
Wrist	-0.01	0.00	-0.36	-2.02	=0.05	-0.52	-0.37	-0.28	8%
Gender	-0.79	0.62	-0.20	-1.26	=0.22	-0.24	-0.25	-0.18	3%
Group	0.04	0.60	0.01	0.07	=0.94	-0.27	0.02	0.01	0%

Table IV.3. Standard multivariate regression model to assess the impact of all simultaneously measures PA positions, group and gender on the disease severity as described by the BODE score

The model revealed that only ankle activity was significantly associated with the BODE score (p<0.01), explaining 16% of the variation. Hip PA only explained 3% (p=0.227), wrist recordings 8% (p=0.054) of the variation in the model.

1.3. Discussion

In order to examine if the placement of a device affects the reported PA results (see Research Question and Objective II in Section 7 of Chapter I), the difference in the position-based accelerometer output from simultaneously acquired PA data at ankle, wrist and hip sites, and its effect on the association between PA and medical outcomes were examined in this study (see Chapter II, Sections 3.2 and 3.4).

Motion sensors can be attached at different positions, but recordings at one location of the body might not be representative for overall activity [221, 224]. It remains unclear whether the sampling location affects the relationship to clinical data. Our study aimed at clarifying this issue. We therefore examined the associations between objective data gathered at different body positions and assessed their relationship to the 6MWD and disease severity in in-clinic patients suffering from COPD and undergoing LTOT.

Recently, Casaburi et al. [282] assessed PA patterns of LTOT patients similar to the present study, but detected no difference in PA. To our knowledge, no previous study simultaneously assessed upper, lower and trunk activity by means of three accelerometers in COPD during an in-patient rehabilitation setting.

Louvaris et al. [283, 284], in a short report, compared the output of 6 different sensors in patients with COPD, also with different body locations, but only assessing correlations among sensor models, not considering location as a possible influence. They found that if similar constructs are assessed by different sensors the outcome is moderately correlated. Although using different body locations in our study, moderate correlations between activity counts acquired at ankle and wrist (GT1M), and hip-measured VMU (RT3) were only found in patients without walker (0.44<r <0.65, p<0.05).

With increasing limitation of mobility, especially in patients using a walker, the activities of ankle and wrist appeared to become less associated. In line with the results reported by Walker et al. [221] we found a good agreement between data from the uniaxial ankle (Actigraph) and triaxial hip worn accelerometer (Stayhealthy) in patients.

Lower limb activity is the key determinant of whole body activity [285], but our results also indicate that patients were limited in their arm movements, although to a lesser extent compared to leg and hip. Wrist accelerometry has recently been shown to be a valid and sensitive instrument to measure upper-extremity movement during PR [286] and is responsive to differences between days. Ankle and wrist assessments are lacking complete agreement with the hip sensor in our study and cannot be fully substituted when determining whole body energy expenditure [221, 224].

We observed a moderate to strong association between 6MWD and the mean ankle activity data. This was not found for the hip or wrist recording. Although the 6MWD is related to mortality and morbidity in COPD and can indicate changes in the functional exercise capacity [287], it does not necessarily track daily activities, at least not under the setting of PR and in the presence of heterogeneous handicaps. Daily activity is certainly not only determined by exercise capacity but also highly influenced by habits, modulated by psychosocial and environmental factors particularly in a rehabilitation setting.

Conclusion

The findings in this study support the notion that the placement of the motion sensor affects the reported PA outcomes. Apart from position-based differences in the count magnitude, particularly different results were observed for the association of activity recordings and the 6MWD. This is underlined by the finding that association between disease severity and PA were only present for the assessment at the ankle. PA is probably an important outcome measure for PR, and, compared to self-reported information, quantitative PA data is better suited for the analysis of quantitative relationships. Currently, only few devices have been validated in COPD and data comparison among devices is hampered by manufacturer-depended peculiarities. Nevertheless, accelerometry in principle can track changes in PA before and after PR programs, even in slow walking patients [288, 289].

1.4. Innovation and limitations

This is the first study to assess PA simultaneously at hip, ankle and wrist in patients suffering from COPD. As PA is predominantly acquired and reported by means of a single motion sensor, attached at a single, but varying position between studies in literature, the position-wise comparison of difference in the amount of PA at multiple locations and the assessment of its influence on medical outcomes, is a strength of this study.

Although a single report compared objective PA data from similar positions, data was acquired in healthy adults during a treadmill protocol, without exploration of the location-wise effect on medical conditions [49].

Moreover, in literature, only very little (subjective) PA information is available in very severe patients with COPD, and especially for those undergoing oxygen therapy. Patients with walking aids have been generally excluded from motion sensor studies, therefore no data on their activity levels was present in literature. Including this group of patients is a strength of this study.

Lastly, there is a lack of PA data for patients undergoing in-patient rehabilitation settings.

The presented study has a couple of limitations. Using two different types of accelerometers at different locations limits the comparability as different sensor models are having different responses to similar activities. The presented results might therefore not only reflect the influence of the body placement but also include differences between the accelerometers (i.e. accuracy, sensitivity) themselves. However, in a very recent report from Vanhelst et al. [290] no significant difference between the output of GT1M and RT3 sensors was found in a group of adolescents when both devices were worn at the same location.

Given the inpatient PR setting of this study, the results might differ from those acquired in free-living, because the training sessions recorded by the accelerometers have also been included in the analysis, and therefore they probably do not reflect what a patient does normally in daily living.

Furthermore, self-exercises and training sessions were individualized and for this reason may differ in intensity and amount in these severely ill patients. Nevertheless, the overall time of prescribed therapy for each group was nearly the same. The higher age and frailty in patients with a walker might have been a confounding factor in activity decline. Despite these limitations, our results underline the importance of sensor position for accelerometry in COPD patients. In patients with very severe COPD, recording at the ankle seems to best reflect the clinical state of the patients.

2. Recording position comparison (KORA-Age)

In this section, the results from the KORA-Age study are presented and discussed. Following a short summary of the accelerometer usability in the elderly, the objective PA data from ankle and hip positions and the position-dependent estimated time corresponding to sedentary, light, moderate and vigorous intensities, are compared in this section.

Results on the usability and reliability

Accelerometer errors occurred in 13 out of 380 measurements (3%), mostly due to a sudden recording stop in relation to a fully (N=5) or strongly (N=6) drained battery. This error appeared in combination with continuously recorded zero values, in two cases. In a single case, a runtime error was present and the data file was corrupted. In another case, zero values were continuously recorded without a premature stop. All errors occurred in a total of 9 subjects. However, in 5 cases, the cohort members agreed to repeat the measurement after the sensors were resent to their home (see Figure IV-5).

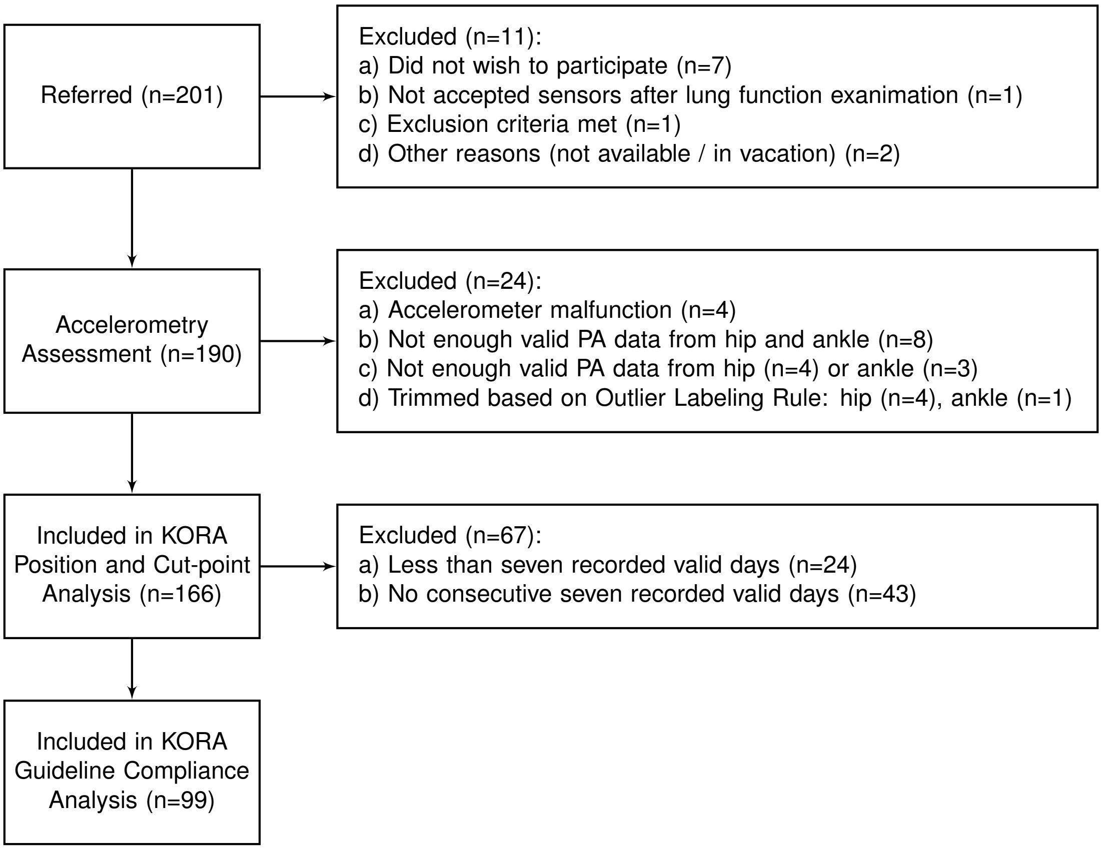


Figure IV-5. Consort chart of included subjects for the analysis

Of initially 190 measured subjects, 171 individuals had four or more valid hip and ankle recordings with a sensor wear time of at least ten hours at 2s epochs as well as at 60s, when the PA data was re-integrated. Five subjects were identified as outliers according to the outlier labeling rule with a specified g of 2.2 [266], and thus, discarded from the analysis (see Figure IV-5). The remaining data from N = 166 elderly subjects entered the analysis, consisting of 1343 valid measurement days per location (i.e. ankle and hip), of which 401 were acquired during weekend days.

2.1. Results from position-dependent PA comparisons

In order to explore the difference between lower and total limb activity, the accelerometer output of the ankle and hip-worn devices, acquired in 166 older adults, are compared based on the mean VMU activity scores at 2s and 60s epochs using descriptive statistics and the Wilcoxon signed-rank test, as well as correlation analysis. The distribution of variables from ankle and hip PA data were assessed by means of descriptive statistics and the Shapiro-Wilk test. Due to the non-parametric distribution of the data at both sampling intervals, median and IQR are reported instead of mean and standard deviation, and Spearman's rank correlation coefficient, as well as the Wilcoxon signed rank test are applied in order to compare the PA data from both positions.

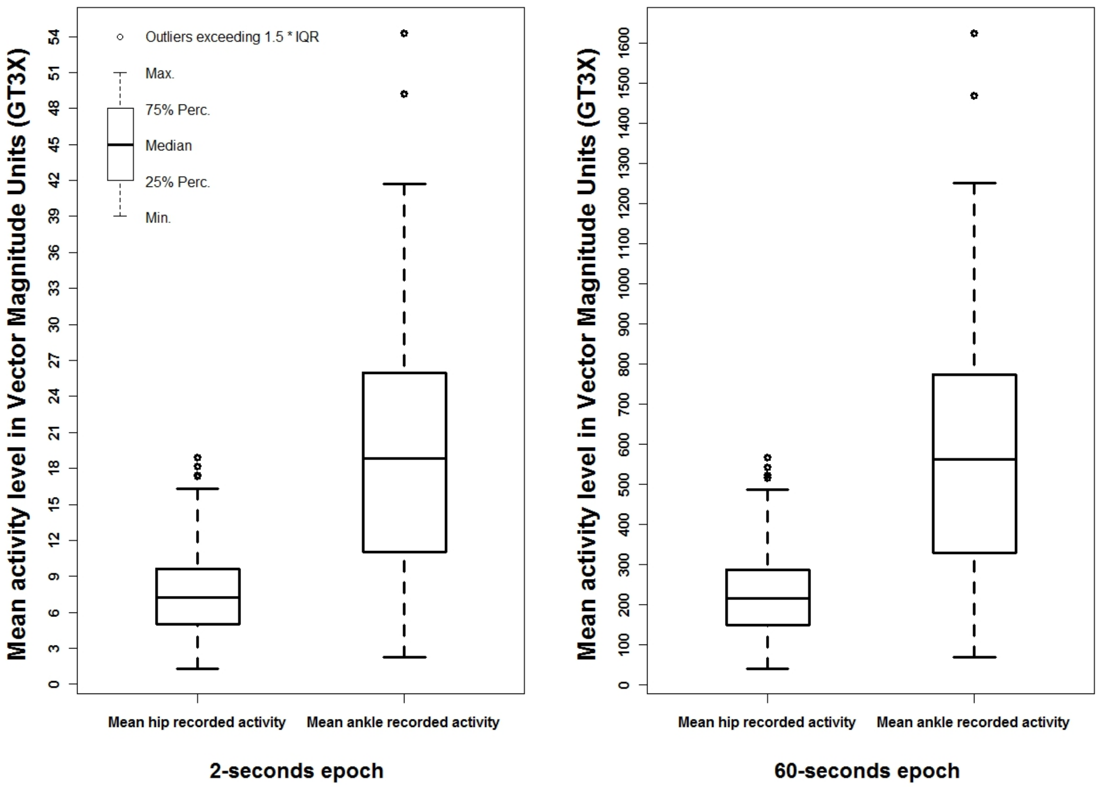


Figure IV-6. Box plots of the mean physical activity for the entire measurement period assessed at ankle and wrist sites in healthy elderly cohort members

On average, each individual engaged in 7.21 counts/2s (IQR: 4.62) during the time the sensor was estimated to be worn for the hip, and 18.84 counts/2s (IQR: 15.00) for the ankle assessment, respectively. The calculated average activity counts for the 60s-epoch were 215.56 counts/min (IQR: 137.38) for the hip and 562.01 counts/min (IQR: 446.62) for the ankle (see Figure IV-6). The difference between ankle and hip recordings was statistically significant for both sampling intervals ($p<0.01$). The median count magnitude was approximately 2.6-fold greater for the ankle recordings compared to the hip measurements based on both epochs. Correlation analysis revealed strong association between activity counts of both recording positions at 2s ($r=0.755$, $p<0.01$) and 60s sampling intervals ($r=0.756$, $p<0.01$).

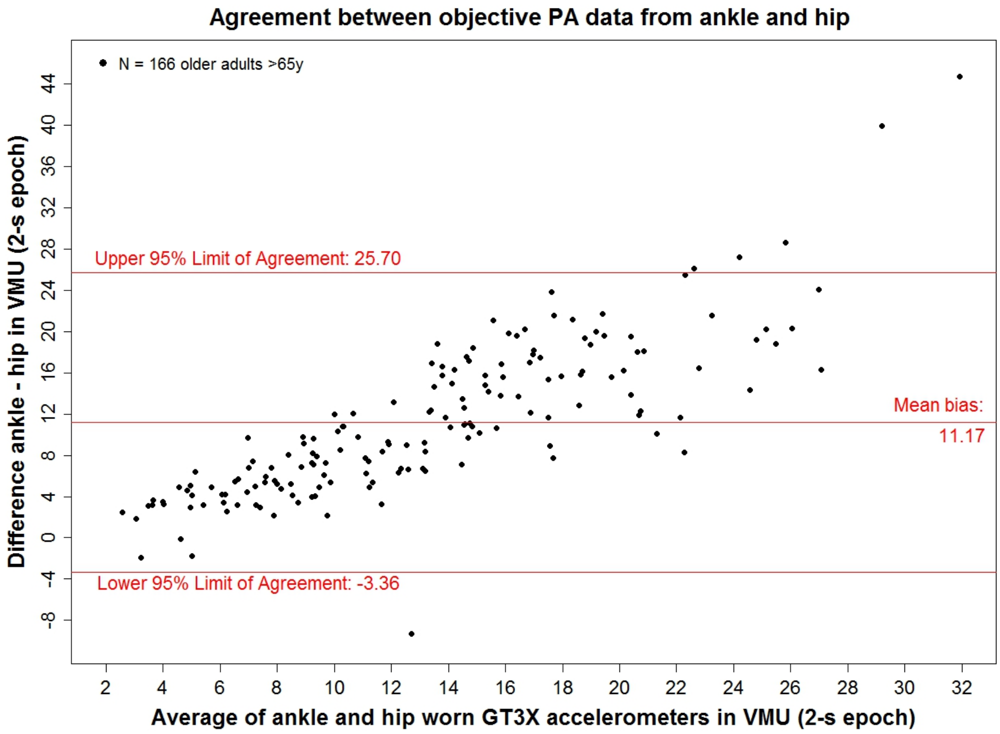


Figure IV-7. Bland-Altman plot comparing triaxial mean ankle and hip measurements

Agreement between the PA data from ankle and hip was assessed using Bland-Altman-Plots [263]. From this analysis an average bias of 11.17 VMU at a sampling interval of 2 seconds was calculated between both methods, with 95% limits of agreement ranging from -3.36 to 25.70 VMU, and the 95% CI of the mean of difference spanning from 10.04 to 12.30 VMU. Only a single value was close to the line of equality and a proportional error can be observed as the difference between both methods increased with a higher average, limiting the agreement (see Figure IV-7). Furthermore, heteroscedasticity was identified by a positive correlation between the absolute difference and the mean of the two measures ($r=0.86$, $p<0.01$). Therefore, the natural logarithm was applied on the ankle and hip PA, resulting in a neglectable slope of $r=0.10$ (see Appendix B-3).

2.2. Results of the position-dependent PA classification

Following the direct comparison of the accelerometer count output from ankle and hip recordings, the calculated time spent in different PA intensities is compared for both positions based on the thresholds developed by Puyau and colleagues [121] and according to individualized cut-points developed in this thesis using a moving average with 5-minutes-window.

Results of the position-dependent PA classification based on published literature

As the work by Puyau et al. was the only publication stating uniaxial thresholds for both measurement positions using the 7164 accelerometer at 60 seconds epoch, the reported thresholds corresponding to sedentary, light, moderate and vigorous intensities were applied for the ankle (<800, <5100, <12000, ≥12000) and hip (<800, <3200, <8200, ≥8200) recordings of the population-based KORA-Age data. The absolute and relative calculated time spent in each intensity level were compared by descriptive statistics and using the Wilcoxon signed-rank test, as the distribution of the absolute and relative values, as well as the mean PA data were non-parametric, with the exception of ankle and hip absolute sedentary minutes.

Table IV.4. Comparison of PA classification based on cut-points for ankle and hip published by Puyau et al.

Pos.	Unit	Sedentary	Light	Moderate	Vigorous	Total
Ankle	Sum of Min	942635	188173	24697	2639	1158144
	Median in % ± IQR	81.65% ± 10.83%	15.75% ± 7.81%	1.57% ± 3.07%	0.00% ± 0.13%	100%
Hip	Sum of Min	999975	81749	8336	1	1090061
	Median in % ± IQR	91.97% ± 6.71%	7.19% ± 5.31%	0.10% ± 0.80%	0.00% ± 0.00%	100%

Table IV.4 summarizes the population-based classification differences in PA when ankle or hip derived cut-points [121] are used to estimate the time spent in different intensity levels. On average, considerably less time is classified as sedentary using the thresholds for the ankle, while relatively more time is classified in light, moderate and vigorous intensities. The difference in the total measurement time of 5% (68.053 minutes) between ankle and hip measurements is a result of the applied wear time algorithm [248], which may have estimated the wear time differently for both position during similar days.

The Wilcoxon Test confirmed statistically significant differences between the PA classifications for sedentary (Z= -11.07), light (Z= -11.11), moderate (Z= -10.10), vigorous (Z= -6.62) and MVPA (Z= -6.183, all p<0.01) intensities between both measurement positions.

Comparison of PA classification based on individualized "cut-points" for ankle and hip

Unlike calibration studies used in literature to derive intensity cut-points using a criterion for EE or METs measurements, a purely data-driven approach was used in this thesis to classify the PA data into four different "performance" levels based on uniaxial, 60 seconds sampling intevals (see Figure IV-8).

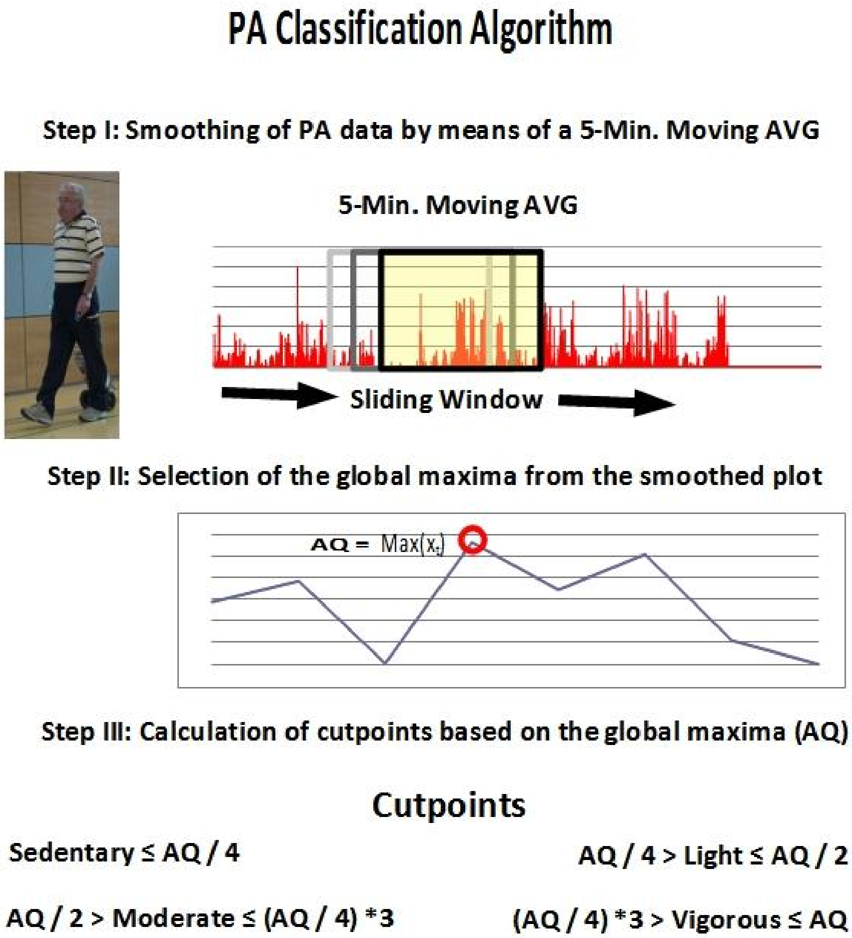


Figure IV-8. Individualized physical activity classification based on activity quartiles (AQ)

For this purpose, moving averages were calculated using a 5-minute sliding window on the PA data acquired from ankle and hip, separately. The derived averaged maximum value was used to create individualized performance-based activity quartiles (AQ) for each elderly subject. The classification results can be found in Table IV.5.

Table IV.5. Comparison of PA classification based on individual cut-points for ankle and hip

Pos.	Unit	AQ_{0-25}	AQ_{26-50}	AQ_{51-75}	AQ_{76-100}	Total
Ankle	Sum of Min	1068479	55307	20005	14353	1158144
	Median in % ± IQR	92.83% ± 5.02%	4.18% ± 3.55%	1.44% ± 1.10%	0.95% ± 1.10%	100%
Hip	Sum of Min	992004	62563	20946	14548	1090061
	Median in % ± IQR	91.99% ± 5.75%	5.33% ± 3.88%	1.75% ± 1.57%	1.18% ± 1.36%	100%

According to the performance-based PA classification, individuals spent on average time predominantly in the lowest activity quartile, consistently in both, the ankle (≈93%) and hip (≈92%) recordings. The difference between the median quartile-based PA classification from ankle and hip measurements is below 1% for the median and the IQR. Irrespective of the measurement position, the individualized "cut-points" (i.e. AQ) resulted in a similar performance-based PA classification on population level.

On individual level, statistically significant differences were found for the calculated time spent in the lowest (AQ_{0-25}: Z= -3.39, $p<0.01$) and second lowest quartile (AQ_{26-50}: Z= -3.98, $p<0.01$) between the ankle and hip classifications using the Wilcoxon rank-sum test. Differences were not statistically significant for the third and fourth quartile corresponding to moderate and vigorous intensities, nor for MVPA level.

Comparing the new PA classification to the one derived by Puyau et al. [121], only the time spent sedentary was statistically not different for the hip (Z= -1.318, p=0.187).

2.3. Discussion

In order to examine if the placement of a device affects the reported PA results (see Research Question and Objective II in Section 7 of Chapter I), the difference in the position-based accelerometer output from simultaneously acquired PA data at ankle and hip sites in healthy elderly subjects during daily free living were examined in this study, as well as resulting differences in the PA classification using published and developed cutpoints (see Chapter II, Sections 3.3 and 3.5). The discussion starts with a comparison of the count magnitude and correlations between acquired PA data from both positions, before addressing results from the PA classificaiton using ankle and hip-derived cutpoints:

A statistically significant difference was revealed between the measurement positions at the lower limb (ankle) and total body activity (hip), indicating that the device output is influenced by the placement of the accelerometer on the human body. This is in agreement with Bouten et al. [83], who found considerable effects of placement and sensor orientation at different positions during walking in two subjects.

Despite strong correlations between the VMU outputs of both devices in this work ($r=0.75$, $p<0.01$), the median activity counts were found to be statistically significantly greater in terms of magnitude at the ankle (i.e. 2.6-fold at 2-s, and 2.4 at 60-s sampling intervals, respectively), and a considerable bias between both positions was observed. The position-based difference regarding activtiy counts and correlations found in this study are compared to published literature in the following paragraphs:

In agreement with our results, Laporte and colleagues found LSI accelerometer readings to be statistically significantly different for hip and ankle PA measurements, with the ankle producing almost 2-fold higher count outputs, compared to the waist attached device in 20 physically active graduate students, during two workdays [291]. Although the device location was found to have a significant effect, PA data from both devices was strongly correlated. Puyau and colleagues compared activity counts at both, the right hip and the lower ankle in 26 children, acquired by means of the model 7164 accelerometers and the omnidirectional AW16 (MiniMitter) devices during structured activities at different intensity levels [121]: For all but one activity in the model 7164, higher counts were recorded at the ankle in both device types (1.8-fold in the model 7164; 1.9-fold in the AW16), with strong correlations between positions per device type ($r=0.77$; $r=0.93$, respectively) and between the two different device models, irrespective of the location ($r=0.82$-0.89). However, Balogun et al. found a significant location effect between Calcount and the Caltrac sensors, which were correlated poorly at the waist, but moderately at chest line during treadmill walking in 20 university students [57].

Both previous studies on the ankle-hip comparisons [121, 291] reported a slightly lower conversion factor between the count outputs at 60-s sampling intervals, despite having measured PA in younger subjects. In contrast to the current work, the uniaxial accelerometers used in the aforementioned studies have not registered bodily movement in the anterioposterior and mediolateral directions. This may explain the greater difference in the magnitude, apart from the differences in the device-internal manufacturer-dependent processing. Device outputs from simultaneously acquired ankle and hip recordings were strongly correlated in all studies, independent if - like in this work - similar devices were used, or different device types: Melanson and Freedson compared the associations between activity counts from a hip-worn Caltrac devices and three model 7164 accelerometers placed at the ankle (r=0.81), the non-preferred hip (r=0.80), and wrist (r=0.76) sides in 28 healthy adults during treadmill walking, finding a comparable ability to quantify amount and intensity of PA [49]. A short comparison of differences in the count output from measurement location around the waist can be found in the Appendix (B.3).

However, the device output might not only be affect by the measurement position, but also by manufacturer-depended peculiarities: Welk and colleagues assessed the influence of monitor position on accelerometry output by placing the model 7164, the Tritrac and the Biotrainer monitors in random order along the right side of the hip at the anterior axillary, mid-axillary, and the posterior axillary line across 42 subjects during walking [93]: Position-dependent significant differences in activity counts were only reported for the model 7164, but not for the VMU and the kcal output of the Tritrac and the Biotrainer devices, indicating that only the Actigraph 7164 model was subject to monitor position effects [93]. This emphasizes the need for comparison studies to better "understand" the differences in the proprietary sensor outputs (see Chapter III).

Overall, only very few studies with very few subjects (i.e. mostly $N \leq 30$) examined the difference in simultaneously acquired accelerometer outputs. For the comparison of ankle and hip recordings, only the single aforementioned study explored differences in young adults during daily free living [291], and another one in children during structured laboratory protocols [121]. As the comparison of study results acquired by means of different sensor with different attachment positions is limited, the derived conversion factor can be applied to enable a comparison between hip or ankle recorded PA with the GT3X in similar individuals. Another objective of this work was to determine if activity estimates from the hip were comparable to ankle PA data, when placement-specific thresholds were applied (see Research Question and Objective II in Section 7 of Chapter I. To explore potential differences in the position-dependent PA classification at ankle and hip sites, published count cutpoints corresponding to sedentary, light, moderate, and vigorous intensity levels were applied on the KORA-Age PA data. The results from this classification are discussed in the following paragraphs:

Despite the differences in the count output between ankle and hip recordings found in this work (see Section 2.1), a similar threshold of 800 has been proposed to classify sedentary intensity in children for both sampling locations by Puyau and colleagues [121]. Using this classification for the relative time spent inactively, a statistically significant difference of roughly 10% was found between the PA data from both accelerometer positions, with implications on the relative time engaged in other intensity levels as well. In fact, approximately only half as much time was spent in light activities based on the hip PA classification ($\approx$ 8% vs. 16%), and almost no time in moderate intensities (i.e. 0.1%), while the corresponding ankle classification (i.e. 1.6%) was statistically significantly different. Moreover, the relative time engaged in vigorous intensities was statistically significantly different between both positions, as well as the time in MVPA ($p<0.01$; not shown in Table IV.4). Results from this work indicate that the PA classification might differ considerably depending on the measurement location when the cut-points proposed by Puyau et al. [121] are applied. Therefore, comparisons of ankle and hip-derived PA classificaiton based on cut-points might be inappropriate. This finding is in line with a very recent report from Routen and colleagues [292], who compared intensity thresholds developed for the hip [121, 250] in comparison to the wrist [204] for the Actiwatch AW16 accelerometer. Similarly, sedentary time was found to be greater for the hip estimates, while significantly less time was spent in light to vigorous intensities, when compared to the wrist recordings.

In order to establish these thresholds, Puyau and colleagues used a combination of 3 treadmill speeds and 6 lifestyle activates, including playing Nintendo or toy play activities, art & crafts as well as aerobic warm-up exercises, tae bo and ball play activities in 26 children. Some of these activities might have only included movements of the lower limb or the torso, and might have been underestimated by either device, resulting in considerably different count outputs, and hence, well different cut-points. Inter-individual variation might have affected the calibration between both measurement positions, as well [293]. However, the CV of ankle (50%) and hip (48%) PA data was not significantly different (F=1.337, p=0.248), indicating a similar transition from low to high counts and vice versa.

To enable a position-independent PA classification, a performance-based quartile classification was developed in this study. The results using this classification method are discussed next:

In order to divide PA into four "intensity" levels, quartiles were used to classify the KORA-Age cohort PA data using a moving average with a 5-minutes window. Individualized performance-based thresholds were calculated to classify the time spent in each of the four quartiles and the results were compared between ankle and hip classifications.

The relative amount of time classified in the third and fourth quartile were compared to traditional MVPA cut-points from calibration studies in Chapter V.

Only moderate, vigorous and MVPA intensities were not statistically different between ankle and hip and significant differences were found between the first two quartiles, representing PA of sedentary and light intensities. However, as individualized thresholds did classify PA into four categories of similar size, a high variation between subjects can be expected. A cut-point corresponding to "sedentary" intensities might therefore be considerably higher in very active participants when compared to the corresponding first quartile of a less active participant. Despite these significant differences in the first two quartiles, the classified time spent in each category did not vary "biologically meaningfully" [292] on the population level, as differences between ankle and hip classification were found to be smaller than 1% for all four PA levels. Therefore, the performance-based classification (partially) enables a comparison of classified PA data from ankle, hip and presumably wrist positions.

Despite the results of this study, the question how many and where to best position accelerometers still remains. An answer to this question is not trivial as it strongly depends on the research question and goal of a study. While accelerometers positioned at the trunk are preferred for the measurement of total body movement and believed to result in more precise PAEE predictions [83], an outcome measure such as steps per day might be more precisely captured by ankle-worn devices, while wrist-mounted accelerometer are assumed to increase compliance to monitoring protocols [292].

In this thesis, activity counts from ankle and hip recordings have been directly compared and significant differences have been found. In order to find a more sound answer to the question where a sensor should be ideally placed for activity estimates, the consequences of these different positions need to be explored in further studies. This can be done by investigating how position-dependent accelerometer outcomes are associated with health parameters, mortality and health benefits. Such differences have been found in the COPD study (see Section 1) and may as well be present in the elderly.

Conclusion

In summary, PA measurements using two accelerometers were feasible in the cohort and the older adults were compliant with the wearing protocol. Activity counts acquired from ankle and hip positions were significantly different in the elderly subjects, with the ankle recording on average 2.6-fold higher VMU/min outputs. Using published, position-dependent Actigraph cutpoints for the classification of the time spent in different intensity levels yielded considerable different results for all intensities (i.e. from sedentary to vigorous as well as for MVPA). This revealed that location-based PA classifications might be inappropriate or only limited comparable. However, using individualized thresholds as a mean to classify PA from ankle and hip, resulted in a more convergent estimation of the time spent in different PA levels between both positions. On population level, differences were smaller as $\pm$ 1%, nevertheless significantly different at both lower activity quartiles. However, the individualized threshold method can be used in future studies to enable a standardization and/or comparison of reports regarding the PA classification (at ankle or hip) in the elderly.

2.4. Innovation and limitations

To the knowledge of the author, this is the first report to explore the difference in triaxial accelerometer output from simultaneously acquired PA data at ankle and hip sites in a large sample of healthy elderly subjects. The PA data has been recorded during daily free living, at a very short epoch. The data processing was conducted according to current recommendations [188]. Despite the widespread use of accelerometers, the key question, where a motion sensor should be positioned has yet not been addressed in an adequate and systematic way. In this regard, the present study provides useful insights in the simultaneously measured PA data from the ankle and the hip. The question whether the classification of PA data is influenced by the sampling location at ankle and hip, has previously not been explored. By default, PA data is classified based on cutpoints derived in calibration studies [226]. This is the first study to develop and compare the classified PA data based on individual, performance-based activity quartiles.

This study shows a couple of limitations: In order to reduce the study burden, a sensor wear time log was not applied. Instead, a modified algorithm of Hecht et al. [248] was used to estimate the wear time of the ankle and hip recordings separately, based on triaxial VMU recordings. Triaxial outputs are assumed to improve the distinction between non-wear time and sedentary episodes compared to uniaxial recordings [249]. However, this algorithm was developed in patients suffering from COPD. Although their reduced PA profile might be comparable to elderly subjects, the difference between the algorithm and the commonly used non-wear time definitions of 60 consecutive minutes of inactivity has not been assessed. Moreover, the total wear time varied to roughly 5% between ankle and leg recordings, despite haven chosen similar days for the analysis. This might have slightly affected the PA estimates and comparisons. Due to the lack of cutpoints for the ankle, Puyau et al. [121] thresholds were selected, although they were developed in children using a predecessor uniaxial device model. The output slightly differs between the model 7164 and more recent Actigraph models including the GT3X [294]. The difference in counts might have affected the developed cutpoints.

Chapter V

Objective 3: Intensity Classification

Contents

In order to translate and interpret proprietary accelerometer signals into physiologically meaningful data, activity counts have usually been validated against DLW or (indirect) calorimetry [117]. From these analyses a variety of different intensity thresholds has been derived in literature, to divide the accelerometer output into light (<3 MET), moderate (3-6 MET) and vigorous (>6 MET) intensities [226]. However, the proposed intensity cutpoints vary depending on the number and age of the included subjects, the selected calibration activities (treadmill, ADL, or both) and the applied statistical analysis (linear or bilinear regression, ROC curves, etc.) [226]. Only few studies compared different cutpoints and a consensus on the "best" PA level classification does not yet exist [226]. As publications concerning cutpoints for elderly subjects are widely lacking, a data-driven approach is used in this chapter, to classify the acquired PA field data from the KORA-Age sub-cohort into time spent in moderate, vigorous and very vigorous intensities (MVPA) (see Sections 3.6). Additionally, the results are compared to the calculated MVPA time based on selected intensity thresholds from literature.

The results from the MVPA cut-point analysis are often used to estimate the compliance with current PA guidelines [129, 295]. The implications of selecting a specific MVPA cut-point on the guideline compliance are examined in addition, as described previously (see Section 3.7).

1. MVPA Classification (KORA-Age)

MVPA plays an essential role in public health. Therefore, the classified time in this intensity level is calculated in this section. As EE was not measured in the scope of KORA-Age, solely PA-derived cutpoints are used in this work (see Figure IV-8). For this, the classified time spent in the AQ_{50-100} interval will be declared as MVPA, under the assumption that greater PA counts correspond to greater EE. Both terms will be used interchangeably. The previous chapter revealed statistically significant differences between ankle and hip positions for all intensity levels when thresholds by Puyau et al. [121] were applied. However, using the uniaxial performance-based classification on the re-integrated PA data (i.e. 60s sampling interval), no statistical differences were observed for the PA levels corresponding to moderate (AQ_{50-74}), vigorous (AQ_{75-100}) and MVPA intensities. To evaluate if the classification of time spent in MVPA is affected by the sampling interval and the amount of measurement axes, the AQ_{50-100} from ankle and hip PA data are calculated based on the vertical accelerometer count output, in comparison to the triaxial VMU representation (see Tables V.1, V.2). This is done by using the PA data of 166 elderly subjects of the KORA-Age sub-cohort (see Figure IV-5).

1.1. Results from uni- and triaxial quartile-based MVPA classification

Table V.1. Classified MVPA time based on uniaxial individual cutpoints for ankle and hip and statistical significance of the difference

Pos.	MVPA (epoch)	Uniaxial (2s)	Uniaxial (60s)	p-Value
Ankle	Sum of Min Median (IQR)	55273 min 4.93% (3.26%)	33010 min 2.62% (2.66%)	$p<0.01$
Hip	Sum of Min Median (IQR)	58925 min 5.27% (2.95%)	35272 min 3.05% (2.58%)	$p<0.01$

The absolute time classified as MVPA was compared between the two different sampling intervals from a single position. From this analysis, both ankle (Z= -11.175) and both hip MVPA estimations (Z= -11.175, both $p<0.01$) were statistically significantly different between the 2s and the 60s epoch. However, when a similar epoch was compared between ankle and hip, no difference was observed in the time classified as MVPA.

Table V.2. Classified MVPA time based on triaxial individual cutpoints for ankle and hip and statistical significance of the difference

Pos.	MVPA (epoch)	Triaxial (2s)	Triaxial (60s)	p-Value
Ankle	Sum of Min Median (IQR)	64646 min 5.50% (3.88%)	39319 min 3.13% (3.17%)	$p<0.01$
Hip	Sum of Min Median (IQR)	128800 min 11.56% (4.94%)	83787 min 7.27% (4.55%)	$p<0.01$

Using all three axes in the VMU representation lead to statistically significant differences in the classified time spent MVPA between both sampling intervals of a single position, and between ankle and hip at a similar epoch (all $p<0.01$).

When uniaxial and triaxial-based MVPA classifications were compared, statistically significantly differences were observed between epochs and positions. Estimations on the time spent in MVPA were greater for all triaxial classifications compared to their uniaxial counterparts. MVPA classifications were lower for the 60s sampling intervals in both, uni- and triaxial thresholds.

1.2. Results of the comparison of published and individualized MVPA classifications

From the available literature on proposed MVPA cutpoints, publications were selected which fulfilled the following criteria:

- The cutpoints were developed for Actigraph accelerometers
- Middle-aged or older adults were included in the calibration protocol
- The cutpoints were derived from validation of activity counts against DLW, or direct or indirect calorimetry

The first two requirements account for the device and population-specific nature of calibration studies, corresponding to our PA measurements by means of an Actigraph device, applied in elderly subjects. In order to exclude studies that derived cut-point based on meta-analysis without a criterion measure, the last requirement was stated.

In addition to the identified cutpoints using the aforementioned criteria, the most commonly applied cutpoints by Freedson et al. [114] are included as a reference, as well those published by Troiano and colleagues, who examined PA in 4867 participants ranging from children to older adults [129]. Pruitt et al. [108] is included, despite now having used a criterion. However, they derived individualized cutpoints based on a 6MWD protocol in the elderly. As elderly-specific triaxial cutpoints are lacking, Haenggi et al. [249] and Sasaki et al. [240] were included for triaxial MVPA calculations.

The final set of publications included treadmill, lifestyle and mixed model calibration protocols and consisted of publications by Freedson et al.[114], Troiano et al. [129], Swartz et al.[116], Hendelman et al.[115], Lopes et al.[296], Pruitt et al.[108], Copeland et al.[297], Ribeiro et al.[298], Haenggi et al. [249], and Sasaki et al. [240]. Details from the uniaxial calibration protocols are summarized in Table C.1 in the Appendix, with the exception of Pruitt and Troiano (no criterion), Copeland (no paper access), and Ribeiro (only abstract available).

Using the aforementioned published cutpoints, the relative time spent in MVPA was calculated and compared by means of a forest plot for 2s and 60s sampling intervals (see Figure V-1). From this analysis, considerable differences were found concerning the relative time spent in MVPA based on uniaxial classifications:

At an epoch of 2s, the relative time classified as MVPA ranged from 3.14% to 16.80%, with a mean of 7.95% $\pm$ 5.30% and a median of 6.67% (IQR: 7.34%), according to the aforementioned publications for uniaxial cutpoints. The uniaxial AQ_{50-100} classification was lower at a median of 5.27% (2.95%) in comparison.

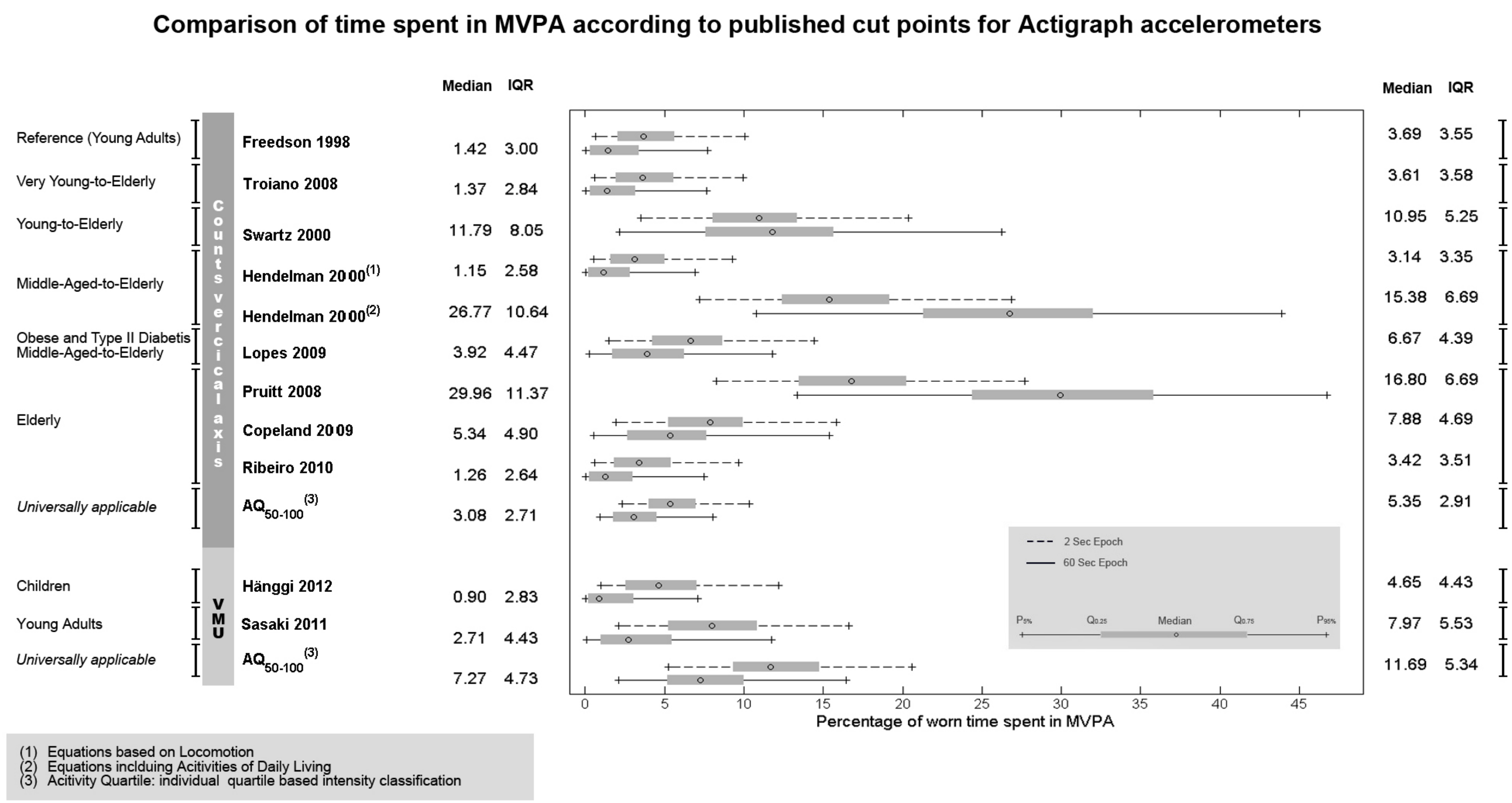


Figure V-1. Forest-plot comparing the time spent in MVPA according to different published cutpoints at 2s and 60s

Correspondingly, for the re-integrated epoch of 60s, MVPA ranged from 1.15%, according to the "all activities equation" of Hendelman et al., to 29.96% based on cutpoints from Pruitt et al., with a mean of 9.19% $\pm$ 11.33%. However, the median concerning the time spent in MVPA was considerably lower at 3.92% (IQR: 10.42%). The developed uniaxial AQ_{50-100} classified 3.05% (2.58%) of the time as MVPA, which is lower than the published MVPA estimates.

In order to compare triaxial cutpoints, only two published studies were available and the estimated relative time spend MVPA using these thresholds was 7.97% with an IQR of 5.53% for 2s sampling intervals and 2.71% (4.42%) for 60s epochs, respectively. Using the developed triaxial AQ_{50-100} classification, the relative time spent in MVPA was significantly greater for 2s epochs (median: 11.56%, IQR: 4.94%), compared to 60s sampling intervals (median: 7.27%, IQR: 4.55%).

Overall, the classified MVPA time is considerably different between published literature. Therefore, the median was used to enable a comparison between the published studies and the developed AQ_{50-100}. The MVPA estimates differed by 1.4% at 2s epoch and by 0.87% at 60s sampling intervals. Differences for all MVPA classifications were present between both sampling intervals. The time spent in MVPA was lower at 60s sampling intervals for thresholds which were derived based on locomotion activities, and greater for cutpoints including activities of daily living (e.g. Swartz and Hendelman regarding the "all activities equation") in the calibration protocol, compared to 2s epochs. As similar cutpoints resulted in different MVPA classifications when PA data from different sampling intervals was used, this "epoch effect" was further examined using a set of artificial cutpoints: Starting at a threshold of 100, the cutpoints were incremented by a constant value until 2000 was reached, thus enabling a comparison of the epoch-dependent difference in MVPA classifications (see Figure V-2). From this analysis, differences were found for the classification of time spent above each of the artificial thresholds, especially for thresholds below 500, which are certainly effecting the classified time spent in sedentary and/or light intensities. This is an important finding, as older adults spend time predominantly in these intensity levels. A similar plot for triaxial recordings can be found in the Appendix (see Figure C-1), as well as a "cross-point" detection between 2s and 60s sampling rates, in which both epochs classify MVPA similarly.

1.3. Effects of the cutpoint selection on the adherence to PA guidelines

In order to examine the effects of the cutpoint selection (see Section 3.7 of Chapter II), the amount of subjects who spent daily more than 30 minutes in MVPA on five of seven consequetive days was calculated in line with the guideline by the AHA and ACSM [152]. The aforementioned self-report-based guideline states that PA in moderate-to-vigorous intensities should be performed in bouts of 10 minutes. However, this requirement was neglected for the objective PA data acquisition in this study, as no older adult met the PA recommendation in a previous report in which accelerometry was used [252]. Furthermore, the adherence was shown to be strongly reduced when 10-minute bouts were applied on the objective PA data in a group of middle-aged postal workers [295]. Results of this analysis based on a subset of the KORA-Age cohort (see Figure IV-5) are summerized in Table V.3.

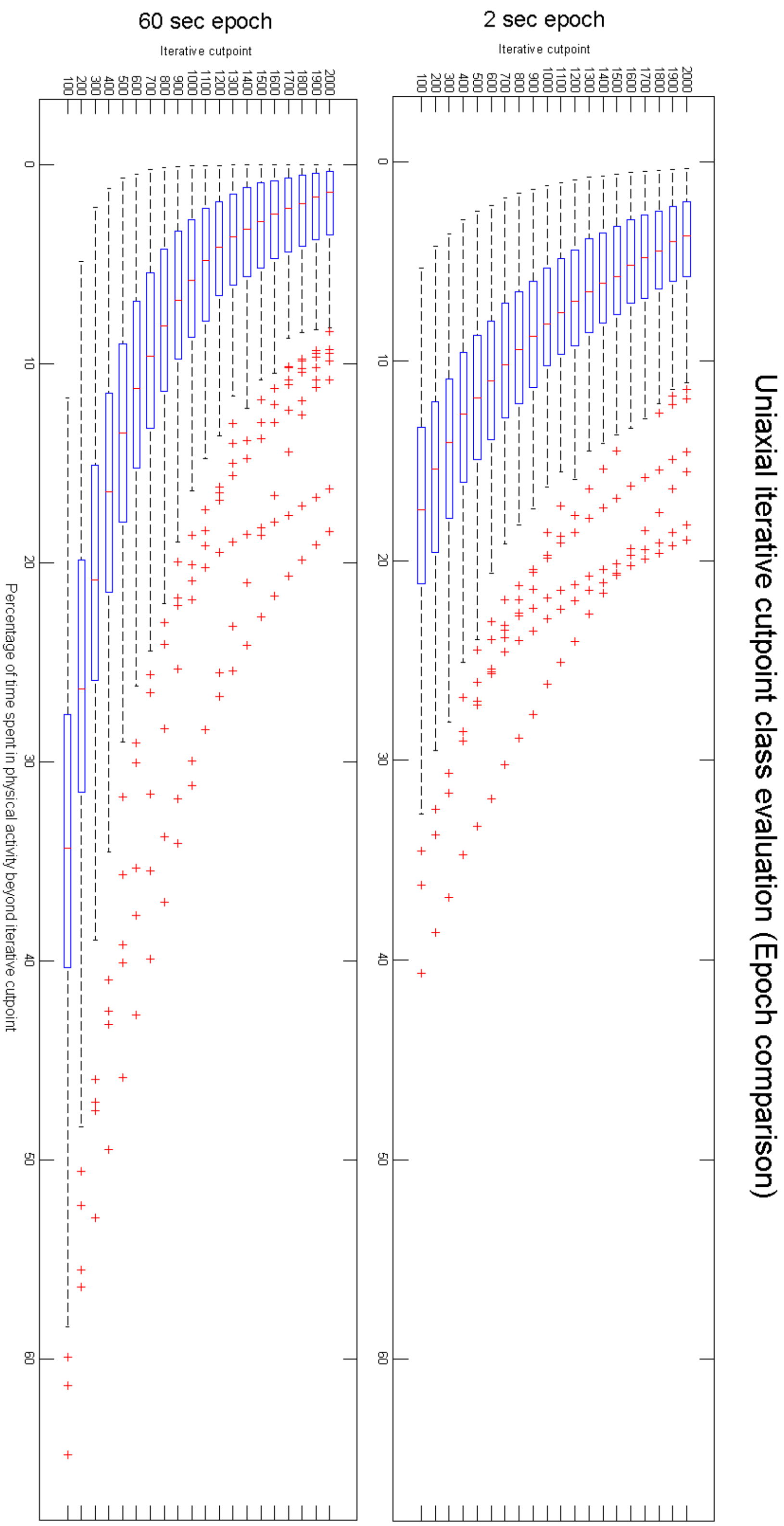


Figure V-2. The effects of artificial thresholds and epoch selection on the PA classification

Table V.3. Amount of subjects who spent at least 30 minutes in MVPA on 5 days of the week depending on selected thresholds and epoch

Epoch	Freedson	Troiano	Swartz	Hendelman (locomotion)	Hendelman	Lopes	Pruitt	Copeland	Ribeiro
2s	36%	35%	93%	30%	100%	67%	100%	84%	32%
60s	17%	15%	89%	12%	100%	35%	100%	50%	13%

Depending on the selected cutpoints and epoch, the relative amount of subjects meeting the recommended PA level ranged from 12% to 100%. The calculated number of older adults adherent to the PA guideline was considerably greater for 2s epoch, compared to 60s sampling intervals.

1.4. Discussion

In order to compare data reduction methods and their implications on the reported amount of subjects meeting a PA guideline (see Research Question and Objective III in Section 7 of Chapter I), the calculated time spent in MVPA according to published and developed count intensity cutpoints were compared in this study (see Chapter II, Sections 3.6 and 3.7).

Before the results of this work are discussed, the need for elderly-specific cutpoints are outlined, and calibration studies including their limitaitons in the elderly are introduced in the next paragraphs. This is necessary to justify the development of performance-based PA cutpoints as part of Objective III.

MVPA is important for public health (see Sections , and thus, considerable work has been carried out to define thresholds by means of calibration studies in children and adolescents, while only few reports derived intensity cutpoints in the elderly [299]. However, Evenson and colleagues demonstrated that elderly-specific calibration studies are necessary, as considerable differences in the estimated time spent in MVPA were found in older adults, when four different artificial threshold (>500, >1000, >1500, >2000) were applied [176].

In these calibration studies, objective PA and EE data are simultaneously measured in subjects by means of accelerometry and a criterion measure such as (in-) direct calorimetry during different activities, treadmill or locomotion protocols, or a combination of both [226]. The acquired data of both procedures is then compared by different statistical methods, such as ROC curves, or (non-, bi-) linear regression models, in order to derive activity count threshold values corresponding to the energy cost of light, moderate, and vigorous levels of PA [119]. For this purpose, the physiological concept of metabolic equivalents (METs) is used (see Equation II.7) [80, 153]. Based on multiples of the RMR, PA can be classified into the typical MET categories of <3 METs, 3-6 METs, >6 METs corresponding to light, moderate, vigorous intensities, respectively. However, the 1 MET equation, which is assumed to be originally derived from data of a single 40 years old subject, was shown to presumably overestimate the resting EE and the actual resting VO2 value in a large heterogeneous sample [153]. Moreover, in the elderly, the RMR was recently found by Hall et al. to be about 32% lower compared to the standard 1 MET equation, concluding that specific intensity thresholds are needed for this age group [300]. Due to the dependence of the RMR on the body composition and age [153–155], relative, instead of absolute METs have been suggested by a recent PA guideline for the classification of intensity levels in the elderly [152]. Thus, Pruitt and colleagues were the first to derive cutpoints by means of a 400 meters walk test protocol based on "meaningful data", instead of the MET classification [108]. Furthermore, the standard MET definition was found to be inappropriate for children [121, 301–303], who have a higher oxygen consumption at rest [166]. As a consequence, alternative METs thresholds have occasionally been chosen for MVPA in children and adolescents, such as 4 METs [120, 228, 304, 305] or 5.7 METs [306].

In the absence of elderly-specific cut points for the estimation of MVPA, researchers have often chosen those proposed by Freedson et al. (MVPA $\geq$1952 counts * min^{-1}), or its closest band ($>$1.999 counts * min^{-1}) in cohorts with older adults [186, 251, 252, 256, 307, 308].

Because of the mentioned limitations in the intensity classifications based on METs in the elderly, the lack of specific cutpoints for this age group, and the recommendation [152] to use relative, individualized intensity levels, a MVPA classification based on performance-based PA quartiles (AQ) has been introduced in this thesis (see Figure IV-8). A comparison of classifications results using these uni- and triaxial AQ at two different sampling rates for estimating the time spent in MVPA, are discussed in the following paragraphs:

Based on the uniaxial AQ classification, the absolute time spent in MVPA was not statistically different between ankle and hip for both sampling rates. This is an important finding, as the uniaxial AQ classification seems to enable a comparison of studies that have estimated the time spent in MVPA at ankle or hip. However, when the triaxial MVPA estimates were compared in VMU, statistical differences were present between both positions. This might be a result of the differences in the movement patterns of the lower limb in comparison to the total body movement, when recordings from the anteroposterior (AP) and the mediolateral (ML) axes are added. Differences in the count output between both positions have been confirmed in the previous chapter (IV.1.1, IV.2.1). Movement of the lower limbs mainly occurs in the vertical axis. This is reflected by a relatively small increase of time spent in MVPA between uniaxial and triaxial measurements for both sampling rates.

On the other hand, for the hip a strong increase in the classified MVPA time (i.e. more than twice as much) was noted at both epochs. This indicates that the additional measurement axes AP and ML strongly affect the MVPA classification of the triaxial AQ at waist level. In contradiction to the results in this work, Vanhelst et al. found only small clinically negligible, but statistical significant differences in the classification of moderate intensities using the cutpoints of Freedson and colleagues [114] in 62 adolescents between hip-mounted uniaxial GT1M and triaxial RT3 accelerometers. However, a direct comparison of both results is limited due to the application of EE vs. PA derived cutpoints and the use of different sensors. Concerning the latter, statistically significant differences were found for the MVPA quantification at 5s epoch lengths between, for instance, the 7164 and GT1M model [149]. Model 7164 classified significantly more time as light and less time as sedentary activity. Sasaki and colleagues found no differences in the count output between the GT1M and the GT3X for the vertical axis, while AP axis as well as VMU based on two axes yielded different results [240]. For the estimation of EE, Howe and colleagues did not find significant improvements using triaxial counts from the RT3 when compared to uniaxial PAEE estimations [309].

For all AQ classifications, the time spent in MVPA was greater for triaxial estimations, impendent of the sampling rates or positions. The chosen sampling rate was found to have a considerable effect on the MVPA estimates at both positions. MVPA estimates were 1.5 to 1.7-fold higher for 2s epochs compared to 60s, in line with previous reports: Nilsson and colleagues found a significant “epoch effect” on the time spent in vigorous and very vigorous intensities, when five different epoch settings were compared in children [310]. Corder et al. found all intensities to differ significantly between 5s and 60s sampling intervals in Indian adolescents [149]. No previous study examined this epoch effect in the elderly. However, the significantly higher classified MVPA time using 2s sampling rates indicates that activity in the higher count range is carried out in very shout bouts in the elderly. This epoch effect was observed for the developed uni- and triaxial MVPA classifications as well as for all published uniaxial and triaxial cutpoint comparisons, based on the PA data of the elderly. Therefore, the smallest epoch possible appears recommendable for the assessment and processing of PA data, in line with the most recent recommendation for accelerometer use in population-based studies [188].

After having compared the performance-based uni- and triaxial AQ classifications for the estimated time spent in MVPA, the aquired results are compared to PA intensity classifications according to published MVPA thresholds in the following paragraphs:

This is done, in order to examine whether the uni- and triaxial AQ_{50-100} are corresponding to the published MET-derived MVPA classifications. For uniaxial comparisons, calibration studies that used Actigraph devices and included elderly subjects in their protocol were selected as well as the reference MVPA cutpoint from Freedson et al. [114]. The publications showed very different MVPA estimates due to differences in the design and protocols of each calibration study, and the applied statistical methods, which were recently shown to affect the derived thresholds [311]. This phenomenon of different cutpoints for MVPA has already been found in children and adolescents and was first defined as “cutpoint conundrum” [312], and specified more recently as “cutpoint non-equivalence” [175].

Noteworthy, studies that included solely locomotion activities during the calibration protocol resulted in higher MVPA thresholds (i.e. Freedson, Hendelman walking equation), and therefore, in lower MVPA estimates. On the other hand, when activities of daily living were added to the protocol, as done by Swartz or Hendelmann, the intensity thresholds were considerably lower, leading to higher MVPA estimates.

According to the uniaxial AQ_{50-100} classification, slightly more time was spent in MVPA compared to solely position-based calibration studies. On the contrary, less MVPA time was estimated compared to mixed models. Due to considerable differences in the MVPA cutpoints, the AQ_{50-100} estimation was compared to the median of all published calibration studies, with acceptable result for 2s sampling intervals (AQ_{50-100}: 5.27% vs. 6.67%) and 60s (3.05% vs. 3.92%), respectively.

A comparison of uni vs. triaxial is discussed next: For a comparison of uni- and triaxial MVPA estimations, only the thresholds from Freedson et al. [114] and Sasaki et al. [240] were included, due to a similar calibration protocol in both studies and a lack of published triaxial elderly-specific cutpoints. The cutpoint proposed by Sasaki and colleagues yielded a 2.16-fold increase of time spent in MVPA compared to Freedson’s uniaxial MVPA classification based on 2s sampling intervals and 1.91-fold greater estimates at 60s epochs. Similarly, the resulting difference in the MVPA classification between the developed uni- and triaxial AQ classifications was compared. The AQ_{50-100} increased by a factor of 2.19 on a 2s sampling interval, and 2.36-fold at 60s epochs.

Between both, published and developed classification methods, the increase of calculated MVPA time between uni- and triaxial cutpoint was found to be comparable at 2s sampling intervals. This finding supports the applicability and feasibility of the AQ in the elderly.

The developed AQ classification methods seems to reflect MVPA considerably well. The advantage of the AQ classifier is its simple implementation and applicability. As the classification is solely based on PA measures, no calibration against EE is needed. Therefore, this method can enhance the comparability between studies and provide a means for the PA classification in the elderly. As these results were not compared to EE measures (validation), the reference MVPA classification by Freedson et al. should be reported in addition.

Conclusion

In this work an individualized PA classification named AQ has been developed and the results were compared to the estimated time spent in MVPA level according to selected published MVPA cutpoints, based on data from the KORA-Age cohort. The classified time spent in MVPA varied strongly between published thresholds, with lower estimates for locomotion-derived cutpoints and greater time for calibration studies that included activities of daily living. The derived uniaxial AQ classified MVPA corresponding activity levels in between, and was found to classify MVPA fairly similar, when compared to the median of all published MVPA estimates. Moreover, no statistical differences were found for classification from ankle and hip data using the developed uniaxial method. This enables a comparison of studies that used these two different sampling locations. The sampling interval was found to have a considerable effect on all PA classifications. The use of shorter epochs might better reflect spontaneous bouts of activity and lead to higher MVPA estimates in the elderly.

1.5. Innovation and limitations

A strength of this comparison is the inclusion of cutpoints from calibration studies including partially or exclusively elderly subjects from different Actigraph generations with a different number of measurement axes. As a result, this work can provide guidance to researchers in the selection of "appropriate" thresholds for older adults. This is important as elderly-specific cutpoints are widely lacking, and traditional MET-based PA intensity classifications might be inappropriate, especially in epidemiological studies.

Based on these considerations and the so called "cutpoint non-equivalence", an innovative method was developed in this thesis to classify PA data individually, based on the average PA performance. The new method was evaluated in direct comparison to the MVPA classification results from calibration-based studies. A strength of this method is its ease and applicability: Researchers can adapt this method in order to enable a comparison of the time spent in different activity levels. This method only relies on the device-measured activity counts and does not require measurements of EE, which are complex and expensive. However, device-dependence and wear time classification are still limiting factors, which ideally need to be matched.

This presented work had a couple of limitations: Due to output differences between accelerometer types, PA data from the applied GT3X accelerometers might vary from the model 7164, and lead to different classification results when device-specific thresholds are compared. This clearly limits the comparability of resulting MVPA estimations of GT3X devices used to classify the time spent in MVPA based on cutpoints derived for the model 7164 and GT1M accelerometers.

As EE was not measured in the scopre of the KORA-Age study, no figures can be made on how accurate or valid the developed AQ method is. Moreover, the AQ classification was assumed to correspond to sedentary, light, moderate and vigorous MET levels.

A published method has been used to estimate wear time. Other studies used 30 or more commonly 60 minutes of consecutive zero values to define non-wear periods, with up to two minutes of allowance above, in elderly subjects. It remains questionable which method is more accurate. A comparison was not conducted in this work, as a wear time log was not used in the cohort.

Chapter VI

Conclusion

PA has been traditionally assessed by means of subjective methods such as questionnaires, interviews or diaries in medical and epidemiological research, in order to estimate the related EE based on inquiries concerning the time spent in certain PA types. However, as these instruments were found to suffer from reporting (e.g. due to social desirability) and/or recall bias, especially in the elderly [297], more accurate and objective PA assessment methods with an acceptable tradeoff between validity and feasibility were desired [75]. Due to the technical evolution of motion sensors regarding their size, memory, battery lifespan, pricing, and their capability to measure continuously the components frequency, duration and intensity of PA in daily free living, accelerometers in particular became widely used in research [75, 107]. However, instead of providing a raw data output in gravitational units (g=m/s^2), current device types convert the measured accelerations at a unit-specific sampling rate (in Hz) into proprietary units (i.e. “activity counts”, “steps”, “time spent in activities or positions”, “EE”, etc.), summed over a user-defined time interval called “epoch”, of which minute-by-minute recordings are most commonly used [191].

As the measured accelerations are internally processed using manufacturer-dependent in-build algorithms, the response to similar activities in different device types or different device generations is (likely) not equal. This might considerably affect the reported PA results (see Research Question and Objective I in Section 7 of Chapter I) . Therefore, the device-dependent responses to similar motions sequences were examined in three widely used commercial accelerometers as part of Objective I (see Chapter III):

Despite a similar accelerometer output representation (i.e. VMU), similar motion sequences carried out by means of a robotic arm resulted in a variation of codomains and measured accelerometer count magnitudes between the different device types. This certainly limits the comparability of results and affects the reported PA levels, and presumably derived EE estimates, due to differences in activity counts between units during calibration. A side effect of this result is the need for calibration studies for each single device, even between two different accelerometer generations from a single manufacturer [249].

The device dependent measurement errors increased at slower movement sequences in all devices, and might pose a challenge when non wear-time is distinguished from sedentary episodes, or effect the accuracy when accelerometers are applied in elderly subjects, who spent time predominantly in sedentary or light intensity activities. Due to difference in the reliability between sensor generations and the black-box nature of accelerometers with post-processed data output, counts from different devices cannot be easily converted and compared using a conversation factor, although a first attempt has been recently published based on field data [281].

Therefore, standardization in the assessment of PA is crucial and raw instead of proprietary data can ease the comparison of results acquired with different sensors. Moreover, the calculation of conversion factors would be eased using raw data outputs, despite sensor differences in terms of technical components and assessment capabilities.

As a final statement to Objective I it can be concluded that, a robotic arm was a feasible method to compare the variability of three commercial accelerometer types, and despite having used only two short repeated movement sequences, difference in the device-dependent outputs and the inter-device reliability could be detected between the three device types. The results of this study indicate strongly, that reported VMU levels are influenced by the selected device.

However, a translation of counts to enable comparability between different devices by means of conversion factors could not be established, as this goal requires knowledge of the in-build signal processing algorithms, or, in order to allow for its approximation, extended study protocols based on a wide range of different amplitude and frequency settings.

Such conversion factors similarly need to be established between sampling positions. Apart from the device selection, the sampling location might be another factor, which has considerable impact on the reported PA outcomes in the assessment of PA (see Research Question and Objective II in Section 7 of Chapter I). Therefore, position-based differences in the accelerometer outputs, the correlations to medical outcomes, as well as the PA classifications using published and developed cutpoints were examined using PA data simultaneously acquired at different measurement positions, as part of Objective II (see Chapter IV):

The question of the placement of sensors is strongly related to the outcome measure of interest. With respect to EE estimations, positions around the center of the body are the most common, while steps per day might be more accurately reflected by ankle locations, as has been recently suggested [313]. However, in this work the direct activity count device output was used for comparison, insteat of derived EE units. From this analysis, an ankle positioned device has been found to best mirror functional capacity and disease severity in patients suffering from COPD. These results suggest that the sampling location might lead to different results regarding associations to medical data. This must be considered when measurements are carried out at different locations, as each location seems to contain unique PA information.

However, due to the dependence of the output on proprietary data it remains questionable, if the results were affected by the device representation or by the comparison of uniaxial ankle vs. triaxial hip measurements in data acquired in the COPD sample. Nevertheless, counts aquired from different positions varied considerably in magnitude in both subject groups, likely affecting reports on the PA behaviour, depending on the sampling location.

Multiple devices can reveal differences in movement patterns as activity can occur predominantly either at upper or the lower limb (as found by means of BAP in this work), leading to vastly different outcomes when individual PA from only a single position is reported. As the magnitude of counts is dependent on the chosen data representation and the measurement position, equations estimating EE are likely affected. When published ankle and hip-derived intensity thresholds were used, the estimated time spent in all intensity levels was significantly different in this work. To enable a more consistent PA classification of activity levels in the elderly, an individualized, performance-based quartile classifier has been introduced, showing a good agreement between the estimated time spent in activity levels corresponding to moderate, vigorous and MVPA for ankle and hip. This is important, as these intensities levels are used to calculate the amount of subjects meeting current PA guidelines.

As a final statement to Objective II it can be concluded that, using objective devices at different positions revealed strong differences in the count magnitude, affected associations to medical outcomes in COPD, and lead to considerably different PA classifications when published cutpoints were applied on the KORA-Age PA data. These findings strongly suggest, that reported PA parameters are strongly affected by the sampling location.

To enable a comparison of count magnitudes, simple converion factors were derived between positions for similar target groups and an individualized, performance-based classifier has been established, which classified the time spent in intensities corresponding to moderate, vigorous and MVPA without similarly for PA data from ankle and hip.

Finally, the selection of applied data reduction methods can influence the reported PA levels, and thus the reported amount of subjects meeting PA guidelines (see Research Question and Objective III in Section 7 of Chapter I). As PA might be (strongly) affected by chronic conditions and/or functional limitations, specific cutpoints are needed in older adults. However, elderly-specific thresholds are widely lacking, and classified time spent in MVPA varied considerably between cutpoints derived from calibration studies that partially or solely included older adults. Due to the lack of standardization in the calibration process, the comparability between studies is hindered. In order to enable such comparisons, a straight forward, easy applicable method was developed, which solely relies on PA data (see Chapter V). This developed method was shown to quantify the time spent in MVPA fairly well, when compared to the median of all publications that derived MVPA threshold including older adults.

In this work, the classified MVPA time was found to be strongly dependent on the sampling interval. Therefore, shorter epochs should be used to track spontaneous bouts of activity in the elderly. As to now, only proprietary data has been used to derive device-specific MVPA cutpoints. The use of high-sampled raw data during the calibration process will lead to more global, and less device-dependent, thresholds and hence, increase the comparability.

As a final statement to Objective III it can be concluded that, an individualized, activity-based quartile classifier (AQ) was developed which was shown to classify MVPA fairly well compared to published cutpoints derived from calibration studies. The intensity classification was found to be strongly dependent on the sampling interval of the PA data. Shorter epochs might better reflect spontaneous bouts of activity and lead to higher MVPA estimates in the elderly. Due to the simple implementation of the AQ classifier, researchers can adapt this method in order to enable a comparison of the time spent in different activity levels in the elderly.

To wrap up: Although PA research and associated methods have evolved tremendously, many methodological questions still remain. Whether PA results in older adults are affects by the device selection, its positioning during field studies and the application of post-processing methods for PA classification purposes on the reported PA behaviour has, therefore, been examined in this work (see Research Question and Objecitves in Section 7 of Chapter I). Based on the results in this thesis, reported PA parameters were shown to be strongly affected by the selected device, its sampling position, and the applied data reduction methods, with each aspect limiting the comparability between studies. However, the possibility to compare results is important regarding the possibilities for meta-analyses or the development of PA guidelines based on objective data. The measured PA activity was shown to be dependent on the in-build singal processing of each device. This proprietary output hinders a comparison of PA data acquired with different accelerometers. Therefore, a conversion factor between different measurement positions can only be derived if a similar device type was used. However, even in such a case, association between the position-specific PA data and medical outcomes might still vary. Another drawback of the arbitrary data representations is the requirement for device-specific calibration studies. Moreover, published position-dependent cutpoints were shown to yield to different PA classification.

Given the lack of standardization in the assessment and processing of objective PA data, attempts were made to ease or enabled the comparability of studies in this thesis. The development of conversion factor between different device types was not feasible as it requires detailled knowledge of the device-dependent in-build signal processing algorithms. However, count conversion factors were derived for the GT1M to enable ankle and wrist count comparisons in patients suffering from COPD, and for ankle and hip translations in elderly subjects using the GT3X accelerometer. Regarding the intensity classification, a solely PA-based classificator was developed, which was shown to classify the time spent in MVPA similarly for ankle and hip recordings. This method can enhance the comparability between studies and provide a means for the PA classification in the elderly.

In future, raw data PA measurements can enhance the comparability between devices, enabling the development conversion factors between devices and positions. This will lead to more accurate intensity thresholds.

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Appendix A

Extended Information on Objective I

1. Excursion on the RT3 reliability assessment using structured laboratory protocols and in free-living

Apart from experiments using mechanical devices, the inter-device variability of the RT3 has been assessed by means of subject-mounted laboratory protocols in literature as well. Although not carried out in this thesis, results from published treadmill experiments indicate a similar speed-dependent increase in the RT3 inter-monitor variability:

Powell and Rowlands reported a between-unit variability of <6% during locomotive activities (i.e. treadmill walking and running), and between 8% and 25% during sit-to-stand position in 23 RT3 devices [314]. Furthermore, they reported that the RT3 between-device variability decreased at each activity as intensity increased, consistent with the laboratory results using mechanical apparatus [125, 180, 258, 271, 314]. Inter-monitor differences were found to be evident at 4, 6, 8, and 10 km/h for the Y and Z axes, and at 6, 8, and 10 km/h for the VMU and X axis [314].

In another report on the inter-monitor reliability of the RT3 devices, Reneman and Helmus included three standardized activities of 5 minutes in duration in 6 subjects with 6 attached RT3 devices per subject at the center of the waist using a belt [315]: From treadmill speeds at 3 and 5 km/h, followed by sitting on a chair, an ICC of 0.75 was reported, with a mean person correlation of 0.78 between the six devices.

Vanhelst and colleagues assessed the intra-unit variability using two RT3 accelerometers during nine structured different PA types in 60 healthy adolescents [316], and the CV was found to be greater for activates of sedentary intensity levels (e.g. watching television) (17%) compared to those of light (16.2%), moderate (9.3%) or vigorous intensities (6.6%).

Reports on RT3 reliability assessment in daily free-living:

Recently, Vanhelst et al. assessed the inter- and intra-device reliability in 15 healthy adults during free-living conditions by attaching 5 RT3 and 8 GT1M devices per person to their back, using an elastic belt [279]. Likewise, they found the inter-monitor CV for the RT3 (12.6 - 35.5%) and the GT1M (3.0 s- 10.5%) to decrease with increasing PA, while the variability was statistically lower for the GT1M devices. This agrees to our data from the mechanical setup, as the observed inter-unit CV was higher for the RT3 in both, the slow and faster movement sequence.

2. Excursion on the GT1M reliability assessment using structured laboratory protocols and in daily free-living

In their comparison of the 7164 and GT1M accelerometers attached at the waist in in 116 subjects (age range: 17 to 74) during self-paced indoor circular hallway locomotion at slow, normal, and fast walking, Kozey and colleagues confirmed the aforementioned cross-over effect [239], which has been reported by Routney et al. [194]. The authors reported a very strong correlation for the count output of both device types in general, as well as at all separate speeds, for which a CV of less than 3.2% was observed [239]. However, the step count at slow speeds (56 ± 30 vs. 34 ± 34, $p<0.05$) and the activity count output at medium speeds (3448 ± 1131 vs. 3264 ± 1126, $p<0.05$) were significantly different between both models [239]. However, John and colleagues reported no significant differences between activity counts from treadmill exanimation in 10 subjects using both devices (7164, GT1M) at walking (3, 5, 7 km/h) or running (8 to 20 km/h, incremented by 2 km/h) [274].

Reports on GT1M reliability assessment in daily free-living:

From data of the field assessments (i.e. free-living) in 27 adolescents, who wore the model 7164 (*60-s epoch*) and the GT1M (*5-s epoch*) centrally on each hip for seven consecutive days, Corder et al. revealed that the count output was on average 9% lower in the GT1M compared to the model 7164, and difference in magnitude randomly increased with intensity of activity, due to heteroscedasticity between monitor model outputs [149].

3. Excursion: GT3X reliability assessment using structured laboratory protocols

Using a treadmill protocol from walking to running at 4, 6, 8, 10 km/h, extended by resting and repeated sit-to-stand exercises, with 12 minutes duration per session and 10 minutes break in-between, the inter-variability of 8 GT3X accelerometers, 4 positioned at the left, 4 at the right hip at waist level, were assessed in one subject by Santos-Lozano et al. [317]. All triaxial inter-unit CV in VMU were reported to be <9.2% except for sit-stands at left (14.9%) and right placement sides (23%) and resting, which has been omitted from analysis due to very low mean scores [317]. A high CV range was observed for the X-axis (9.1 - 45.3%) compared to Y (1.4 - 20.4%) and Z (2.2 - 19.6%). The recorded counts were found to be significantly different between each condition, indicating that the GT3X accelerometer is likely to distinguish different modes and intensities of PA [317]. Moreover, it was concluded, that the addition of X and Z axis does not provide further benefits compared to classical uniaxial vertical activity assessments [317].

Appendix B

Extended Information on Objective II

1. Additional Bland-Altman Plots (COPD-Study)

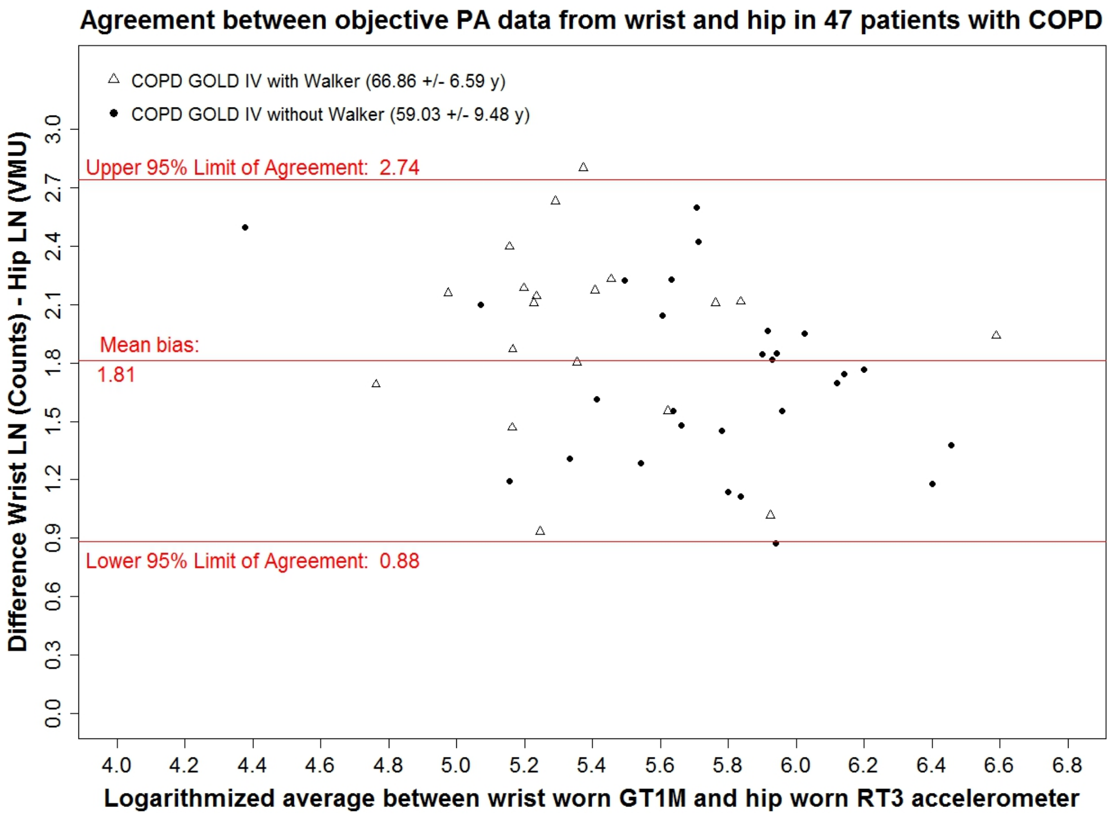

Figure B-1. Log transformed Bland-Altman plot comparing triaxial ankle hip measurements

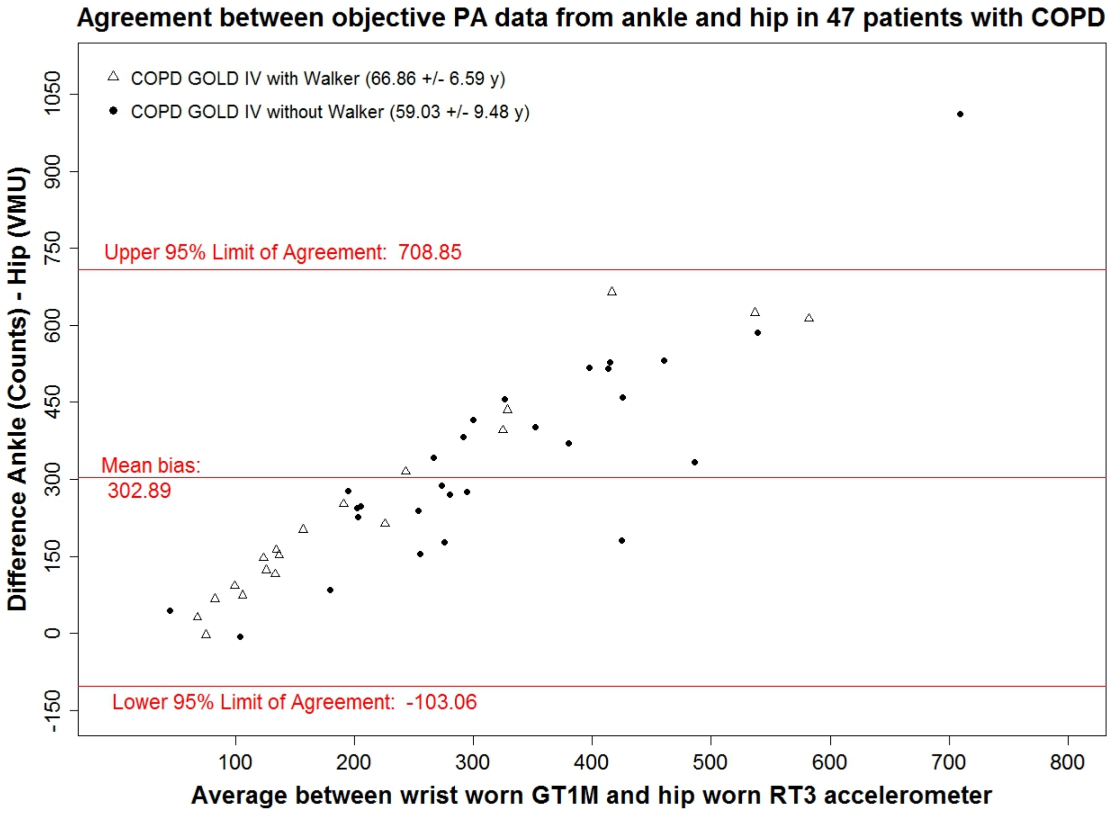

Figure B-2. Bland-Altman plot comparing uniaxial mean ankle and hip measurements

2. Additional Bland-Altman Plots (KORA-Study)

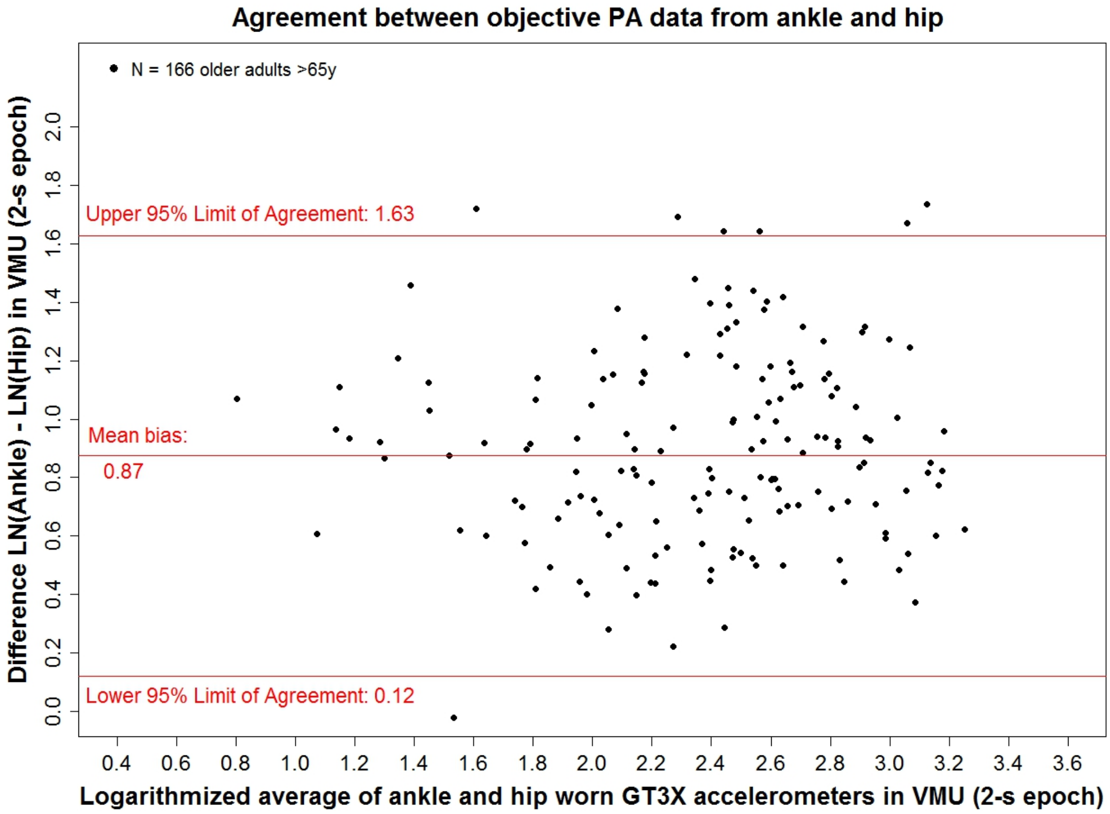

Figure B-3. Log transformed Bland-Altman plot comparing triaxial ankle hip measurements

3. Excursion on the count-based comparison of measurement positions (waist-level)

No statistically significant count difference were found between the left and right using the model 7164 hip in 30 children during three treadmill speeds by Trost et al. [318] whereas, Fairweather and colleagues found small significant difference in 10 subjects over two days using the same device type and positions [273].

Less controversial results were published for comparisons between hip and middle or lower back positions: Using the model 7164 accelerometer during laboratory settings in 28 healthy adults, and in free-living over a week in 34 subjects, Yngve and colleagues found accelerometers counts to be significantly different in the laboratory assessments, with a higher device outputs for the hip, but not in the field study, indicating that placements around the waist do not affect the sensor outcomes [276]. No significant differences were found by Nilsson et al. for the total amount of PA and the intensity levels between recordings at the hip and the back in 16 children, using the same device model [310], and at normal and fast walking using the LSI and Caltrac accelerometers in 17 subjects according to Washburn and Laporte [225].

In a comparison of total vs. upper limb activity in 88 subjects, hip counts were shown to be greater during walking compared to the wrist, but lower for sedentary activities [319]. Eslinger et al. [181] reported comparable results when comparing recordings from GENEA accelerometer in 60 participants from the waist to those placed at the left and right wrist. The wrist positioned devices had a simmilar output, and recorded higher outcomes than did the waist unit for lifestyle but not for walking activies [181].

Swartz and colleagues compared accelerometer recordings (model 7164) at the hip and the nondominant wrist side in 70 healthy adults using a total of 28 randonly assigned activities [116]: The highest accelerometer outputs were reported to be produced by different activites for the hip and the wrist, with the wrist counts being on average *2.3-fold* greater than the hip assessments. However, in 6 activities, namely all four walking tasks (two times slow and brisk walking, with or without load) and the manual and the power mowing, the wrist counts were approximately *0.8-fold* smaller compared to the hip, while being on average *3.4-fold* greater in the remaing 22 activities [116]

4. Excursion on the position-dependence for PAEE predictions

Bouten and colleagues [83] explored the influence of location and position of accelerometers on PAEE predictions by placing devices at the upper ankle, lower ankle, upper arm, lower arm, the chest and lower back segment in two subjects during walking. No significant influences on the correlations with the PAEE estimates were found. According to their report, activity counts from each place of attachment were strongly correlated to PAEE, with the lower back providing the best results in explaining variance in PAEE, followed by the chest and the upper arm when the gravitational component of the accelerometer signal was excluded, and in reversed order if not [83]. However, the correction of the gravital component was stated to be not worth the effort as difference in the accelerometer output were minimal (i.e. explained variance in PAEE for the low back with gravitational correction 89% vs. 85% without) [83]. It was concluded that each location can be used to predict PAEE with high accuracy; however, using multiple accelerometer on several locations only improved PAEE estimates modestly [83].

In another report comparing multiple positions for EE estimates, Leenders et al. [80] attached a single model 7164 accelerometer at the left hip, a Mini Logger 2000 (Minimitter Corp) 2.5 cm anterior, a triaxial R3D sensor on the opposite hip side, and a pedometer (Yamax-Digiwalker-500) on the right anterior superior iliac spine in 28 healthy adults during treadmill examination at speeds from causal to very brisk. From this analysis, they reported that all hip worn sensors showed a moderate to high performance (i.e. Yamax r^2 = 0.60, Mini Logger r^2 = 0.69, model 7164 r^2 = 0.74, TriTrac r^2 = 0.81), while ankle and wrist worn uniaxial Actigraph accelerometer only reached a low predictability (r^2 = 0.27, 0.28, respectively) and did not significantly improve the prediction of EE.

In the validation of the GENEA accelerometer, Eslinger et al. [181] compared PAEE estimates from waist (r=0.87) and both wrist sides (left: r=0.86, right: r=0.83), with the waist being a notch better than the left hip.

In agreement of these results, Swartz and colleagues [116] established EE prediction models from accelerometer recordings (model 7164) at the hip (right anterior axillary line at waist level) and the non-dominant wrist side in 70 healthy adults using a total of 28 randomly assigned activities: Hip counts explained 32% of the variance in MET, wrist less than 5%, and a regression equation from both sensors was reported to only add 2.6% compared with the hip alone when predicting EE [116]. Inline, Kumahara, Tanaka and Schutz [319] assessed EE during a 24-h period in a respiratory chamber in 88 subjects at wrist and hip, finding that the explained variance in PAEE prediction improved only improved by 2% when wrist PA measurements were added to the hip.

Comparing similar positions (i.e. hip and wrist), Chen and colleagues measured EE via indirect room calorimetry and body movements to predict of PAEE during a 24-h period in 60 healthy sedentary female adults, who performed structured exercises and ADL [304]: Each participant wore a triaxial R3D sensor placed in a nylon pouch and secured to a belt, on the right hip at waistline, as well as an uniaxial accelerometer (ActiWatch AW64, Minimitter) at the wrist of the dominant hand. In terms of r^2 (i.e. estimated vs. measured EE), the developed EE prediction model from the hip worn accelerometer was found to be significantly better than the wrist model [304], inline to the reports from Swartz and Leenders [80, 116]. However, the authors concluded that a combined model using data from both accelerometers better estimated PAEE across all intensities compared with the single sensor equations [304].

Contradicting results were published by Melanson and Freedson [49], who found the wrist device to be minimally better in PAEE predictions during treadmill walking when comparing the validity of a hip-placed Caltrac and three model 7164 accelerometers, placed at the non-preferred hip, wrist and ankle sides. The authors noted that count output from both sensor types was moderately to strongly correlated to EE, regardless of the sampling location (wrist r=0.81, hip r=0.80, and ankle r=0.66). EE prediction models using subjects body mass and counts from all three Actigraph accelerometers at ground level as variables were most accurate (ankle & wrist & hip: R = 0.95, Standard Error of Estimate (SEE) = 0.85, 92% explained variance in EE) compared to the best multivariate regression model using data from two sensors (wrist & ankle or wrist & hip: 0.94, 0.75 - 0.93, 85 - 89%) and single sensor equation (wrist: 0.85, 0.86, 82%, respectively) [49].

Another single report, published by Puyau and colleagues [121], found the ankle position for PAEE predictions better than the hip placement, assessing the correlations between EE and activity counts based on data from the model 7164 and the AW16 (MiniMitter) at the right hip and the lower ankle during room respiration calorimetry in 26 children [121]: Mean correlations to EE were found to be higher for the ankle positioned devices (0.73, 0.80), compared to the hip (0.66, 0.78), with the AW16 showing slightly higher associations at both positions.

Despite all difference and indicated contradictions, the validity from left and right hip-positioned model 7164 accelerometers for estimating PAEE was found to be almost identical by Trost and colleagues [318].

Appendix C

Extended Information on Objective III

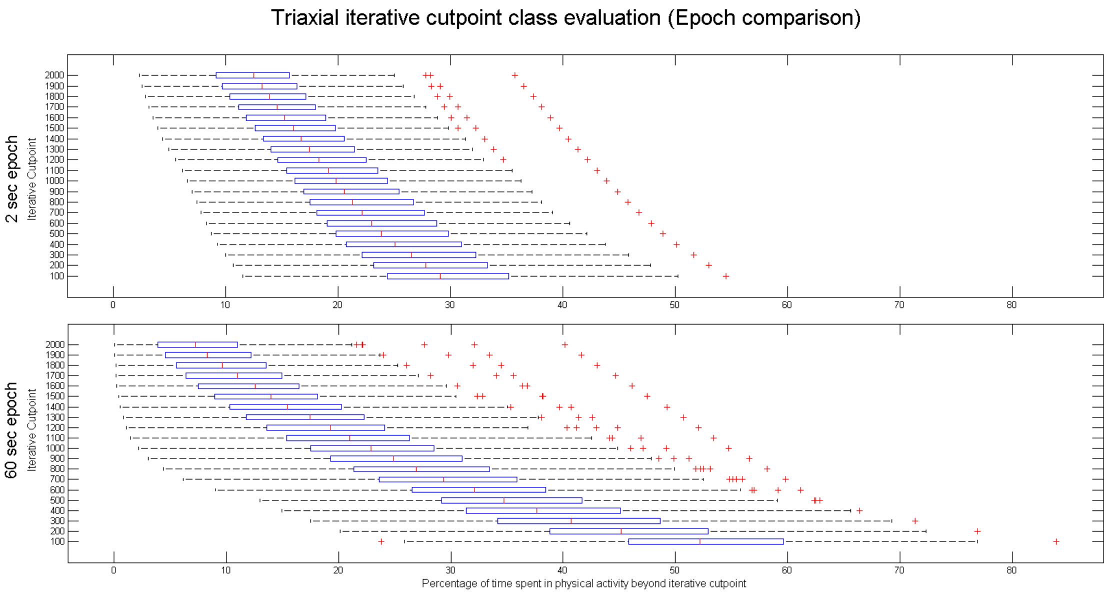

Figure C-1. The effects of artifical triaxial thresholds and epoch selection on the PA classification

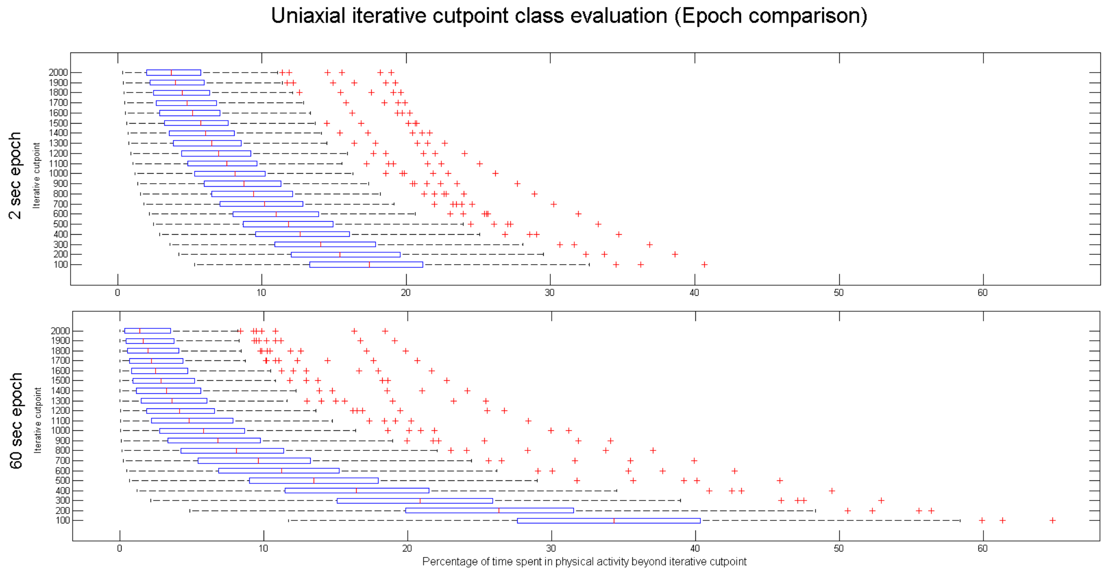

Figure C-2. The effects of artifical uniaxial thresholds and epoch selection on the PA classification

Ref.	Subjects	Sensor	Calibration	
	N (fem.) Age ± SD (Range)	Name Axis Epoch Position	*Method* Protocol	*Statistical Method* MVPA levels
Freedson	50 (25) 23.9 ± 4.0	7164	*Treadmill at 3 speeds (km/h)*:	*Linear regression*
		uniaxial	Slow walking (4.8)	MPA: 1952 - 5724
		60s	Fast walking (6.4)	VPA: 5725 - 9498
		Hip	Jogging (9.7)	VVPA: >9498
Swartz	70 (39) 41 ± 15 (19 - 74)	7164	*4 Treadmill (km/h) &* *24 Lifesytle Activities*:	*Linear regression*
		uniaxial	walking without (4.7, 6.0), and with loads (4.0, 5.6)	MPA: 574 - 4945
		60s	In- & outdoor houshold	VPA.: >4945
		Hip	Family care, recreation	(e.g. tennis, golf)
Hendelmann	25 (15) 40.8 ± 7.2 (30 - 50)	7164	*Self-paced indoor track walking at 4 speeds (km/h ± SD)*:	*Linear regression*
		uniaxial	Leisurely walk. (3.8 ± 0.8)	MPA: 2191 - 6893
		60s	Comfort.walk. (4.8 ± 0.7)	VPA: >6893
		Hip	Mod. & brisk walk. (5.7 &	6.7 ± 0.5)
Lopes	26 (12) 62.6 ± 6.5		*Treadmill at 3 speeds (km/h) & 3 Lifesytle Activities*:	*ROC*
			Resting, seating, standing	MPA: 2400
			walk I (2.5), walk II (5.0), walk III (6.0)	
Sasaki	36 27.8 ± 8.6	GT3X	*Treadmill at 3 speeds (km/h)*:	*Linear regression*
		triaxial	Slow walking (4.8)	MPA: 2690 - 6166
		60s	Fast walking (6.4)	VPA: 6167 - 9642
		Hip	Jogging (9.7)	VVPA: >9642

Table C.1. Extended information on the calibration protocols from selected publications for the MVPA analysis