Objective measurement of activity limitations in complex regional pain syndrome type I; development and application of an Upper Limb-Activity Monitor

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Objective measurement of activity limitations in complex regional pain syndrome type I; development and application of an Upper Limb-Activity Monitor

Het objectief meten van beperkingen in activiteiten van patiënten met complex regionaal pijn syndroom type I; ontwikkeling en toepassing van de Upper Limb-Activity Monitor

Proefschrift

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Contents

1 General introduction

1.1 Introduction

Studies that describe the disorder presently known as Complex Regional Pain Syndrome type I (CRPSI) have been published since the second half of the nineteenth century [1-5]. Since then, a large number of names have been introduced for this disorder, until it was renamed CRPSI: the name the International Association for the Study of Pain (IASP) agreed upon in 1994 [6, 7]. CRPSI is a symptom complex that may have several consequences on everyday life for the person concerned. Such consequences can be classified according to the International Classification of Functioning (ICF, defined by the World Health Organisation) at the three following levels; impaired body function or structure at the level of the body, activity limitations at the level of the person, and participation restrictions at the level of the society [8-10]. As for the consequences of CRPSI on everyday life, CRPSI may comprise a combination of sensory impairments (e.g. neuropathic pain, allodynia, hyperalgesia, hyperaesthesia, anaesthesia), autonomic impairments (e.g. oedema, hyperhydrosis, skin colour change, change of temperature), trophic impairments (e.g. atrophy of skin, nails, muscles and bone), and motor impairments (e.g. dystonia, muscle weakness, spasms, tremor, difficulty initiating movement, and increase of complaints after exercise). In addition to impairments, activity limitations during everyday life (including occupation) and participation problems such as social functioning and role fulfilment have also been described as possible consequences of CRPSI. When CRPSI occurs, it usually follows surgery or trauma and it is generally expressed in the extremities. Its course shows large variability, which makes interpretation of clinical findings and research data difficult.

The controversial syndrome of CRPSI has been increasingly investigated from various perspectives all over the world, and it may be said that health care professionals and researchers become more and more intrigued by this complicated syndrome. This growing interest and curiosity can, for example, be illustrated by the substantial number of theses that has been written about CRPSI during the last ten years in the Netherlands with only one thesis before this period of time, namely in 1972 [11]. In 1995, Veldman [12] provided a comprehensive overview of clinical aspects of CRPSI and analysed some treatment problems from the perspective of general surgery. After that, Kurvers [13] performed a clinical and experimental study on the effects of partial nerve injury on activity and sensitivity of the sympathetic nervous system from the perspective of neurology. Geertzen [14] studied CRPSI from the perspective of rehabilitation medicine; treatment effectiveness in early CPRSI, the role of social life events and psychological aspects, measurement error for range of motion and muscle strength instruments, and long term outcome of CRPSI in terms of impairments, disability, general health and vocational outcome. Oerlemans' [15] thesis described the development of measurement instruments and the outcome of a randomised controlled clinical study on physiotherapy and occupational therapy. This thesis originated from the department of allied health services. Another thesis from

the perspective of surgery by vanderLaan [16] was a clinical and experimental study on the pathophysiological mechanisms of CRPSI. Moesker [17] studied the relationship between plasma carnitine levels and age, and the effects of treatment with ketanserin (relieving vasoconstriction) and carnitine (correcting metabolic changes) from the viewpoint of anesthesiology. Kemler [18] performed a study on the effectiveness of spinal cord stimulation on the intensity of pain, function, depression, sensory characteristics and health-related quality of life in chronic CRPSI, also from the perspective of surgery. A second thesis originating with rehabilitation medicine was the thesis on pain and motor impairments by Ribbers [19]. Ribbers performed clinical studies on pain management, as well as experimental studies on motor impairments and immunology. Once more from the perspective of neurology, vandeBeek [20] described clinical, pathophysiological and etiological aspects of CRPSI with a special focus on mechanisms of development of dystonia and dryness of the eyes.

Even though CRPSI has often been investigated, its etiology and pathophysiology are not yet fully understood. Several theories with respect to the pathogenesis of CRPSI have been proposed throughout the years. Currently, the main theories that are still standing are hyperactivity of the sympathetic nervous system accompanied with peripheral and central sensitisation, an exaggerated inflammatory response with the production of toxic free oxygen radicals and accompanying ischemia, although both theories have been topic of discussion and neither has been irrefragably confirmed. This lack of consensus regarding pathogenesis does not affect the research that is described in the present thesis, however. This thesis is written from the perspective of Rehabilitation medicine, which focuses on the consequences that disorders, such as CRPSI, may have on everyday life and functioning as described in the ICF rather than pathophysiological mechanisms. Since extensive overviews of the different definitions of CRPSI, the heterogeneity with respect to diagnostic criteria for CRPSI, the as yet poorly understood pathogenesis of CRPSI plus the large number of treatment modalities for CRPSI have already provided by others in their theses [12-20], and such overviews can also be found in scientific medical literature, it was considered superfluous to repeat these in this introduction.

The aim of this introduction is to explain what another thesis on CPRSI from the perspective of rehabilitation medicine has to add to the understanding of the complicated entity CRPSI. Since the goal of rehabilitation medicine is regaining and/or maintaining of functionality by decreasing the consequences of a disease or disorder, measurement instruments that focus on everyday life are of fundamental importance. Feasible, reliable and valid instruments that objectively measure during everyday life are essential to provide insight into activity limitations of patient groups. For this reason, a research line on ambulatory monitoring of daily functioning was set up at the Institute of Rehabilitation Medicine in the early nineteen-nineties by Henk Stam and Hans Bussmann. Ambulatory monitoring means continuous observation of free-moving subjects in real-life situations and enables non space-bound data

gathering on postures, transitions between postures, and movements of the human body. Due to technological developments in ambulatory accelerometry at that time it was possible to develop and validate the Activity Monitor (AM) [21-26]. The AM consists of acceleration sensors attached on thighs and trunk, connected to a small recorder worn around the waist. The AM is aimed at the measurement of quantity, quality and physical strain of exclusively mobility-related activities and could not be used for patient groups with an upper limb disorder. Since CRPSI affects the upper limb(s) in approximately half of the patient population, and because an upper limb problem such as CRPSI is thought to negatively affect performance of activities during everyday life with several possible consequences with that respect, it was decided to extend the technique and possibilities of the AM. Moreover, more commonly used techniques of actometers / actigraphy to measure activity of upper limbs (or other body parts) [27-34] were, in our opinion, not specific enough to determine limitations of everyday activity in an upper limb CRPSI population sufficiently. Therefore, a novel Upper Limb-Activity Monitor (ULAM) with two additional acceleration sensors on both forearms was developed. Based on our definition of upper limb usage (i.e. active movement of (parts of) the upper limb(s) in relation to proximal parts, holding and leaning), a framework was compiled to classify several forms of upper limb usage and upper limb non-usage. The development and validation of this ULAM and its application in research with subjects with upper limb CRPSI will be described in the present thesis. In this way, the ULAM will add to the understanding of CRPSI because its consequences on everyday activity can now be determined and quantified objectively. Which, in turn, enables objective determination of treatment effect on everyday activity in future studies which is extremely important for CRPSI patients, research and clinic.

1.2 Outline of this thesis

First, in **chapter 2**, a large number of outcome measures that have been used in CRPSI research was classified according to the International Classification of Functioning (ICF), which describes the consequences of a disease. For each outcome measure a description of concept, operationalisation into variables and instrument was given to determine the availability of preferably objective outcome measures that are relevant for rehabilitation medicine. The lack of relevant outcome measures to determine presence or absence of activity limitations in subjects with CRPSI was the rationale for and starting point of the development of the ULAM, which is described in **chapter 3**. In this chapter, the feasibility of the ULAM to discriminate between upper limb usage and non-usage during performance of mobility-related activities in healthy and disabled subjects was investigated with video recordings as a reference method. **Chapter 4** provides a more extensive technical description of the ULAM. In **chapter 5**, the long-term impact of upper limb CRPSI on general mobility and upper limb usage during everyday life was determined. Several ULAM outcome measures were compared between ten female patients with chronic CRPSI and ten control subjects. The primary aim of **chapter 6** was to determine the

relationship between impairments and activity limitations in a group of thirty chronic CRPSI subjects. To measure the degree of impairment, we used a validated set of five items (temperature, pain 2x, active range of motion, volume) that has been previously developed especially for subjects with upper limb CRPSI and described by Oerlemans [15, 35]. The ULAM outcome measures to determine activity limitations were the mean intensity of upper limb activity of the involved side, the percentage of upper limb activity of the involved side, the proportion of activity between both upper limbs and the percentage of dynamic mobility-related activities. Because the measurement technique of the ULAM clearly differs from what is commonly used in research and clinic with respect to methodological and practical criteria, in **chapter 7**, it is described how several questionnaires that also aim to measure activity limitations (and participation problems) are related to each other and the ULAM. Emphasis was placed on the ULAM because it is important to know its place in the field of outcome assessment. In contrast to the chronic CRPSI patients that were studied in all other chapters, in **chapter 8,** four patients with acute CRPSI are studied, who each wore the ULAM four times for 24 hours. This was done in order to explore upper limb activity over time as measurd with the ULAM, and to compare the time course of the ULAM outcome measures to the time course of other outcome measures at the impairment and activity levels. Finally, in the general discussion in **chapter 9**, some of the issues already discussed will be brought together to discuss them from a more general viewpoint and some new issues will be introduced.

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2 Outcome measures for complex regional pain syndrome type I: an overview in the context of the international classification of impairments disabilities and handicaps

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2.1 Abstract

Purpose: To determine the availability of relevant and objective outcome measures concerning Complex Regional Pain Syndrome Type I (CRPSI) for Rehabilitation Medicine. **Method:** Outcome measures were classified according to the International Classification of Impairments, Disabilities and Handicaps. For each outcome measure a description of concept, operationalisation into variables and instrument was given. We performed a PUBMED MEDLINE search (1980-1998) using the following keywords: complex regional pain syndrome, reflex sympathetic dystrophy, impairment, disability, handicap, (long-term) outcome and effect/efficacy. **Results:** Most outcome measures were concentrated on impairments, whereas measures at the level of disabilities and handicaps, the most relevant levels for rehabilitation medicine, were mentioned in very few studies. Objective outcome measures were merely found at the level of impairment. **Conclusion:** The results indicate a need for the development of relevant outcome measures at the level of disabilities and handicaps that can objectively measure treatment efficacy for CRPSI.

2.2 Introduction

Complex Regional Pain Syndrome Type I (CRPSI; also known as Reflex Sympathetic Dystrophy) is a poorly understood and not well defined symptom complex comprising a combination of sensory, trophic, autonomic and motor impairments [1, 2]. The syndrome usually follows surgery or trauma, and is generally expressed in the extremities. In addition to the impairments, CRPSI can lead to serious disabilities in performing activities of daily life and handicap [3, 4]. In the acute phase of CRPSI, pain in particular may constitute a major cause of disability and/or handicap, whereas during the later stages CRPSI associated motor impairments, together with pain, are thought to bring about disabilities and/or handicaps [1, 5, 6]. The complex entity of CRPSI has often been investigated, leading, however, to confusing and conflicting results and theories about the aetiology and pathophysiology [7]. As the disease is not yet understood, plus the fact that each speciality has its own discipline-specific approach, a wide variety of treatments (more than 50) are found in literature [8]. As a consequence, numerous measures to determine treatment outcome have been described.

In the present paper, the numerous measures that are used to determine treatment outcome in CRPSI research and clinical practice will be classified. So far, one of the difficulties in interpreting reports on treatment efficacy in CRPSI, has been the (objective) quantification of patient findings and the lack of uniform measurement of treatment outcome [9, 10]. Classification of outcome measures may not only be a useful tool to indicate the extent of the (obvious) inconsistency in defining treatment outcome in CRPSI research. The main aim of classifying outcome measures in the present paper is to determine whether relevant and objective outcome measures for rehabilitation medicine are available. It is clear that objective outcome measures are preferable to subjective outcome measures; the latter are more likely to endanger reliability and validity of measurements. As for the relevance of outcome measures: outcome measures are considered most relevant for rehabilitation medicine when they concern the goal of rehabilitation, that is regaining and/or maintaining of functionality by decreasing the consequences of a disease [11, 12]. Outcome measures concerning impairments are considered less relevant for rehabilitation medicine, especially since the relation between the consequences of a disease is often found to be rather ambiguous [13-15].

The international classification of impairments, disabilities and handicaps (ICIDH) [16] is an often-used classification, in which three hierarchical levels of the consequences of a disease on everyday life of patients are distinguished. Outcome measures on the level of impairments, disabilities and handicaps concern the consequences of diseases at the level of the body, the person and the person as a social being, respectively. As for CRPSI, the consequences at the ICIDH level of impairments can be categorised into sensory impairments (e.g. neuropathic pain, allodynia,

hyperalgesia, hypesthesia, anaesthesia, dysesthesia, hyperpathia), autonomic impairments (e.g. oedema, hyperhydrosis, skin colour change, change of temperature), trophic impairments (e.g. atrophy of skin, nails, muscles and bone), and motor impairments (e.g. dystonia, weakness, spasms, tremor, difficulty initiating movement, increased tone and reflexes, and increase of complaints after exercise) [8]. Disabilities associated with CRPSI are those directly related to the involved extremity (e.g. problems with getting dressed with upper extremity CRPSI or climbing stairs with lower extremity CRPSI) and general disabilities in daily functioning (e.g. slow performance of activities of daily living). Handicaps associated with CRPSI concern limitations in social functioning (e.g. alienation) and problems with role fulfilment (e.g. a grandmother with CRPSI cannot play with her grandchild), as a consequence of pain, other impairments or disabilities [17]. From this list of consequences it becomes clear that CRPSI encompasses all three levels of the consequences of a disease as described in the ICIDH. Although some discussion continues about the sometimes unclear distinction between the theoretical levels of the ICIDH [18, 19], we consider the ICIDH framework useful to classify outcome measures in order to make a statement on availability of relevant and objective outcome measures for rehabilitation medicine.

2.3 Method and data sources

To obtain data, a PUBMED MEDLINE search (1980-1998) was performed using 'complex regional pain syndrome', 'reflex sympathetic dystrophy', 'impairment', 'disability', 'handicap', '(long term) outcome' and 'effect' as keywords. The initial idea of only using randomised clinical trial studies and quasi-experimental studies was not feasible given the relatively small number of studies performed up till now. Therefore, non-experimental and transversal studies with descriptions of one or more outcome measures were also included. Only journal articles in the English or Dutch languages were used. Publications without MEDLINE abstract and studies with less than 8 subjects were excluded. To provide insight in the kind of research that is performed concerning CRPSI, we studied some characteristics of the publications used for classification of outcome measures.

To determine the success of treatment in a reliable and valid manner, well-defined and methodologically sound outcome measures are of major importance [20-22]. In general, an outcome measure can be considered methodologically sound when the theoretical definition of the outcome measure (at the conceptual level) is clearly operationalised into one or more variables [21]. Moreover, an appropriate instrument to assign a value to variables has to be chosen [21]. In this study, we represented each outcome measure in a scheme, in which the concept to be measured, the operationalisation of this concept into variable(s), and the instrument to assign a value to the variables were described. It was not our aim to take reliability and validity of measurements with different instruments into account. Each outcome measure was classified according to the three levels of a consequence of a disease

(impairment, disability and handicap). The earlier described categorisation of impairments [8] was also applied in the tables.

Each publication was analysed to find information about concept, operationalisation of concept into variable(s), instrument and level of the ICIDH classification of the described outcome measures. Almost identical descriptions of concept, operationalisation and/or instrument of two or more outcome measures in different publications were represented as one outcome measure to limit the size of the tables. In case the concepts of outcome measures in different publications were similar, but different operationalisations and/or instruments were described, the outcome measures were shown separately.

2.4 Results

To provide insight in the kind of research that is performed concerning CRPSI, some characteristics of the studies were described (table 2.1). In addition to information about the first author and year of publication, studies were categorized as either transversal or longitudinal depending on the number of measurements. Transversal studies were categorized as either retrospective or prospective depending on whether measurements are done with data that already existed before defining the research questions or yet to be acquired data. Longitudinal studies were categorized as either experimental or non-experimental depending on whether the researcher actively intervenes in the research process or not. Specification of the type of treatment and research field, based on the first author, were presented, as well.

Table 2.1: Overview of several aspects of the publications studied.

Author(s) (+ref. no.)	*Year*	*Design†*	*Subjects (n)*	*Type of treatment*	*Research field*
Atkins *et al.*[39]	1990	tran., pros.	60	No treatment	Orthopaedic Surgery
Bickerstaff *et al.*[41]	1991	long., exp.	20 (+20 control)	Nasal calcitonine (Sandoz Basle)	Hum. Metabolism & Clin.Biochemistry
Bickerstaff *et al.*[42]	1994	long., non-exp.	274	No treatment	Hum. Metabolism & Clin.Biochemistry
Braus *et al.*[66]	1994	long., exp.	36	Oral corticosteroids (methyl prednisolone)+daily physical therapy	Neuropathology
Cortet *et al.*[30]	1997	long., exp.	23	Intravenous 2nd generation biphosphonate pamidronate (APD)	Rheumatology
Davidoff *et al.*[10]	1988	long., exp.	17	Exercise program (8 weeks)+corticosteroids or sympathetic blockade	Rehabilitation Medicine
Field *et al.*[37]	1992	long., exp.	55	Intravenous regional anaesthesia+cast immobilisation (4 weeks)	Orthopaedics
Field *et al.*[38]	1993	long., exp.	17	Serial regional intravenous guanethidine blockade	Orthopaedics
Geertzen *et al.*[40]	1994	long., exp.	26	Regional intravenous ismelin blocks (n = 13)+radical scavenger DMSO (n = 13)	Rehabilitation Medicine
Geertzen *et al.*[15,45]	1998	tran., retro.+pros.	65	No particular treatment (follow-up after various treatments)	Rehabilitation Medicine
Gobelet *et al.*[9]	1991	long., exp.	33 (+33 control)	Physical therapy combined with calcitonine	Rehabilitation Medicine
Hamanci *et al.*[26]	1996	long., exp.	24 (+16 control)	Intramuscular salmon calcitonine treatment	Rehabilitation Medicine
Hassenbusch *et al.*[32]	1996	long., exp.	30	Peripheral nerve stimulation	Neurosurgery
Hord *et al.*[34]	1992	long., exp.	12	Intravenous regional bretylium and lidocaine	Anaesthesiology+Orthopaedics
Kaplan *et al.*[33]	1996	long., exp.	53	Intravenous regional guanethidine Bier block	Anaesthesiology+Pain Management
Kozin *et al.*[78]	1981	tran., pros.	48 (+16 control)	No particular treatment	Radiology
Langendijk *et al.*[25]	1993	long., exp.	37	Dimethylsulfoxide DMSO (50%) in a fatty cream	Pharmacy
Mailis *et al.*[62]	1997	long., exp.	15 (+21 control)	Intravenous administration of sodyum amytal, a medium action barbiturate	Pain Investigation Unit
Muramatsu *et al.*[29]	1998	long., exp.	17	Movelat cream manipulation (MIRA) therapy and regional anesthesia	Orthopaedic Surgery
*Poplawski *et al.*[27]	1983	tran., retro.+ pros.	62	No particular treatment	Orthopaedics
*Poplawski *et al.*[27]	1983	long., exp.	27	Regional intravenous block (+corticosteroids) followed by physical therapy	Orthopaedics
Ramamurthy *et al.*[28]	1995	long., exp.	30 (+30 control)	Intravenous regional block with guanethidine	Anaesthesiology
Rauck *et al.*[36]	1993	long., exp.	26	Epidural clonidine	Anaesthesiology
Robaina *et al.*[73]	1989	long., exp.	35	Transcutaneous electrical nerve stimulation + spinal cord stimulation (n = 6 of 35)	Neurosurgery+Anaesthesiology
Schwartzman *et al.*[24]	1997	tran., retro.	29	Transthoracic or lumbar sympathectomy	Neurology
Subbarao *et al.*[68]	1981	tran., retro.+ pros.	77	No particular treatment (follow-up after various treatments)	Rehabilitation Medicine
Tu *et al.*[44]	1994	tran., pros.	8	Surgical sympathectomy	Radiology
Vande Streek *et al.*[63]	1998	tran., pros.	?	No treatment	Nuclear Medicine
Veldman *et al.*[35]	1995	long., exp.	71	Injection of bupivacaine+methylprednisolone for RSD shoulder complaints	Surgery
Zuurmond *et al.*[31]	1996	long., exp.	16 (+15 control)	Dimethylsulfoxide in a fatty cream	Anaesthesiology

* The study of Poplawski *et al.* consists of two parts with distinct designs that are shown separately.
† long. = more than one measurement, tran. = one measurement, retro. = data already available, pros. = data yet to be aquired, exp.= active intervention, non-exp. = no active intervention

2.4.1 Outcome measure at the level of impairment

Sensory impairments
A variety of outcome measures at the ICIDH level of sensory impairments were found (table 2.2). However, only few of the earlier described familiar CRPSI-associated sensory impairments [8, 23] were used as concepts of outcome measures. It is clear that the concept of pain is most frequently used in CRPSI research and practice.

Although there was general acceptance of pain as the main concept, operationalization of this concept differed considerably (table 2.2). In some publications, pain was operationalized by simply describing the type [24] or location [9, 10] of pain. Other operationalizations of the concept of pain were focused on the level of pain, indicated by using the terms degree [25], score [26], intensity [10, 15, 27, 28] or severity [27-29] of pain. Changes in the level of pain were indicated by usage of the terms decrease [30], change [31-33], relief [25, 34, 35] or reduction [32, 36]. These differences in operationalization were not related to the design of the study. From a methodological perspective, it may be expected that pain was operationalized as changes in pain level in longitudinal studies and as pain level in transversal studies, which was, however, not consistently done. In general, operationalizing pain was considered obvious and was not extensively described. In addition to pain, tenderness was the only other sensory impairment that was used as an outcome measure concept in more than one publication. As for the instruments to measure pain, it appeared that pain was mainly measured by scales and questionnaires and virtually no objective instruments were used.

Table 2.2: Outcome measures used in CRPSI research to measure sensory impairments. Insufficient descriptive detail in publications is represented by a question mark.

Concept	*Operationalization*	*Instrument(s)*	*Reference no.*
Pain	Burning pain	Visual analogue scale (VAS)	24
Pain	Change in level of diffuse pain	Visual analogue scale (VAS)	31
Pain	Change in level of diffuse pain	Examination: pressure exerted over tendons	35
Pain	Change in level of mechanical allodynic + spontaneous pain	Verbal digital scale (0–10)	32
Pain	Change in level of pain	Verbal digital scale (0–10)	30
Pain	Change in level of pain	Visual analogue scale (VAS)	25, 30, 34
Pain	Change in level of pain	4-point scale	33
Pain	Change in level of pain	Question(naire) or patient's estimate	32
Pain	Change in level of sensory, affective + miscellaneous pain	McGill pain questionnaire (PRI)	36
Pain	Level of pain	Visual analogue scale (VAS)	10, 26, 36, 40, 47, 73
Pain	Level of pain	McGill pain questionnaire	28, 73
Pain	Level of pain	3, 4 or 6-point scale	27, 29, 66
Pain	Presence or absence of pain	Question(naire) or patient's estimate	39, 41, 42
Pain	Joint pain (at rest or during movement) by palpation	4 or 5-point score	9, 10
Pain	Affective, sensory + evaluative aspects pain	McGill pain questionnaire (PRI + NWC)	10
Pain	Pain as part of general health	RAND-36 questionnaire	79
Hyperalgesia	Intensity of hyperalgesia	6-point scale	66
Tenderness	Tenderness of wrist, MCP, PIP, DIP	Investigation	26
Tenderness	Bony tenderness in response to load compared to other hand	Dolorimeter ratio (kg/m^2)	37–39, 41, 42
?	Moving two-point discrimination volar tip thumb + index finger	Disk Discriminator (mm)	79

Autonomic impairments

Autonomic impairments of CRPSI patients can be categorized as changes in temperature, changes in skin colour, changes in volume and changes in sweat secretion [8]. These four autonomic impairments associated with CRPSI have all been used as outcome measure concepts (table 2.3): a large variety of 'autonomic' outcome measures were found. Some authors consider autonomic impairments as a cluster of signs or symptoms, which was represented by conceptual umbrella terms, such as 'vasomotor instability' [29, 37-39] or 'vasomotor changes' [32]. Most authors, however, did not use such umbrella terms. For clarity, the initial concepts of tumour [31], oedema [9, 15, 26, 40] and swelling [10, 25, 27, 29, 37-39, 41, 42] were grouped as volume. Operationalizations shown in table 2.3 are original operationalizations and were not renamed. Of the autonomic impairments, (changes in) volume was clearly most often used as concept of outcome measures.

Table 2.3: Outcome measures used in CRPSI research to measure autonomic impairments. Insufficient descriptive detail in publications is represented by a question mark. The bottom three rows represent outcome measures that do not fit into the categories of Kurvers (1997).

Concept	*Operationalization*	*Instrument(s)*	*Reference no.*
skin temperature			
calor	elevated skin temperature compared to other side	dorsal side observer's hand + patient's estimate	25, 31
?	bilateral skin temperature	?	28
vasomotor instability	abnormal temperature affected hand	2-point questionnaire	42
calor	2-point temperature profile skin compared to other side	?	10
vasomotor instability	(7-point) temperature profile skin compared to other side	portable thermography	32, 38
?	skin temperature response (to electrical stimulation)	thermometer	34, 62
skin colour			
discoloration	difference in skin colour compared to other side	3-point scale	15, 40
rubor	difference in skin colour compared to other side	observation/examination	25, 31
vasomotor tone changes	change in skin colour compared to other side	examination on 4-point scale	32
vasomotor instability	abnormal skin colour affected hand	2-point questionnaire	42
volume			
volume	diffuse oedema	observation/examination	31
volume	degree of oedema compared to other side	observation	25
vasomotor tone changes	degree of swelling compared to other side	observation	32
volume	degree or severity of oedema dorsal side throughout day	4-point scale	29
autonomic problem	degree or severity of distal oedema	4-point scale	66
volume	degree or severity of oedema	3 or 4 point scale (examination)	9, 15, 26, 40
volume	volume hand compared to other side	ratio water displacement (+ assessment)	10, 37–39, 41, 4
volume	digital circumference compared to other side	arthrocircameter or measuring tape	15, 27, 38, 39
volume	skin thickness compared to other side	skinfold calipers on dorsum hand (mm)	39
perspiration			
vasomotor instability	hyperhidrosis affected hand	2-point questionnaire	42
?	hyperhidrosis affected hand compared to other side	observation	25
?	bilateral electrodermal activity from sweat glands	electrical stimulation and macroelectrode recording	62
vasomotor instability	response to external factors/environmental changes	questionnaire	37–39, 42
?	asymmetrical blood flow in extremities	scintigraphy	43
vasoconctrictor tone	blood flow distal artery muscle affected side	colour duplex Doppler ultrasound	44

Operationalizations of the autonomic impairment concepts, as well as the instruments to measure autonomic impairments were not uniform. Part of the outcome measure operationalizations were expressed as a ratio of affected and unaffected side, whereas the other part only took the affected side into account. The three outcome measures at the bottom of table 2.3 were separated from the other outcome measures. This was done because they could either be considered as an outcome measure with a general operationalization of more than one of the four autonomic impairments [37-39, 42, 43], or because none of the four autonomic symptoms were mentioned specifically in the text [44].

Trophic impairments

Only few outcome measures at the level of trophic impairments were found (table 2.4). Nearly all of these outcome measures were used by highly specialised disciplines, such as Nuclear medicine and Human metabolism & clinical biochemistry.

Table 2.4: Outcome measures used in CRPSI research to measure trophic impairments. Insufficient descriptive detail in publications is represented by a question mark.

Concept	*Operationalization*	*Instrument(s)*	*Reference no.*
trophic changes	degree of trophic changes	examination, 4-point scale	32
?	abnormal hair or nail growth compared to other side	observation	25
skeletal changes	trabecular bone evaluation	radiographic scoring system	41
skeletal changes	cortical bone evaluation of metacarpals	morphometry	41
skeletal changes	bone mineral density compared to other side	Nuclear Data ND 1100 scanner	41
dynamic bone changes	periarticular bone uptake compared to other side	Three-Phase-Bone-Scan (TPBS)	63
osteoporosis	demineralisation	radiography	43
?	increased periarticular activity compared to other side	scintigraphy	43

Motor impairments

A large number of 'motor' outcome measures at the ICIDH level of impairments were found (table 2.5). Lack of unity in defining outcome measures was very obvious with motor impairments: concepts, operationalization as well as instruments differed enormously. Studies mainly focused on operationalization and instruments mentioning the concept to be measured. Information about concepts had to be extracted from all sections of the publications, which made some interpretation unavoidable. In several publications [10, 15, 38, 41, 42] information about concepts could not be found.

Range of Motion (ROM) was the most frequently adopted operationalization of motor impairment outcome measures. Measurement of active or passive ROM was not always specified. Moreover, ROM was not consistently measured in the same joints of upper or lower extremity. In one study [29] the instrument to determine ROM was not specifically mentioned, which forces one to make assumptions when trying to classify the different outcome measures.

Table 2.5: Outcome measures used in CRPSI research to measure motor impairments. Insufficient descriptive detail about concepts in publications is represented by a question mark.

Concept	*Operationalization*	*Instrument(s)*	*Reference no.*
loss of motor function	pinch grip, elbow flexion and shoulder abduction	Motricity index	26
weakness	grip strength compared to other side	hand held strength gauge	41, 42
joint function	grip strength compared to other side	sphygmomanometer	39
?	grip strength compared to other side	dynamometer	15,38
motor deficits	degree of motor weakness	4 or 6-point scale, examination	32, 66
?	stiffness in fingers	questionnaire	41, 42
loss of motion	stiffness during day	4-point scale on palpation or complaints	27, 29
functio laesa	limited active ROM	observation/examination	31
inflammatory symptom	limited active or passive ROM shoulder	observation/examination	35
motor function	painless passive ROM shoulder	4-point scale with goniometer	66
motor function	passive ROM shoulder, wrist and MCP	goniometer	26
contracture	ROM PIP joint, severity compared to other side	4-point scale	29
joint function	ROM shoulder, elbow and finger	clinical assessment and goniometry	39
joint mobility	ROM fingers	goniometry	37
loss of mobility	ROM compared to other side	4-point mobility scale	9
stiffness	ROM all finger joints compared to other side	goniometer	38
loss of motion	ROM digital joints compared to other side	goniometer	27,28
motor function limitation	ROM fingers when making fist compared to other side	measurement tape	15, 40
motor function limitation	ROM thumb	6-point scale	15,40
motor function limitation	active ROM shoulder + elbow + wrist compared to ROM normal ADL	goniometer	15
?	active ROM compared to other side	measurement tape and goniometer	10

2.4.2 Outcome measures at the level of disability and handicap

Relatively few studies expressed the outcome of a CRPSI treatment in terms of disability and/or handicap (table 2.6). Therefore, we decided to describe the outcome measures of these two levels together. Concepts as well as operationalizations of outcome measures were described in very different ways, although the majority of outcome measure concepts at the level of disabilities were related to occupation. Instruments to assess 'disability' and 'handicap' were scales and questionnaires.

Operationalization into activity level categories in ordinal scales was not always consistent and scales or interviews sometimes contained items with different levels of abstraction [32, 42] including some items at the level of impairments, which made interpretation of treatment outcome difficult. Some instruments (e.g. RAND-36 Questionnaire) contain items at both the level of disabilities and at the level of handicaps [45]. Topics of the structured interview were not always reported [9].

Table 2.6: Outcome measures used in CRPSI research to measure disabilities and handicaps. Insufficient descriptive detail in publications is represented by a question mark.

Concept	*Operationalization*	*Instrument(s)*	*Reference no.*
Disability			
activity level	rating of restriction of activities of daily living related to full-time job (100%)	11-point scale	32
status of daily activities	improvement in certain daily activities	interview 3rd party	32
daily activities	difficulties with using hands last 24 hrs (in upper extremity CRPS)	Visual analog scale (VAS) All Daily Activities	40
hand function	among others: restriction of everyday activities + performing simple tasks	de Bruijn (1987) scoring system	42
vocational or educational status	changes in vocational or educational status compared to premorbid level	questionnaire	68
work status ?	ability to perform occupational activity or ADL after 8 weeks of treatment	analysis/interview	9
employment status	changes in job and/or working time compared to prior CRPS	questionnaire, interview	27
occupational status	long-term changes in occupation	structured interview, 4 categories	45
Handicap			
functional social activity level	subjective grade of ability to return to premorbid levels	questionnaire	68
general health status	9 subscales (e.g. social functioning, role limitation, pain, mental health)	RAND-36 questionnaire	45

2.5 Discussion and conclusion

2.5.1 Level of impairments

Sensory impairments

The almost unanimous choice of pain as the main 'sensory' outcome measure concept may be attributed to the fact that pain is often described as the most unpleasant feature of CRPSI for the majority of patients [1, 5, 8, 46, 47]. The large variability of other sensory impairments between patients and the lack of valid and reliable instruments may also play a role in this choice.

An important aspect in the evaluation of pain that was not taken into account in any of the studies is that, in CRPSI, acute pain in early stages of the disease most likely changes into chronic pain in later stages. Acute and chronic pain can be considered as different clinical entities [48], which may not involve the same dimensions [49, 50]. Therefore, one has to carefully consider the moments of measurement and the choice for a specific instrument to determine long-term pain evaluation in CRPSI; not all instruments are designed to reflect these different dimensions of acute and chronic pain.

To clearly classify the numerous outcome measures, we tried to fit each outcome measure in the scheme of concept, operationalization and instrument. With respect to the operationalization of the outcome measure concept of pain, this gave rise to some difficulties because authors usually failed to present an explicit operationalization. It appeared that the majority of authors consider pain as a clear-

cut concept, thus making some interpretation unavoidable. We realise that one may ask whether 'level of pain' and 'changes in level of pain' are actually operationalizations of pain, but in these cases thorough analysis of the publications failed to provide more detailed information.

Pain clearly is a very complex and diverse concept that can be interpreted or classified in several ways [51]. In one publication, pain was operationalized as mechanical allodynia and spontaneous deep pain [32]. These operationalizations, however, are both discrete sensory impairments in the framework of the ICIDH. In contrast to this framework, in which pain is considered as one of the sensory impairments in CRPSI, pain can also be considered as a separate entity [10, 52], that can be classified into several levels of abstraction: nociception, pain, suffering and pain behaviour [51, 53]. Because pain is often described as the most unpleasant feature of CRPSI and especially since it is the impairment that particularly leads to disability (which can be described in terms of pain behaviour), one may consider this latter classification also applicable to classify the CRPSI outcome measures. Although we acknowledge that the ICIDH is not ideal to classify the concept of pain, there are two reasons why we think the ICIDH is the most suitable framework to classify the numerous outcome measures. First, pain clearly is not the only consequence of CRPSI; using this other classification would not do justice to the other impairments that are found in CRPSI. Second, pain is not present in all CRPSI patients [54, 55]; about ten percent of the patients do not have pain, which makes the alternative classification not applicable to determine outcome for this part of the patient group.

Pain and other sensory impairments were usually measured by scales and questionnaires. A major disadvantage of these instruments is their subjective character [56, 57]. Another problem with measuring pain in CRPSI is that pain of individual patients can change often during the day and the pain level between patients can also vary widely [58]. The instruments to measure pain are not capable of detecting variation in pain level throughout the day. A possibility to overcome these problems is to evaluate 'pain behaviour' in addition to pain as a sensory impairment [51, 53, 59], especially because latest technological developments provide possibilities to objectively measure pain behaviour [60]. For rehabilitation medicine, measuring the concept pain behaviour operationalized as (changes in) the activity pattern is more relevant than measuring pain alone because pain behaviour is an outcome measure at the ICIDH level of disability and not at the level of impairment.

Autonomic impairments

It is clear that the number of 'autonomic' outcome measures by far exceeds the number of other outcome measures at the level of impairments, with the exception of pain. The popularity of 'autonomic' outcome measures together with 'sensory' outcome measures may be related to the current ideas concerning aetiology and pathophysiology of CRPSI. Sensory and autonomic impairments represent the most important features of an inflammatory reaction (dolor, calor, rubor and tumor) which

are thought to play a role in the acute phase of CRPSI [55, 61]. The acute phase is the focus of the majority of CRPSI studies. However, the greater part of CRPSI patients in rehabilitation practice in the Netherlands are already in the later stages of the disease, which makes autonomic outcome measures less relevant for determining treatment efficacy. Autonomic outcome measures are frequently measured by subjective purpose-formulated scales or questionnaires, although objective instruments are available [15, 27, 32, 34, 38, 39, 62].

Trophic impairments

Trophic impairments are not often used as outcome measures. This may be because these impairments are only found in a minority of CRPSI patients [43, 55] which makes 'trophic' outcome measures a less logical choice. Even though objective measurement of trophic impairments is possible, a major disadvantage is that instruments are usually costly and not always available. Moreover, objective measurement requires trained personnel. Trophic impairments are generally measured for diagnosis of CRPSI and not to determine the effect of a treatment, although some authors have investigated the possibilities of using them as outcome measures [63]. It was concluded that the bone scan could be part of an algorithm rather than a discrete outcome measure. Trophic impairments are closely related to autonomic impairment; changes in the nutritional state are one of the consequences of changes in local blood flow, which, for some researchers, may make use of these measures redundant.

Motor impairments

Whether active range of motion (AROM) or passive range of motion (PROM) was measured was not always clear. This is a very important issue, however, because measuring PROM is assumed to be not appropriate for patients with CRPSI since the pain threshold is generally reached quickly [58]. In addition, ROM measurements in CRPSI patients are subject to considerable variation [64], which may have an impact on the objectivity and reliability of measurements. This is also true for grip strength: it was found that for objective medical reports on hand muscle strength, it is recommendable to measure three times in more than one session and, if possible, by more than one person [65]. In the studies that used grip strength as an outcome measure, only few actually used a (potentially) objective method [15, 38, 39, 41, 42]. In only one of these studies [15] was information presented about repeated measurement. Even though motor impairments form a well-known aspect of CRPSI, epidemiological data on this matter are still scarce [6]. Whether this is a matter of lack of interest or lack of objective, reliable and valid instruments is not clear. However, it may be that researchers usually focus on the early stages of CRPSI, whereas motor impairments become more obvious in the later stages.

Sum scores

In order to indicate the 'overall' condition of patients, in several studies, scores were assigned to a number of outcome measures and added to sum scores called reflex

sympathetic dystrophy-score [15, 40], also reflex sympathetic dystrophy-score [25, 31] or shoulder hand syndrome-score [66]. Reflex sympathetic dystrophy (RSD) and shoulder hand syndrome (SHS) are two of the numerous names that are used to describe the disease. In the present study, we decided to use the term CRPSI because this is the term the International Association for the Study of Pain recently agreed upon [67]. Sum scores were made up of a varying numbers of outcome measures that usually had different relative contributions to the total score. This may be related to the discipline involved (e.g. ROM is more important to a rehabilitation specialist or an orthopaedist, whereas changes in temperature may be more relevant for an anaesthesiologist). In these five sum scores, pain was generally considered (one of) the most important concept(s) of outcome measures. In the selection of other outcome measures, however, little consistency in order of importance was found which makes interpretation of treatment outcome and comparison of different studies very complicated. An additional sum score, the impairment level sum score (ISS)[58], was published after the initial MEDLINE-search. In this weighted sum score, pain is also the most important outcome measure concept.

Since the consequences of CRPSI encompass all three levels of the ICIDH, assessing treatment outcome by sum scores of different outcome measures at different ICIDH levels can be considered as a logical strategy. However, with the exception of the variable VAS-ADL in one of the RSD scores [15, 40] and the affective and evaluative variables of the McGill pain questionnaire in the impairment level sum score [58], all of the variables in these scores were exclusively on the level of impairments. Variability among patients regarding the functional impact of various impairments was reported as a reason to solely focus on the level of impairments [58].

2.5.2 Level of Disabilities and Handicaps

The small number of ‘disability’ and ‘handicap’ outcome measures that were found, were assessed by means of scales and questionnaires; no objective instruments were used. About half of the outcome measures at the level of disability and/or handicap were employed by researchers in the field of rehabilitation (table 2.1). Apparently, outcome measures at these levels are also considered relevant by researchers in other research fields. With the exception of two studies [27, 68], all studies in which outcome measures at the ICIDH level of disabilities and/or handicaps in CRPSI research were used are written in the last few years. This may also be related to increasing general recognition that the evaluation of treatments should include assessment of a broad set of outcome measures that are important to patients, especially functionality (level of disabilities), role performance (level of handicaps) and quality of life [69-72].

Clearly, assessing treatment outcome at the level of disabilities and/or handicaps is difficult: particularly when it comes to objective outcome measures. In one study [73], it was mentioned that the outcome measures ‘increase in hours of sleep’ and ‘increase

in physical activity' were taken into account. However, the authors failed to report on these outcome measures, which may also indicate that objectively assessing outcome at these two levels is considered relevant but difficult.

2.5.3 General discussion and conclusion

The aim of the present paper was to determine the availability of relevant and objective outcome measures concerning CRPSI for rehabilitation medicine. It appears that there clearly is a gap in the availability of these measures. Gaps in availability of appropriate outcome measures may be the starting point for the development of new instruments that are capable of objective measurement at the higher levels of the ICIDH. This does not implicate that we consider outcome measures at the level of impairment irrelevant for rehabilitation medicine. These outcome measures would be very relevant if there were an unambiguous relationship between impairments and changes in functionality; no clear evidence for such a relation in CRPSI has yet been found. Studies investigating whether patients benefit from treatment in terms of improvement of functional health require disability and/or handicap measures [74]. Insight into a patient's disabilities and handicaps is also important for the choice of treatment.

For this overview of outcome measures used in CRPSI research and clinical practice, 30 publications were analysed. It was not our intention to be fully exhaustive: we omitted studies with small patient numbers because these studies usually report on preliminary results of employment of 'new' outcome measures. Classifying these outcome measures may result in an overview of one-time employed outcome measures, which was not the objective of this study. In the data selection we did not perform cross-referencing because we think that the outcome measures currently classified are representative for the outcome measures applied in CRPSI research in general. In our opinion, cross-referencing would not have added many other outcome measures; it would merely result in a larger number of references in the reference number columns in tables 2.2-2.6. Again, it was not our intention to be fully exhaustive.

The clinical picture of CRPSI has been described by authors from different clinical disciplines, such as anaesthesiologists, hand surgeons, orthopaedists, psychiatrists, and rheumatologists [7]. These different disciplines have not unexpectedly emphasised different signs, symptoms, diagnostic criteria, treatments and outcome measures, which may be a reason for some of the difficulties in reviewing the literature on CRPSI. The fact that little controlled research on CRPSI is done from the perspective of rehabilitation [75] may have contributed to the lack of relevant outcome measures at the level of disabilities and/or handicaps. On the other hand, all disciplines should attempt to determine whether patients benefit from treatment in terms of improvement of functional health.

Due to the lack of consensus about pathogenesis, current treatments do not always have a rational basis [8]; this may have had an impact on the selection of outcome measures for determining treatment efficacy. Ideally, the selection of certain outcome measures depends on the questions to be answered in different studies [74]; namely, whether the treatment has a biological effect or a clinical effect. Research and treatment of CRPSI may still be in an early experimental phase, despite the amount of research that has already been performed. For studies on pathogenesis, impairment outcome measures probably are the best choice. Clinical decision making can be improved by measuring at the level of disability, however, because these measures provide important and patient relevant information on whether a treatment improves the patient's functional health. Moreover, expressing outcome in terms of disabilities and handicaps, in addition to impairments, facilitates communication between disciplines and between specialists and patients.

In summary, classification of outcome measures in CRPSI research according to the hierarchical levels of the ICIDH shows that the majority of outcome measures describe treatment success at the level of impairment. Little consistency was found in concepts, operationalization of these concepts into variables and the instruments used. Outcome measures at the levels of disability and handicap, the most relevant levels for Rehabilitation Medicine, were mentioned in only very few studies. Objective outcome measures were merely found at the level of impairment. The shortage of relevant and objective outcome measures can not be due to lack of interest in such outcome measures or in CRPSI. This finding calls for development of relevant outcome measures that can objectively measure treatment efficacy at the level of disabilities and handicaps. Recent developments in the field of ambulatory activity monitoring [76, 77] seem to offer good perspectives.

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3 Ambulatory measurement of upper limb usage and mobility-related activities during normal daily life with an Upper Limb-Activity Monitor: a feasibility study

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3.1 Abstract

Aim: To assess the ability of an Upper Limb-Activity Monitor (ULAM) to discriminate between upper limb usage and non-usage in healthy and disabled subjects during normal daily life. **Methods:** The ULAM was based on ambulatory accelerometry and consisted of several acceleration sensors connected to a small recorder worn around the waist. While wearing this ULAM, four healthy and four disabled subjects performed an activity protocol representing normal daily life upper limb usage or non-usage. The motility feature (derived from the raw acceleration signals) was used as a measure for the extent of upper limb usage. Agreement scores between ULAM output and videotape recordings (reference method) were calculated. **Results:** ULAM data that were of special interest for rehabilitation were detected satisfactorily (overall agreement 83.9%). There were no systematic differences in the agreement percentages between healthy and disabled subjects for mobility-related activities ($p=0.345$) and the different forms of upper limb usage or non-usage ($p=0.715$). **Conclusion:** It is considered feasible to use the ULAM in future studies in subjects with upper limb disorders to discriminate between upper limb usage and non-usage during performance of mobility-related activities in order to determine activity limitations.

3.2 Introduction

For many medical disciplines, and especially for rehabilitation medicine, instruments that focus on physical activities are of fundamental importance [1]. Instruments that objectively measure during normal daily life are essential to provide insight into activity limitations of patient groups. Until recently, reliable and valid instruments that objectively measure these activity limitations were lacking [2-4]. Therefore, an Activity Monitor (AM) based on ambulatory accelerometry was developed that consisted of acceleration sensors attached to the thighs and trunk, connected to a small recorder worn around the waist [5-9]. This device allows a number of mobility-related activities (such as lying, sitting, standing, walking, cycling and general movement) to be automatically detected for a period of 24-72 hours [10, 11]. Measurement of these activities allows the assessment of activity limitations. Indicators for these limitations are, for example, lying down or sitting the greater part of the day, or a low number of transitions between postures.

Activity limitations of subjects with disorders related to the upper limbs are not primarily expressed in mobility-related activities. Although these disorders can have some impact on the performance of mobility-related activities, the main limitations are those directly related to upper limb usage during normal daily life. The present configuration of the 'classic' AM, with sensors on thighs and trunk, is insufficient to measure upper limb usage. To make a statement about limited upper limb usage, valid measurement of 'normal' upper limb usage is a prerequisite. Therefore, it is necessary to adapt the 'classic' AM, which implies increasing the number of sensors and extending the analysis program. The aim of this study was to determine the feasibility of an Upper Limb-Activity Monitor (ULAM) to discriminate between (different forms of) upper limb usage and non-usage during normal daily life.

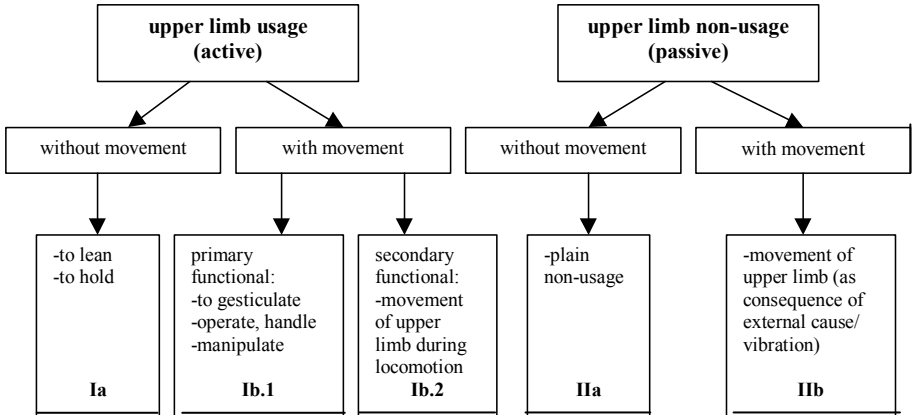
3.3 Method

Three subsequent steps were taken to explore the feasibility: 1) determination of the most appropriate sensor configuration, 2) writing of the 'Upper Limb Usage Analysis Program' consisting of several software algorithms needed for signal processing and analysis, and 3) validating the ULAM and its sensor configuration to discriminate between upper limb usage and non-usage in both healthy subjects and subjects with a disorder involving one upper limb.

Definition and operationalisation of upper limb usage
Upper limb usage can be defined as the movement of parts of the upper limbs. Although upper limb movement is an important aspect of functional upper limb usage, such an approach can lead to validity problems because, in normal daily life, upper limb movements are sometimes non-functional and, *vice versa*, upper limb non-movements are sometimes functional. Therefore, to determine the overall feasibility

of the ULAM to measure 24 h real-life upper limb usage, we used the following definition: active movement of (parts of) the upper limb(s) in relation to proximal parts, holding objects and/or leaning. Based on this definition, a framework was compiled to classify upper limb usage and non-usage (figure 3.1).

Figure 3.1: Overview of the different classes of real-life upper limb usage and non-usage based on the following definition of upper limb usage: active movement of (parts of) the upper limb(s) in relation to proximal parts, holding objects and/or leaning.



The key feature of upper limb usage is that it is active ('by the limb itself'). Upper limb usage without movement comprises holding objects and leaning (class Ia). Within the category upper limb usage with movement (Ib) a distinction is made between primary and secondary functional usage. Primary functional upper limb usage (Ib.1) comprises positioning of a limb subsequently to handle (gross movements) or manipulate (fine movements). Class Ib.1 also includes communicative upper limb usage (gesticulation). Secondary functional upper limb usage (Ib.2) comprises movement during locomotion. Secondary functional usage implies that there is no goal of the movements with regard to activities of normal daily living.

The key feature of non-usage is that it is passive. Upper limb non-usage without movement (class IIa) cannot be misunderstood, this is plain non-usage. Upper limb non-usage with movement (IIb), however, requires further explanation. This class was formulated because there are certain activities during which the limb is passively displaced due to body movement (e.g. nervously wiggling, tics, tremors) or external sources (e.g. during riding a car or public transport). Also, in subjects with an upper limb disorder, the involved limb is often passively displaced with the uninvolved limb.

ULAM output categories

We considered the valid detection of primary functional upper limb usage (Ib.1) most important because limitations directly related to upper limb usage are mainly

expressed in this form of usage. This choice made discrimination between primary functional usage (Ib.1), secondary functional usage (Ib.2) and plain non-usage (IIa) very relevant. Although we considered upper limb usage without movement (leaning and holding, class Ia) to be of secondary importance, this form was also studied, to determine the overall feasibility of the ULAM. Therefore, upper limb non-usage with movement (IIb) was also taken into account, even though this form was not expected to represent a great part of normal daily life.

We also determined which mobility-related activity was performed each second, because this can improve the detection of upper limb (non-)usage. Combined detection of upper limb (non-)usage and mobility-related activities provides more specific information, because such combinations make up normal daily life. Moreover, activity limitations are, in our opinion, mainly expressed in some specific combinations. These are, for example, primary functional usage during lying, sitting and standing, plain non-usage during sitting and leaning and holding during standing. Hence, for data analysis, three discrete output categories were considered: the five forms of upper limb (non-)usage, the mobility-related activities and, most importantly, certain combinations of forms of upper limb (non-)usage and mobility-related activities.

Subjects

Eight healthy subjects (four male and four female; average age 25.3 (range 21-28) years) volunteered to participate in the first two steps of the study (i.e. to determine sensor configuration and write analysis software). One subject was left handed, seven were right-handed; dominancy was based on writing.

During the third step of the study (validation of the the ULAM), the analysis software was tested on an independent group of eight right-handed subjects (three male and five female): four healthy subjects (average age 24.5, range 21-26 years) and four disabled subjects (average age 44.8, range 26-57 years) with limited upper limb usage due to an upper limb disorder. Three of the latter subjects had limitations at their dominant side and one at the non-dominant side, as a consequence of complex regional pain syndrome type I (n=3) and traumatic injury of the upper limb (n=1). Informed consent was obtained from all subjects.

Activity protocol

To determine the optimum configuration and to write the analysis program (steps 1 and 2), together with an occupational therapist we compiled a list of activities representing the five forms of upper limb usage or non-usage (configuration protocol, table 3.1). The subjects performed these activities in a quasi-natural setting (Occupational Therapy section of the hospital). Subjects were asked to perform activities in their own way and at their own pace. Five subjects performed a short configuration protocol (table 3.1), which represented forms of upper limb non-usage

with movement (class IIb, framework) during transportation; these data were used only to determine the most appropriate configuration and not for validation.

After preliminary analysis of the results in this first group of eight healthy subjects, it appeared that upper limb (non-)usage during certain activities (e.g. cleaning the kitchen sink, watching television, washing hands and putting tableware in closet) had agreement percentages of 96-100%. Therefore, to avoid fatiguing the disabled subjects participating in the third study step, we composed a shortened validation protocol with 'critical' activities (table 3.1), which had lower agreement percentages in the preliminary analysis. It should be noted that use of such a strict protocol will inevitably have a negative impact on the results.

Apparatus
Uni-axial piezoresistive acceleration sensors (Analog Devices, ADXL201) were used (size 1.0x1.0x0.5 cm). The raw acceleration signals were a combination of two components: the gravitational acceleration and accelerations due to movement and are expressed in g (ms^{-2}) [11, 12]. The magnitude of these components depends on the magnitude and direction of the accelerations with regard to the sensitive direction. Raw acceleration signals were stored digitally on a PCMCIA flash card with a sample frequency of 32 Hz. After measurements, the raw acceleration signals were downloaded onto a PC for analysis. The data recorder is a digital recorder (9.0x15.0x4.5 cm, 700 g) with energy supplied by four penlite batteries.

To detect mobility-related activities, two sensors were placed on the left and right thighs halfway between spina iliaca anterior superior and upper side of the patella (sensitive direction in the sagittal plane) and two sensors on the sternum (sensitive direction in sagittal and longitudinal plane) (figure 3.2). The four remaining sensors were attached on both upper limbs: being in the anatomical position, just proximal from the wrist joint on the forearm, sensitive direction perpendicular to the body segment in the sagittal and transversal directions. The sensors were fixed on Rolian Kushionflex™ or silicone-based stickers (Schwamedico) by double-sided tape; both materials can be fixed directly on the skin.

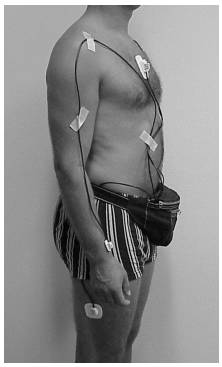


Figure 3.2: A subject wearing the configuration of the Upper Limb-Activity Monitor with acceleration sensors at the thigh, trunk and forearms.

Table 3.1: Overview of the activity protocols. The configuration protocol was used to determine the sensor configuration and to write analysis software. The validation protocol was used to validate the ULAM.

Activities (indicated per room)	Configuration protocol	Validation protocol
Activities performed in kitchen:		
peel, cut and eat apple	×	×
make fresh orange juice with electric squeezer	×	×
fill water boiler and pour out in bowl	×	×
make instant soup (use scissors), stir and eat it with spoon	×	×
clean kitchen sink and wring out dishcloth	×	
get soap from pump and wash and dry hands	×	
put tableware in closet	×	
Activities performed in living room:		
moving one ('involved') upper limb with other ('healthy')*	×	×
reading newspaper in (easy) chair	×	×
turn pages of book that is lying on table	×	×
watch television while sitting upright	×	
watch television while leaning backwards	×	
act as if being nervous/having tic (moving leg with and without hand on leg)	×	×
make telephone call	×	×
Activities performed in hall and stairwell:		
walk up and down stairs without using banisters	×	×
walk up and down stairs using banisters	×	
place ('involved') limb in protective position near trunk and stand still like this*	×	
walk up and down stairs with limb in protective position*	×	×
walk to and fro in the hall with limb in protective position*	×	
take tray and walk up and down stairs	×	
walk to and fro in hall	×	×
pick up shopping bag and walk to and fro in hall	×	×
pick up and hold umbrella and walk to and fro in hall	×	
Activities performed outside:		
push wheelchair (alternative trolley) on smooth ground	×	
push wheelchair (alternative trolley) on rough ground	×	
ride bicycle on smooth ground	×	×
ride bicycle on rough ground	×	
keep feet still while riding bicycle (alternative moped) on smooth ground	×	×
keep feet still while riding bicycle (alternative moped) on rough ground	×	
Activities performed in hobby room:		
typing on personal computer	×	×
writing on piece of paper with ballpoint	×	×
saw board in two	×	×
vacuum hobby room	×	×
Activities performed in bed and bathroom:		
get undressed and put on nightclothes	×	
brush teeth	×	×
lie in bed on right and left side	×	
read magazine and turn pages in bed while lying on side	×	×
take off nightclothes and get dressed	×	
Activities related to transportation (performed by five subjects):		
sitting in subway	×	
standing in subway	×	
reading book in subway	×	
as passenger in car	×	
driving car	×	

*Indicates patient-specific activities

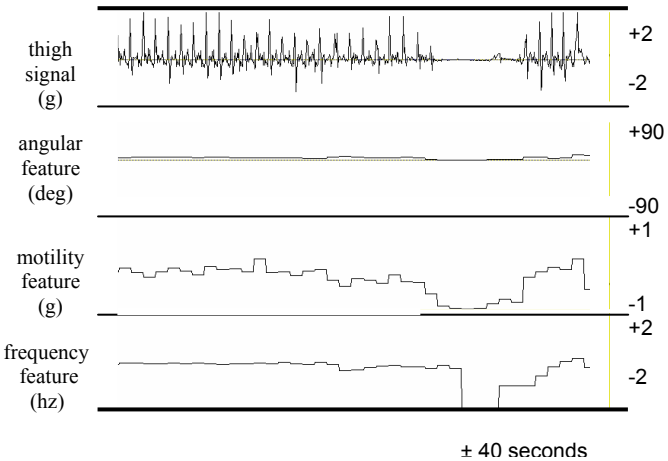
Reference method
Videotape recordings were chosen as the reference method and were recorded together with the acceleration signals. The videotape recordings had a digital time code (resolution of 1 s) that was visible on screen. To allow correct comparison between video data and ULAM data, the timing of the instruments was synchronised: each time a series of activities started and ended, the subjects stood still for 3-5 seconds with both upper limbs flexed 90 degrees at the elbows after which a research assistant tapped one thigh sensor three times (all this was videotaped).

After synchronisation, intervals of various durations (minimum duration > 1 second) were marked on the raw upper limb acceleration signals according to the five forms of upper limb usage and non-usage from the framework. For each subject, for each activity performed, intervals were coded based on the class of usage or non-usage that was displayed on video at that time. Dominant and non-dominant sides were analysed separately, because the form of (non-)usage did not necessarily have to be the same for both upper limbs. The intervals of the eight healthy subjects participating in the first two study steps were used to determine the sensor configuration and to write the analysis program. The intervals of the other eight subjects (four healthy and four disabled) were used to validate the ULAM and to make a statement about feasibility (third step of the study). About 100-120 intervals per subject per side were marked for this latter step.

Detection method: signal processing and analysis
Detection of mobility-related activities was done by standard automatic kinematic analysis using the 'classic activity detection analysis program', which is based on signal processing and inferencing language (SPIL) routines, yielding ´C´-code [13]. For this detection, three feature signals are derived from each raw acceleration signal (sampled at 32 Hz): the angular, frequency and motility feature signals (time resolution 1 s) (figure 3.3).

The angular feature was created after low-pass filtering (finite impulse response, cut-off frequency 0.3 Hz) and subsequent decimation down to 1 Hz and to angles via arcsine transformation (range +90 to –90 degrees). The frequency feature was based upon a band-pass filtered derivative (0.3-2 Hz for the legs; 0.6-4 Hz for the trunk), also using finite impulse response filters. This band-passed signal is the input of the fast time frequency transform (FTFT) procedure [14]. If this signal met the pre-set criteria, a valid frequency was assigned and compressed to 1 Hz. The motility feature was the envelope of AC component above 0.3 Hz and was created after zero-phase finite impulse response high pass filtering (0.3-16 Hz), rectifying and averaging over 1 s. This signal depended on the variability of the raw signal around the mean and was expressed in g (=9.81 ms^{-2}).

Figure 3.3: A raw thigh acceleration signal and its three features (duration approximately 40 seconds).



The subsequent steps for the detection of mobility-related activities were activity detection & post-processing [5-7, 11]. Briefly, for each activity and for each feature signal, minimum and maximum values were pre-set. Each second, the ´distance´ from the actual feature signal value to the pre-set range was calculated. If a feature signal was within this range, this distance was zero, i.e. it did not add to the total distance for that activity. The mobility-related activity with the lowest total distance was detected. There were some (optional) post-processing procedures; activity duration thresholds (using time windows), statistics or reports on duration of activities, or the number of walking periods longer than 10 s. Manual editing was another option during post-processing, which we used (if required) to correct wrongly detected mobility-related activities. This manual editing (with the help of a SPIL routine) was carried out before the upper limb analysis program was applied in the third study step in order to obtain an unobtrusive indication of the feasibility of the ULAM to measure upper limb (non-)usage.

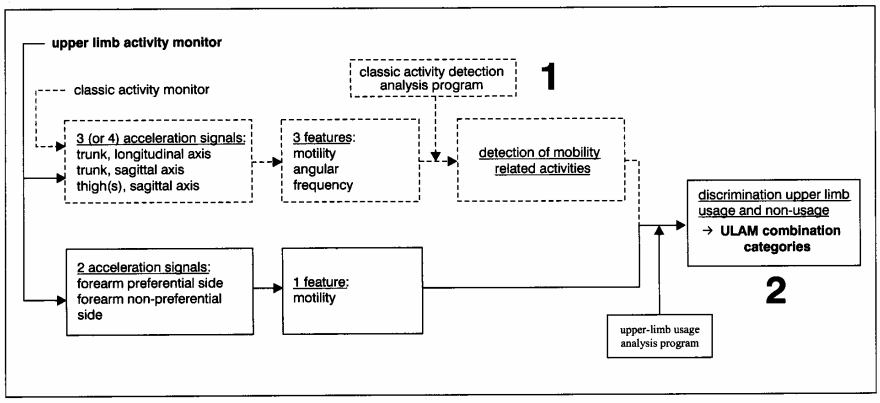
The variability of the raw signal around the mean, as expressed in the motility feature (cutoff frequency 0.3 Hz), can be regarded as a measure of the extent of upper limb movement: the more the limbs are moved, the higher the variability of the raw signal and the higher the motility value. We used the motility feature in all three study steps. To determine the most appropriate sensor position (first step), the average motility values of the marked intervals for the sagittal and transversal upper limb sensors were calculated. The position that yielded the (average) highest motility values for classess of upper limb usage and (average) lowest motility values for classes of upper limb non-usage was considered most appropriate.

To write the software algorithms for the ´upper limb usage analysis program´ (second step) we also used the motility value. Ideally, upper limb usage would result in motility values higher than zero *(mot > 0)* and non-usage would result in motility values of around zero *(mot ≈ 0).* However, we did not expect this ideal situation, because motility values can be similar, for example, during advanced typing and while watching television. Tamura et al. [15] also reported wrist accelerations when a subject was in a sitting position in a chair.

Because mutual exclusiveness between usage and non-usage could not be guaranteed, we set thresholds on the motility values. Motility values exceeding a threshold were regarded as usage and values under a threshold as non-usage. These motility-threshold values could be varied for the different mobility-related activities to compensate for general body movements due to postural sway or head movements. Such general body movements are more prominent during standing than during sitting, and are especially prominent when compared with lying flat. Because of this, upper limb motility during non-usage may have a certain ´basic value´ that is higher during standing than during sitting and/or lying. The motility thresholds providing the least misdetection in the first group of eight subjects were used as algorithms for the 'upper limb usage analysis program'.

To validate the ULAM and to determine its feasibility (third step), the data from the second group of eight subjects had to be analysed for the three discrete ULAM output categories (see paragraph on ULAM output categories). The ULAM analysis program was based on and included the 'classic' activity monitor (figure 3.4). Discrimination between upper limb usage and non-usage was made in two subsequent steps. First, mobility-related activities were detected with the existing classic activity detection analysis program. Subsequently, the upper limb usage analysis program (consisting of SPIL routines, including pre-set motility thresholds) was applied to determine whether or not the upper limbs were used, combining the motility signals from the forearms and the output of the classic activity detection analysis program (i.e. mobility-related activities). The ULAM combination categories were therefore characterised by specific ranges of one or more of the three features derived from the raw acceleration signals.

Figure 3.4: The Upper Limb-Activity Monitor and its analysis program (1+2) in relation to the classic version of the Activity Monitor and its analysis program (1). The 'classic' AM is indicated in patterned grey and black.



To validate the upper limb usage analysis program, we determined the degree to which each videotape category from the framework (representing classes of upper limb usage and non-usage actually performed) was detected correctly by the ULAM. Agreement was calculated according to the equation: agreement for videotape category X = (number of identical samples of videotape recording and ULAM data when videotape category is X / total number of samples for videotape category X) * 100%. Although overall agreement percentages between classic AM output and video recordings for the detection of mobility-related activities have already been described [5-8, 16], we also determined this percentage for the present study.

Statistics

To determine the most appropriate position for the upper limb sensors, average motility values of the sagittal and transversal sensors were compared and analysed using the Wilcoxon matched pairs signed rank sum test. The Wilcoxon matched pairs test was used to determine whether there were unwanted systematic differences in the detection of the five classes of upper limb (non-)usage between the healthy and disabled subjects. For each class of (non)-usage, the Mann-Whitney two samples t-test was used to determine differences in agreement percentages between the healthy and disabled groups. The Mann-Whitney t-test (unequal variances assumed) and the Kruskall-Wallis test were used to determine whether there were any unwanted systematic differences in the discrimination between the dominant, non-dominant, involved and non-involved sides.

3.4 Results

Sensor configuration
For the classes of upper limb usage (Ia, Ib.1 and Ib.2), the sagittal direction resulted in significantly higher motility values than the transversal direction (p=0.001) (table 3.2). There was no significant difference between sagittal and transversal motility values for the forms of upper limb non-usage (IIa and IIb) (p=0.361). The sagittal direction also resulted in higher motility values for upper limb usage and lower values for non-usage for activities related to transportation performed by five subjects (configuration protocol, table 3.1). Therefore, we considered the sagittal sensor most suitable to discriminate between upper limb usage and non-usage: only the sagittal sensor was used during the subsequent study steps.

Upper Limb Usage Analysis Program
Because there was no mutual exclusiveness between usage and non-usage, thresholds for the upper limb usage analysis program were set such that agreement percentages between videotape recordings and ULAM output for the intervals from the first group of subjects were as high as possible for both upper limb usage and upper limb non-usage. In this manner, motility thresholds providing the least misdetection were used as algorithms for the upper limb usage analysis program.

Validating the Upper Limb Usage Analysis Program
For validation, three output categories (mobility-related activities, classes of upper limb (non-) usage and combinations of upper limb (non-)usage and mobility-related activities) were considered separately. The total time analysed was 15 604 samples of 1 s each, which is almost 4.5 hours.

Upper limb (non-)usage
The overall percentage of agreement between videotape recordings and ULAM data for the five classes of upper limb usage and non-usage from the framework was 69.5% (minimum 60.5%, maximum 74.9%, sd 4.8%) (table 3.3). There were no significant differences in agreement percentages between healthy and disabled subjects for these five forms of usage and non-usage (p=0.715).

Table 3.2: Average motility values of sagittal and transversal sensors for the different classes of upper limb usage (Ia, Ib.1 and Ib.2) and non-usage (IIa and IIb). Average motility values were only calculated if a certain form of upper limb usage or non-usage during a certain activity from the Configuration protocol was performed by five or more of the eight subjects participating in the first two steps of the study.

Upper limb usage								Upper limb non-usage			
Ia		Ib.1		Ib.1		Ib.2		2a		2b	
sagittal	transversal	sagittal	transversal	sagittal	transversal	sagittal	transversal	sagittal	transversal	sagittal	transversal
0.11	0.14	0.39	0.77	0.13	0.11	0.50	0.35	0.07	0.06	0.52	0.94
0.04	0.02	0.38	0.37	0.49	0.48	0.61	0.52	0.04	0.04	0.41	1.10
0.04	0.04	0.30	0.61	1.24	1.91	0.41	0.36	0.02	0.02	0.58	0.91
0.53	0.50	0.29	0.65	0.62	0.67	0.61	0.51	0.02	0.02	0.10	0.17
0.32	0.35	0.58	0.48	0.74	0.89	0.49	0.37	0.01	0.01	0.11	0.23
0.62	0.48	0.64	0.82	0.34	0.51	0.67	0.46	0.02	0.03	0.25	0.21
0.22	0.17	0.75	0.39	0.40	0.39	0.70	0.56	0.02	0.01		
0.08	0.06	0.44	0.69	0.87	0.69	0.56	0.47	0.12	0.13		
0.15	0.13	0.37	0.21	0.46	0.38	0.61	0.43	0.14	0.13		
0.06	0.03	0.54	0.36	0.37	0.59	0.47	0.37	0.04	0.04		
0.01	0.01	0.39	0.51	0.35	0.72	0.54	0.41	0.08	0.09		
0.07	0.05	1.63	0.67	1.06	0.93	0.57	0.47	0.05	0.02		
0.01	0.01	0.37	0.29	0.65	0.41	0.49	0.44	0.03	0.05		
0.10	0.10	0.30	0.20	0.44	0.20			0.03	0.04		
0.01	0.01	0.11	0.05	0.61	0.29			0.02	0.02		
0.23	0.26	0.40	0.32	0.46	0.29			0.01	0.01		
0.61	0.48	0.14	0.12	0.48	0.37			0.02	0.01		
0.35	0.37	1.14	0.99	0.67	0.65			0.02	0.01		
0.64	0.47	1.35	1.07	1.23	1.06						
0.26	0.21	0.99	0.64	1.75	1.00						
0.21	0.17	1.88	0.98	1.50	0.92						
0.14	0.08	1.72	0.98	0.47	0.60						
0.07	0.11	0.63	0.68	0.36	0.43						
		0.35	0.40	0.87	1.12						
		1.10	1.10	0.08	0.10						
		0.07	0.09	0.53	0.46						
		0.14	0.09	0.80	0.71						
		0.56	0.38	0.52	0.39						
		1.24	1.65	0.11	0.19						
		0.82	0.65	0.45	0.47						
		0.63	0.39	0.61	0.58						
		0.17	0.22	0.88	0.99						
		0.44	0.36	0.39	0.56						
		0.14	0.11	0.97	0.59						
		0.81	0.63	0.28	0.35						

Table 3.3: Overview of total duration (in seconds) and agreement between ULAM output and video recordings (in %) for the five classes of usage described in the framework for the healthy, disabled and total group.

	healthy subjects		disabled subjects		all the subjects	
type of usage	**duration (sec)**	**agreement (%)**	**duration (sec)**	**agreement (%)**	**duration (sec)**	**agreement (%)**
Ia to lean and hold	2706	36.1	1545	38.7	4251	37.0
Ib.1 primary functional usage	4143	81.8	3788	82.6	7931	82.2
Ib.2 secondary functional	513	100.0	459	100.0	972	100.0
IIa plain non-usage	1018	83.7	895	90.1	1913	86.7
IIb involuntary	398	32.3	140	0.0	538	23.9
usage of upper limbs	7362	66.2	5792	72.3	13153	68.9
non-usage of upper limbs	1417	69.2	1034	77.9	2451	72.9
total	8779	66.7	6826	73.1	15604	69.5

The different classes of upper limb usage and non-usage were not equally well detected (table 3.3). Detection of primary functional usage (Ib.1) and plain non-usage without movement (IIa) was good in 82.2% and 86.7%, respectively, of their total duration. Secondary functional usage (Ib.2) was always well detected (100%). Detection of upper limb usage without movement during leaning and holding (Ia) and involuntary/passive non-usage with movement (IIb) was less than optimum, with agreement percentages of 37% and 23.9%, respectively. After separate analysis of the five different classes of usage and non-usage, only the agreement percentages of non-usage with movement (form IIb) showed a significant difference between healthy and disabled subjects ($p= 0.004$).

Percentage agreement of the ULAM for primary functional usage (Ib.1) (82.2%) was considerably decreased because of wrong detection of operative and/or handling movements of the upper limbs during specific activities (<85%): turning the pages of a book that was lying on a table (52.9%), eating soup or an apple (52.1%), pouring water into bowl (29.2%), moving one ('involved') upper limb with the other ('healthy') limb (55.3%) and reading a magazine in bed and turning the pages (58%). The activities during which manipulative movements of the upper limb were well detected in less than 85% of the time were: writing on a piece of paper (62.6%), stirring soup (53.1%), typing on a PC (77.1%), and pushing buttons to dial a telephone number (77.1%).

There were no systematic differences in the upper limb usage and non-usage agreement percentages between the two groups ($p= 0.631$). There were also no systematic differences in agreement percentages between the four different sides ($p=0.405$), between the non-involved and involved sides of the disabled subjects ($p= 0.180$), between the dominant and non-dominant side of the healthy subjects ($p= 0.684$), between the non-involved side of the disabled subjects and the dominant side of the healthy subjects ($p= 0.191$), and between the involved side of disabled subjects and the non-dominant side of healthy subjects ($p= 0.704$).

Mobility-related activities
Overall agreement between videotape data and ULAM output for mobility-related activities was 94.6%. The 5.4% misdetection was mainly due to general movement, which was detected as cycling. There was no significant difference in agreement percentages between healthy and disabled subjects (p= 0.345) for the various mobility-related activities.

Combination upper limb (non-)usage and mobility-related activities
Agreement percentages for the ULAM combination categories are given in table 3.4. No percentage was calculated for plain non-usage (IIa) during lying down, because there was no activity in the validation protocol that represented this ULAM output category. Holding objects and leaning (Ia) during standing (35.5%) were poorly detected. Some misdetection occurred for primary functional usage (Ib.1), positioning to subsequently handle or manipulate, during lying down (64.3%) and sitting (68.1%) and plain non-usage (IIa) during standing (70.7%). Overall percentage of agreement for the ULAM combination categories was 83.9%.

Table 3.4: Overview of total duration (in seconds) and agreement between ULAM output and video recordings (in %) for several ULAM combination categories.

form of (non)-usage	mobility-related activity	duration (sec)	agreement (%)
primary functional	lying	488	64.3
primary functional	sitting	3558	68.1
primary functional	standing	2639	96.7
primary functional	walking	591	99.8
secondary functional	walking	972	100.0
plain non-usage	lying	(well-detected in configuration protocol)	
plain non-usage	sitting	1293	95.4
plain non-usage	standing	590	70.7

3.5 Discussion and conclusion

General
The aim of this study was to determine the feasibility of an ULAM to discriminate between upper limb usage and non-usage during normal daily life. There were three subsequent steps: 1) determining the most appropriate configuration for the upper limb sensors, 2) writing the upper limb usage analysis program for signal processing and analysis, and 3) validating the ULAM and its sensor configuration to determine the feasibility.

Sensor configuration
With respect to the sensor configuration, using the motility feature, the sagittal direction was the most suitable to discriminate between upper limb usage and non-usage. Because acceleration sensors are not completely waterproof and some subjects cannot bear sensors attached to hand or fingers, two options for forearm attachment we investigated. All subjects considered this to be a convenient solution and all found the ULAM comfortable to wear.

For practical reasons, we did not investigate the possibility of using two- or three-axial sensors. The use of multiple-axial sensors would probably not have influenced our findings because studies using three-axial sensors encountered shortcomings similar to those with the ULAM: i.e. low sensitivity to sedentary activities and inability to register static exercise [17, 18]. In addition, the signals of the two forearm sensors in this study were closely related (correlation of 0.81).

Agreement percentages
Overall agreement between ULAM output and videotape recordings for mobility-related activities (94.6%) was in accordance with earlier studies [5-8, 16]. The overall agreement percentages for (non-)usage during mobility-related activities and the ULAM combination categories were 69.5% and 83.9%, respectively. At first sight these findings may seem somewhat disappointing. However, because the Validation protocol mainly contained the critical activities, this inevitably made the agreement lower. In addition, overall agreement percentages largely depend on the proportion of each category in the protocol used. We considered agreement percentages for each separate form of usage and ULAM output category of greater value than overall percentages, because these proportions are unknown in the real-life situation. These proportions may be totally different from the proportions in the protocol.

ULAM combination categories
As was expected, some of these categories were poorly detected. However, the combinations of upper limb (non-)usage and mobility-related activities that we considered most important were detected satisfactorily. Most of the relatively poor agreement percentages can be explained. Primary functional usage (Ib.1) during lying and sitting had agreement percentages of 64.3% and 68.1%, respectively. Manipulative (fine) movements are practically solely responsible for the low agreement percentages. True non-usage (IIa) (agreement 70.7%) during standing, for example, is poorly detected because, after slight general trunk movements, the upper limbs are also displaced. In view of the technique used, it is logical that holding of objects and leaning (Ia) were most difficult to detect. When holding a cup or reading a book, for example, the upper limbs are displaced as little as possible. The same applies to leaning, which automatically implies absence of movements.

Despite some low agreement percentages, this will not necessarily hamper future usage of the ULAM. In normal upper limb usage leaning and holding, as well as

primary functional manipulation, are usually preceded and followed by active upper limb movements to bring the limb in the right position to lean, hold or manipulate. Thus, a well-detectable class of usage in normal daily life situations, usually accompanies poorly detected classes of usage. If a subject has limitations directly related to upper limb usage, then less leaning, holding and manipulating will be performed with the involved side. Most probably, well-detectable movements will also be performed less.

In our opinion, activity limitations in leaning, holding and manipulating will (indirectly) be expressed in the number of upper limb movements. This is in accordance with Taub et al. [19] and Uswatte et al. [20], who also used threshold filters to correct for erratic fluctuations in arm acceleration influencing measurement of the amount of movement. Although, it was not possible to yield a direct measure of the amount of *functional* upper limb *usage*, the amount of upper limb movement was considered a meaningful parameter. It was considered highly likely that an increase in upper limb movement is associated with an increase of usage of that upper limb [20]. With the ULAM it is possible to yield detailed information because mobility-related activities are measured at the same time. Since we used different pre-set motility thresholds for different mobility-related activities to optimise detection, the ULAM combination categories are, in our opinion, even more meaningful parameters.

Possible applications
In this study, the feasibility of the ULAM to measure all forms of upper limb usage and non-usage during normal daily life was investigated. It appeared that the ULAM does not allow valid measurement of every aspect of upper limb usage. However, if outcome measures to determine activity limitations are defined such that upper limb *movement or activity* is measured, we think that future studies will allow to make a statement on the degree of limitations of subjects with an upper limb disorder. Such outcome measures are, for example, the intensity of upper limb activity of the involved side during sitting (expressed in motility values), the absolute extent of upper limb activity of the involved side during standing (expressed at the percentage of the time an upper limb is moved when a subject is standing), or the relative extent of upper limb activity of the involved side relative to the non-involved side during lying. Such outcome measures can be used to determine activity limitations of subjects with neurological disorders, musculoskeletal disorders or chronic (benign) pain, to monitor natural recovery, to determine treatment effects or to describe the relationship between impairments and activity limitations, provided that it is emphasized exactly how activity limitations are defined.

Current developments
The development of an instrument such as the ULAM is an ongoing process of extending possibilities and optimising properties. We are currently working on the automatic detection of activities related to transportation and wheelchair driving that, until now, could only be determined by visual inspection. In addition, dimensions,

weight and impermeability to water of the data recorder can also be improved. In the current version of the classic activity detection analysis program, the pre-set feature ranges for cycling have been redefined and a time window has been included for cycling, which rejects a period of cycling of less than 10 seconds duration, hereby improving misdetection of mobility-related activities.

It is not yet possible to automatically discriminate between primary and secondary functional usage during walking, i.e. to determine whether a subject is performing ordinary walking or carrying a bag while walking. Currently, this can only be done by visual inspection. Since the acceleration signals and its derived features certainly differ between these types of upper limb usage, calibrating the ordinary walking of a subject at the beginning of a measurement period may be a solution.

Other techniques
Upper limb movements have a non-cyclic character and many degrees of freedom. Therefore, use of the motility feature alone is not sufficient to discriminate between functional upper limb usage and non-usage. The motility feature is a technique comparable to the more often used Wrist Activity Monitor/Actometer/Actigraph [21-25]. The additional value of the ULAM, however, is the combination of both mobility-related activities and upper limb motility scores, plus the fact that both upper limbs are measured. Improved detection of upper limb usage and non-usage may be achieved with electromyogram (EMG) recordings in addition to accelerometers. Keil and colleages [26] considered the two techniques complimentary and suggested to use them simultaneously. However, this may not be desirable, because ambulatory EMG measurement during a 24-hour period is not yet feasible or convenient for the subjects.

Systematic differences
No differences in agreement percentages were found, except for a significant difference between healthy and disabled subjects for upper limb non-usage class IIb. However, this latter form of usage represents a very small proportion of the total time analysed and it is questionable what part of 24-hour real life it will represent. We focused on systematic differences, because the absence of such differences allows comparison between disabled and healthy subjects. The presence of systematic differences would hamper use of the ULAM in future patient studies.

3.6 Conclusion

Although, the ULAM, with its two additional sensors on the forearms, does not yet allow valid measurement of *every* aspect of upper limb (non-)usage, its use is considered feasible in future studies in subjects with upper limb disorders to discriminate between upper limb usage and non-usage during performance of mobility-related activities to determine activity limitations.

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4 Technical description of the Upper Limb - Activity Monitor

Partly based on:

Bussmann JBJ, Martens WLJ, Tulen JHM, Schasfoort FC, vandenBerg-Emons HJG, Stam HJ
'Measuring daily behaviour using ambulatory accelerometry: the Activity Monitor.'
Behavior Research Methods, Instruments & Computers 2001, 33(3):349-56.

4.1 Abstract

Due to developments in data recording and sensor technology, advanced ambulatory systems that measure aspects of human functioning and behaviour during everyday life have become available. One such instrument is the Upper Limb-Activity Monitor (ULAM). This chapter provides a technical description of the ULAM. The ULAM is an extended version of the Activity Monitor (AM); both instruments are based on ambulatory accelerometry and aim at assessing body postures and motions, and in case of the ULAM also activity of the upper limbs. Signals from body-fixed acceleration sensors are recorded for a period of at least 24 hours in a subject's home environment during everyday life and continuously stored in a digital portable recorder. During post-measurement analysis, body postures, body motions and upper limb activity are detected by means of custom-made software programs.

4.2 Background

Human behaviour can be regarded as a complex of physical activities: body postures, body motions, and transitions between postures. Measuring human behaviour is of major importance for fundamental and applied clinical research in a large number of disciplines. If unobtrusive, objective and valid measurements of a large and specific set of body postures and motions (i.e. mobility-related activities) during everyday life in a subject's personal environment are required, most of the available techniques, such as questionnaires, observations and diaries are inadequate [1]. Recent developments in data recording (small, portable and digital data logger systems with increased data processing and –storage capacities) and simultaneous developments in sensor technology (small, non-drifting and robust sensors), however, enabled objective measurements for longer periods during everyday life using ambulatory monitoring devices. Two of such devices are the Activity Monitor (AM) and the Upper Limb-Activity Monitor (ULAM) [2-8]. Both AM and ULAM consist of several body-fixed acceleration sensors connected to a recorder that is worn in a belt around the waist and aim at long-term (24 hours) assessment of physical activity during everyday life.

The primary goal of rehabilitation medicine, i.e. regaining and/or maintaining functionality by decreasing the consequences that a disease or disorder may have on everyday life, provided the rationale for development of the AM and ULAM. The AM can be used to determine whether a subject is lying, sitting or standing (body postures), walking, running, climbing stairs, cycling, driving a wheelchair or performing general (non-cyclic) movements (body motions), or the transitions between the different body postures. Measuring such body postures and motions allows assessment of activity limitations. Indicators for activity limitations are, for example, lying down or sitting the greater part of the day, or a low number of transitions between postures. Because the AM was insufficient to detect activity limitations that are characteristic of upper limb disorders, the possibilities of the AM were extended using additional accelerometers on the forearms which resulted in the ULAM [8]. The ULAM is based on the following definition of upper limb usage: active movement of (parts of) the upper limb(s) in relation to proximal parts, holding and leaning. Its key characteristic is combined measurement of mobility-related activities and upper limb activity of both upper limbs. Although we have published [8] on the ULAM´s feasibility to measure normal and limited upper limb usage through measurement of upper limb activity, a comprehensive technical description of the analysis scheme and software programs of the ULAM has not been provided.

4.3 Technical description of the ULAM

Piezo-resistive accelerometers

The ULAM consists of five (or six) ADXL202 piezo-resistive accelerometers (Analog Devices, Breda, the Netherlands, adapted by Temec Instruments, Kerkrade, the Netherlands). Piezo-resistive accelerometers consist of a mass, connected to a frame by beams, which can be represented by a damped spring (figure 4.1) [6, 9, 10]. Piezo-resistors are mounted in the beams and form a bridge circuit. The value of the resistors depends on the magnitude of acceleration. The raw acceleration signals yielded by the piezo-resistive accelerometers are a combination of the gravitational acceleration ($\bar{a}_{grav}$, 9.81 ms^{-2}) and a component of the inertial acceleration ($\bar{a}_{inert}$). The part of $\bar{a}_{grav}$ that is measured ($\bar{a}_{grav,\ sens}$) depends on the angle φ_2 between the sensitive axis of the sensor and $\bar{a}_{grav.}$ The part of $\bar{a}_{inert}$ that is measured ($\bar{a}_{inert,\ sens}$) depends on the angle φ_1 between the sensitive axis of the sensor and $\bar{a}_{inert}$. Because the gravitational force acts on the mass and the inertial forces act on the frame of the sensor, $\bar{a}_{grav}$, and $\bar{a}_{inert}$ have opposite effects on the spring. Therefore, the raw signal ($\bar{a}_{sens}$) produced by the sensor at a certain moment (t) can be expressed as $\bar{a}_{sens}$ (t) = $\bar{a}_{inert,\ sens}$ (t) - $\bar{a}_{grav,sens}$ (t). Theoretically, a constant $\bar{a}_{sens}$ smaller than 9.81 ms^{-2} can be the result of either a constant $\bar{a}_{inert}$ or the result of $\bar{a}_{grav}$; this can not be determined with a single accelerometer. The occurrence of a constant $\bar{a}_{inert}$ of several seconds duration is unlikely during the performance of dynamic mobility-related activities or upper limb activity in everyday life, however. Therefore, it is assumed that the body part that the sensor is attached to is active when the raw accelerometer signal is time varying (i.e. body motions are performed or there is upper limb movement). In contrast, the body part that the sensor is attached to it inactive when the raw accelerometer signal is constant (i.e. a body positions are performed or there is no upper limb movement). Assuming angular deviations in one plane, from a constant raw signal the angle between the accelerometer axis and the gravity vector can be determined, which gives information about the orientation of the accelerometer [10, 11].

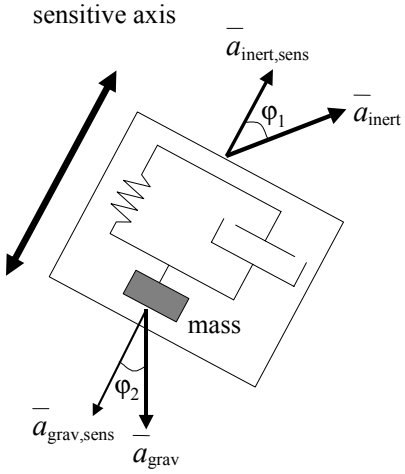


Figure 4.1: Scheme of a piezoresistive accelerometer. $\bar{a}_{grav,}$ gravitational acceleration; $\bar{a}_{inert.}$ inertial acceleration; $\bar{a}_{***sens,}$ the part of the gravitational or inertial acceleration measured by the accelerometer.

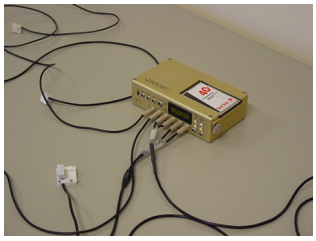
Measurement set-up

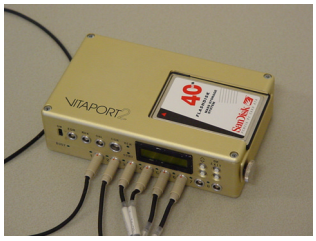
The acceleration sensors (size about 1.5x1.5x1.0 cm) are fixed on Rolian Kushionflex (Smith & Nephew, Hoofddorp, the Netherlands) or silicone based stickers (Schwa-Medico, Ehringshausen, Germany) by double-sided tape; both materials can be fixed directly on the skin. One sensor is attached at the lateral side of the thigh, at the level halfway between trochantor major and knee joint. A sensor on the other thigh is optional. The sensitive axis of this uni-axial sensor is in sagittal direction while the subject is in the anatomical position. A bi-axial (or two uni-axial) sensor(s) is (are) attached on the lower part of the sternum, with sensitive axes in the sagittal and longitudinal direction. These accelerometers have to be attached with their sensitive axis as parallel as possible to the related anatomical axis; for the thigh and trunk sensors a deviation of 15 degrees is allowed. If a sensor cannot be attached within this range, a wedge is used. For the ULAM two additional uni-axial sensors are attached to the forearms, just proximal from the wrist joint with the sensitive axis in the sagittal direction while the subject is in the anatomical position. It has to be noticed that sometimes concessions have to be made with respect to proximal-distal sensor attachment as a consequence of the upper limb disorder under investigation. An important aspect for the forearm sensors is identical placement on both upper limbs. Each accelerometer is attached to a data recorder by means of separate lemo-jackets. The recorder is worn in a belt around the waist and before measurements are started, the accelerometers are calibrated (+1g and –1g).

Recorder

The data recorder should allow measurements of at least 24 hours with respect to data storage and energy supply, be able to measure (at least) five accelerometer signals, have small dimensions and low weight, and be easy to handle by researchers and clinicians. For the ULAM, a Vitaport2™ (Temec Instruments) digital recorder (9x15x4.5 cm, 500 grams) with energy supplied by four penlite batteries was used (figure 4.2). The Vitaport2™ universal module allows simultaneous measurement of up to eight signals; data are stored on a flash card of 40 MB). Continuous measurement (without changing batteries or disks) of over three days is possible, but until now only 24-h measurements have been performed. The data recorder must contain a ´definition file´ representing the measurement set-up. The measurement set-up consists (among other things) of calibration and offset factors, sample frequency (32 Hz), resolution (12 bits) and filters (30 Hz low-pass). Signals are continuously measured and stored. After the measurements, the data are downloaded onto a PC for analysis.

Figure 4.2: The Vitaport2™ used for the application studies with the ULAM.





Signal analysis

After the measurements, detection of mobility-related activities and upper limb (in)activity takes place by means of proprietary ´signal processing and inferencing language´(SPIL), yielding C-code [12]. In this automatic analysis, several parts can be distinguished (figure 4.3).

1) The first part is feature extraction, which means that new signals (feature signals) with specific characteristics are derived and computed from each raw acceleration signal. For the trunk and thigh signals, three features (low pass (LP) /angular, motility and frequency) are derived, and for the forearm signals only the motility and LP/angular features are derived.

2) The second part of analysis of the trunk and thigh signals consists of body posture and motion detection, which means that body postures and body motions are classified on the basis of the feature signals from trunk and thigh sensors. In this part of the analysis also some post-processing takes place. The pattern of body postures and motions (also referred to as mobility-related activities) is the basis for the detection of upper limb (in)activity in the subsequent parts of data analysis.

3) Upper Limb Activity detection:

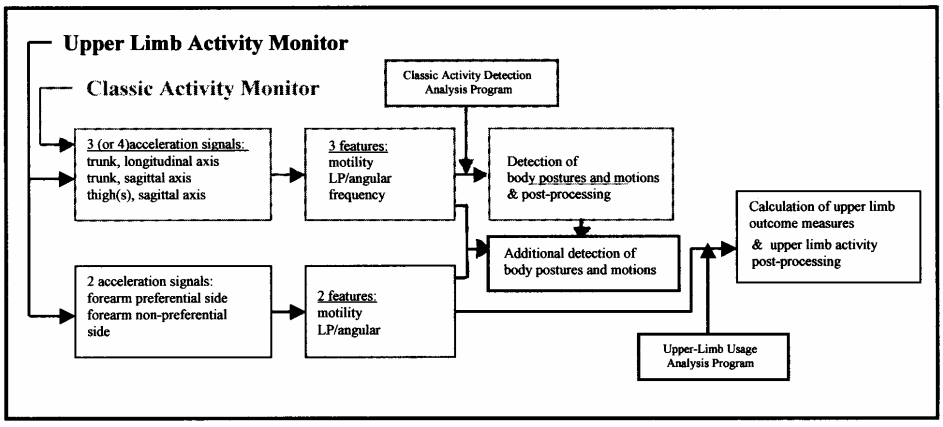
a) Additional body posture and motion detection using features from the signals of the forearms.

b) Based on information on body postures and motions and feature signal data from the forearms, a set of Upper Limb Activity measures are calculated.

c) Upper limb activity post-processing.

These subsequent parts will be described in the following paragraphs.

Figure 4.3: The Upper Limb-Activity Monitor and its analysis program in relation to the classic version of the Activity Monitor and its analysis program.



Feature extraction

The feature signals are continuously computed from each measured accelerometer signal (see also figures 3.3 chapter 3 and 5.1 chapter 5, this thesis). The *LP/angular feature* signals are created after low-pass filtering (finite impulse response filter, cut-off frequency 0.3 Hz). These signals are subsequently averaged over 1 second intervals and converted to angles via an arcsine transformation (range –90º to + 90º), although the translation to an angular position of the sensor is not straightforward (e.g. during motion and multidimensional angular positions). The *frequency feature* signals are based on a band-pass-filtered derivative (0.6-4 Hz for the trunk signals and 0.3-2 Hz for signals from other sites of attachment), also with the use of finite impulse response filters. This band-passed signal (which ideally has a sinusoid shape with the movement frequency of the segment the sensor is attached to) is the input of the fast time frequency transform (FTFT) procedure [13]. This procedure constitutes a particular type of instantaneous frequency analysis for signals and determines instantaneously the frequency and amplitude/envelope of the band-passed signal. To be regarded as valid, this raw instantaneous frequency must meet three criteria, pre-set in the so-called FTFT knowledge base: the frequency range, the amplitude (power) range of the band-pass-filtered signal, and the variability of the detected frequency. If the current signal does not meet all the pre-set criteria, no valid frequency is assigned; otherwise, the frequency is assigned to a frequency feature signal and averaged over 1 second intervals. The *motility feature* signals are created after subsequent filtering at 0.3-16 Hz and applying a root-mean-square (RMS) procedure during subsequent 1-second windows of filtered data; the RMS value is assigned to the motility feature signal (1Hz). This value depends on the variability of the measured signal around the mean.

Posture/motion detection

Based on the three feature signals derived from the measured trunk and thigh signals, more than 20 (sub) body postures and body motions are distinguished in the analysis program. For each subcategory and for each feature signal, a minimum and maximum value is a pre-set in the activity detection knowledge base. For consecutive intervals of 1 second, for each subcategory and for each feature signal, the ‘distance’ is calculated from the actual feature signal value to the pre-set range of feature signal values. Since the three features (LP/angular, frequency and motility) have different units (degrees, Hz and g, respectively), some features are scaled to allow a proportional influence of all features. If an actual feature signal value is within the pre-set range of a specific posture/motion subcategory, the calculated distance is zero – that is, it does not add to the total distance for that subcategory. The calculated distances of the feature signals are added for each subcategory; the body posture/motion with the lowest total distance in the end will be selected and detected. If a posture/motion is detected, but the distance is above a pre-set general threshold value, indicating a relatively high degree of unreliability, the category ‘unknown’ is selected.

There are some (optional) post-processing procedures after posture/motion detection. The first option is to reduce the number of categories from subcategories to main categories. Although most of the 23 subcategories are initially required to avoid misdetection, not all have to be of interest in a later phase, especially when subjects with an upper limb disorder are the topic of investigation. In our studies, the most often used main categories are the body postures lying, sitting and standing, including transitions, and the body motions walking, running, climbing stairs, cycling and general non-cyclic movements. A second post-processing option is applying duration thresholds, which means that postures/motions below certain duration are rejected because these may not be of clinical or methodological interest. In fact, each sample within a time window of n seconds around sample s is examined; the posture/motion that is most frequently detected in that window is assigned to sample s. The size of the frame determines the duration threshold (usually 5 seconds). Manual editing is the third option in post-processing. Although the validity of the AM is high, not all postures/motions are currently correctly detected (e.g. driving a car can only be determined by visual inspection at the moment, but it may be desirable to distinguish driving from sitting). In such situations, it is possible to manually correct or insert categories. If necessary, this type of manual post-processing has to be done before the SPIL routines for automatic detection of upper limb activity are applied in order to obtain unobtrusive information about upper limb (in)activity.

Detection of (limited) upper limb activity

As mentioned, the detection of upper limb (in)activity takes place after standard detection of mobility-related activities with the 'classic activity detection analysis program' (figure 4.3). The ULAM upper-limb usage analysis program consists of several sub-programs in which the SPIL-routines consisting of Boolean operators and pre-set motility thresholds are described [8, 12].

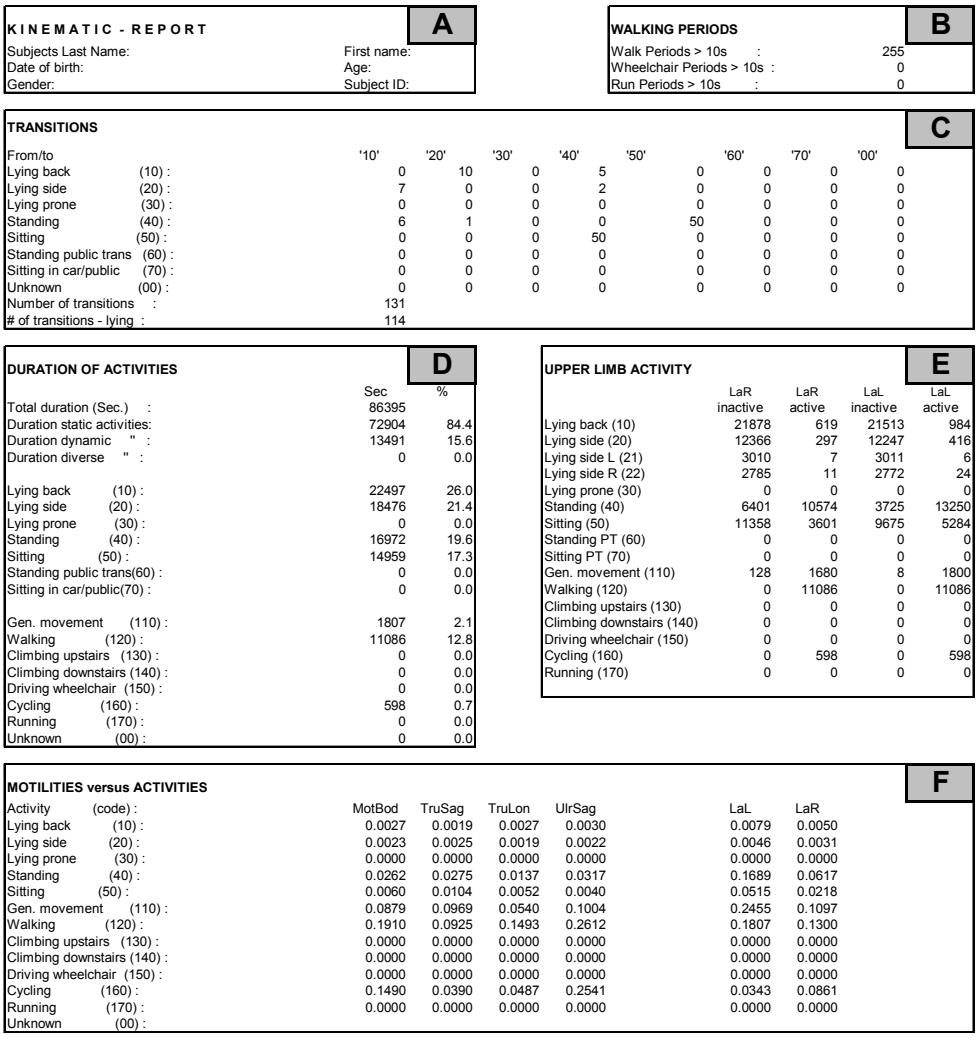
a) The first sub-program that is used generates additional body postures and motions (mobility-related activities) that were not yet detected with the classic activity detection analysis program. On the bases of the motility and LP/angular signals of the forearms and the average value of the trunk and thigh motility signals the following mobility-related activities are additionally detected: lying on the side undefined, lying on the right side, lying on the left side and sitting or standing during (public) transportation.

b) The second sub-program that is used performs the actual detection of upper limb activity and inactivity, for both upper limbs separately. For each forearm sensor, a new signal is generated that indicates per second whether there is upper limb activity or not; for each body posture and body motion, distinct pre-set thresholds were used for the motility signals of the forearm sensors in order to compensate for differences in general body movements due to postural sway or head movements during different mobility-related activities (see also [8]).

c) Post-processing in the 'upper limb usage analysis program' consists of creating statistics/reports. For each mobility-related activity an overview is provided of the number of samples (i.e. seconds) that the individual upper limbs were active or not. Also, the average motility value of the forearm sensors for each mobility-related activity can be obtained. The so-called ´report-files´ can be exported to Microsoft EXCEL to further calculate a large number of outcome measures (figure 4.4). The calculation of ULAM outcome measures may comprise the whole measurement period or one or more parts of it.

In the report files, some standard information is provided about the subject that was measured with the ULAM (part A, figure 4.4). Part B shows the number of walking, wheelchair (if applicable) or running periods of more than 10 seconds. Then in part C, an overview of transitions from one (coded) body position to another (coded) body position is provided. The number of transitions is also summed up, both for the total number of transitions and for the number of transitions with the transitions between different forms of lying excluded. Part D gives an overview of the duration (in seconds and in % of the measurement period) of each body posture and motion (i.e. mobility-related activity). Part E demonstrates the duration of upper limb activity and inactivity for both forearm sensors LaR and LaL separately for each of the body postures and motions. LaR refers to the involved upper limb when a patient is measured or to the dominant limb when a healthy subject is measured and LaL refers to the non-involved upper limb when a patient is measured or to the non-dominant limb when a healthy subject is measured. The bottom part (F) of the report shows the average motility values per acceleration sensor, for each body posture and motion separately. TruSag and TruLon refer to the sensor on the trunk with axes in the sagital and longitudinal direction. UlrSag refers to the sensor on the right upper leg with the axis in the sagital direction. MotBod is the average of summed motility values of the trunk and leg sensors. We would like to refer to the application studies described in this thesis (chapters 5-8) for a description of the ULAM outcome measures that were calculated from these report files and were actually used.

Figure 4.4: Example of a report file.



K I N E M A T I C - R E P O R T — **A**

Subjects Last Name:	First name:
Date of birth:	Age:
Gender:	Subject ID:

WALKING PERIODS — **B**

Walk Periods > 10s :	255
Wheelchair Periods > 10s :	0
Run Periods > 10s :	0

TRANSITIONS — **C**

From/to	'10'	'20'	'30'	'40'	'50'	'60'	'70'	'00'
Lying back (10) :	0	10	0	5	0	0	0	0
Lying side (20) :	7	0	0	2	0	0	0	0
Lying prone (30) :	0	0	0	0	0	0	0	0
Standing (40) :	6	1	0	0	50	0	0	0
Sitting (50) :	0	0	0	50	0	0	0	0
Standing public trans (60) :	0	0	0	0	0	0	0	0
Sitting in car/public (70) :	0	0	0	0	0	0	0	0
Unknown (00) :	0	0	0	0	0	0	0	0
Number of transitions :	131							
# of transitions - lying :	114							

DURATION OF ACTIVITIES — **D**

	Sec	%
Total duration (Sec.) :	86395	
Duration static activities:	72904	84.4
Duration dynamic " :	13491	15.6
Duration diverse " :	0	0.0
Lying back (10) :	22497	26.0
Lying side (20) :	18476	21.4
Lying prone (30) :	0	0.0
Standing (40) :	16972	19.6
Sitting (50) :	14959	17.3
Standing public trans(60) :	0	0.0
Sitting in car/public(70) :	0	0.0
Gen. movement (110) :	1807	2.1
Walking (120) :	11086	12.8
Climbing upstairs (130) :	0	0.0
Climbing downstairs (140) :	0	0.0
Driving wheelchair (150) :	0	0.0
Cycling (160) :	598	0.7
Running (170) :	0	0.0
Unknown (00) :	0	0.0

UPPER LIMB ACTIVITY — **E**

	LaR inactive	LaR active	LaL inactive	LaL active
Lying back (10)	21878	619	21513	984
Lying side (20)	12366	297	12247	416
Lying side L (21)	3010	7	3011	6
Lying side R (22)	2785	11	2772	24
Lying prone (30)	0	0	0	0
Standing (40)	6401	10574	3725	13250
Sitting (50)	11358	3601	9675	5284
Standing PT (60)	0	0	0	0
Sitting PT (70)	0	0	0	0
Gen. movement (110)	128	1680	8	1800
Walking (120)	0	11086	0	11086
Climbing upstairs (130)	0	0	0	0
Climbing downstairs (140)	0	0	0	0
Driving wheelchair (150)	0	0	0	0
Cycling (160)	0	598	0	598
Running (170)	0	0	0	0

MOTILITIES versus ACTIVITIES — **F**

Activity (code) :	MotBod	TruSag	TruLon	UlrSag	LaL	LaR
Lying back (10) :	0.0027	0.0019	0.0027	0.0030	0.0079	0.0050
Lying side (20) :	0.0023	0.0025	0.0019	0.0022	0.0046	0.0031
Lying prone (30) :	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Standing (40) :	0.0262	0.0275	0.0137	0.0317	0.1689	0.0617
Sitting (50) :	0.0060	0.0104	0.0052	0.0040	0.0515	0.0218
Gen. movement (110) :	0.0879	0.0969	0.0540	0.1004	0.2455	0.1097
Walking (120) :	0.1910	0.0925	0.1493	0.2612	0.1807	0.1300
Climbing upstairs (130) :	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Climbing downstairs (140) :	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Driving wheelchair (150) :	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Cycling (160) :	0.1490	0.0390	0.0487	0.2541	0.0343	0.0861
Running (170) :	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Unknown (00) :						

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5 Impact of upper limb complex regional pain syndrome type I on everyday life measured with a novel upper limb-activity monitor

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5.1 Abstract

Background: Complex regional pain syndrome type I (CRPSI) often leads to serious activity limitations in everyday life. To date, however, limitations in patients with CRPSI of an upper limb have not been objectively measured. **Aim:** To determine the long-term impact of upper limb CRPSI on general mobility and upper limb usage during everyday life, as measured with a novel upper limb-activity monitor (ULAM). **Method:** In ten female chronic CRPSI patients and ten healthy control subjects, 24-h activity patterns were measured with the ULAM. This ULAM consists of body-fixed acceleration sensors, connected to a recorder worn around the waist. The ULAM automatically detects upper limb activity during mobility-related activities. Several outcome measures related to general mobility and upper limb usage were compared between patients and controls. **Results:** CRPSI in the dominant upper limb had modest impact on general mobility; i.e. on the percentages spent in body positions and body motions and on mean intensity of body activity. For upper limb usage outcome measures during sitting there was a marked difference between CRPSI patients and controls. Especially patients with dominant side involvement clearly showed less activity of their involved limb during sitting, indicated by significant differences for the mean intensity ($p=0.014$), percentage ($p=0.004$) and proportion ($p=0.032$) of upper limb activity. **Conclusion:** These ten chronic CRPSI patients still had limitations in upper limb usage during everyday life 3.7 years (average) after the causative event.

5.2 Introduction

Complex Regional Pain Syndrome type I (CRPSI; also known as reflex sympathetic dystrophy or posttraumatic dystrophy) is a complex entity comprising a combination of sensory, trophic, autonomic and motor impairments that usually follows trauma or surgery and is generally expressed in the extremities [1]. Etiology and pathophysiology of this syndrome have been studied, but with conflicting results and theories [2, 3]. Because CRPSI is not yet fully understood and variously defined, it remains a topic of discussion [4-11]. Moreover, a wide variety of treatments and numerous measures to determine treatment outcome have been described [2]. Most outcome measures for CRPSI concentrate on impairments [12], which is remarkable because CRPSI can lead to serious activity limitations in everyday life [5, 13-21]. Activity limitations associated with upper limb CRPSI are directly related to upper limb usage during everyday life (e.g. problems with getting dressed or personal hygiene). In addition, limitations in general mobility may also occur (e.g. hypoactivity). In spite of numerous research reports on CRPSI, there is little information on activity limitations [19, 22, 23]. So far, studies on activity limitations of patients with CRPSI have only used (retrospective) scales and questionnaires: no instruments have been employed that measure what patients *actually do* and whether they *actually use the upper limbs* during everyday physical activities [12]. The importance of such objective outcome measures for CRPSI research has recently been stressed in a consensus report [24].

The Activity Monitor (AM), developed and validated in our department [25-30], is a portable device based on ambulatory accelerometry that can be used for long-term measurement of mobility-related activities (body positions and body motions, including transitions). The AM consists of acceleration sensors attached to thighs and trunk, connected to a small recorder that is worn in a padded bag around the waist. The device allows to automatically detect mobility-related activities (e.g. lying, sitting, standing, walking, cycling and general movement). Measurement of these activities enables assessment of limited general mobility, e.g. lying down or sitting most of the day, or a low number of transitions. To determine activity limitations of subjects with disorders related to upper limbs, such as CRPSI, we extended the possibilities of the AM, resulting in an upper limb-activity monitor (ULAM) [31]. The ULAM enables to determine whether or not the upper limbs are active when a subject is performing one of the mobility-related activities. In a feasibility study [31], subjects performed an activity protocol, representing several forms of real-life upper limb (non-)usage that were described in a framework. Agreement scores between the ULAM output categories and video recordings (reference method) were calculated. The ULAM output categories that were of special interest from a rehabilitation point of view were satisfactorily detected. It was considered feasible to use the ULAM in future studies in patients with an upper limb disorder. The combination of data on mobility-related activities and activity of both upper limbs allows to obtain more specific information than with the more frequently used, less advanced techniques, such as a wrist

activity monitor/actigraph/actometer [32-36]. The ULAM enables detailed measurement of what subjects actually do and can therefore be used to determine the impact of upper limb disorders, such as CRPSI, on everyday life. Such an instrument has never been used before in CRPSI research. Therefore, the aim of this study was to determine the long-term impact of CRPSI in one of the upper limbs on everyday life, as measured with the ULAM.

The research questions were:

- Does CRPSI in one upper limb have an impact on general mobility during everyday life?
- Does CRPSI in one upper limb have an impact on upper limb usage during everyday life?
- Does the impact depend on whether the dominant or non-dominant side is involved?

5.3 Methods

Design and subjects
Twenty subjects volunteered to participate in this descriptive comparison study: ten female chronic CRPSI patients and ten healthy controls with the same age (± 3 years), gender and family situation. In five patients the dominant side was involved and in the other five the non-dominant side; the right side was dominant in all control subjects. Mean age was 50.2 (sd ± 15.7) years in the patients and 50.3 (sd ± 16.6) years in the controls. Inclusion criteria for CRPSI were 1) presence of the criteria of Veldman [37] at the moment of diagnosis, and 2) presence of CRPSI-related complaints at the moment of measurement. The criteria of Veldman were a) four or five of the following: unexplained diffuse pain, different skin color relative to other side, diffuse edema, different skin temperature relative to other side, limited active range of motion, b) occurrence or increase of signs and symptoms after use, and c) presence of signs and symptoms in an area larger than primary involved, including the area distal to primary injury. These criteria do not substantially differ from the criteria formulated by the International Association for the Study of Pain (IASP) [1, 8]. Table 5.1 presents some patient characteristics, which were measured with the following instruments: a Visual Analogue Scale (VAS), goniometry, hand-held dynamometry, a volumeter (Volumeters Unlimited) and an infrared thermometer (Braun Pro 3000 Type 6014). None of the patients had contractures or dystonia. All the patients reported perceiving activity limitations as a consequence of CRPSI. Written and oral information was given, and informed consent was obtained. The study was approved by the Medical Ethics Committee of Erasmus MC.

Table 5.1: Characteristics of the ten patients for both subgroups separately.

Patient number	Dominant side	Involved side	Age (years)	Duration since onset (months)	Time between onset & diagnosis (months)	Currently treated	Preceding event
1	left	left	19	34.5	2	Y both	fractures
4	right	right	47	41	18.5	Y ther	spontaneously
5	right	right	56	143.5	1.5	Y phar	fracture
7	left	left	44	10	4.5	Y ther	fracture
9	left	left	54	33	1	N	spontaneously
2	right	left	80	39.5	0.5	N	heamorrhage
3	right	left	36	16.5	1	Y phar	fractures
6	right	left	56	9.5	2.5	Y ther	dupuytren
8	right	left	58	30	1.5	N	fracture
10	right	left	53	89.5	0.5	N	fracture

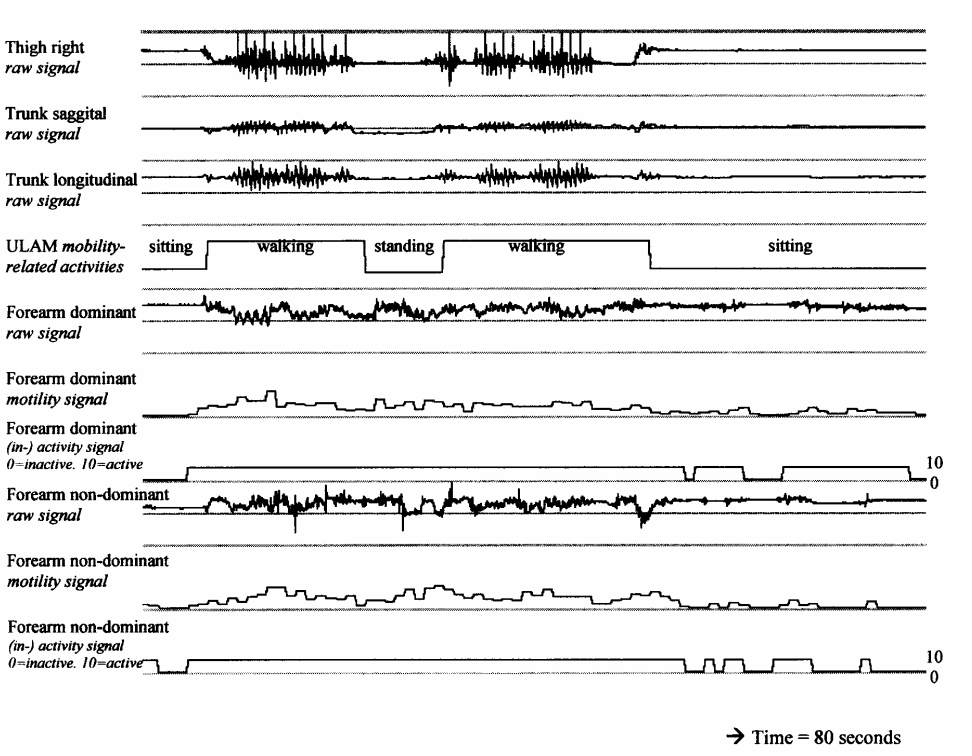
Patient group	Momentary pain	Pain after strain	Active Range of Motion	Grip strength	Temperature hand	Volume hand	Productivity status
dom	+ +	+ +	+ +	+	o	-	Social services
dom	+	+ +	+ +	+ +	-	-	Work compensation
dom	+	+	+ +	+	- -	-	Work compensation
dom	+	+ +	+ +	+ +	o	o	Work compensation
dom	+	+ +	+ +	+ +	- -	+ +	Work compensation
nondom	+	+	+	o	-	o	Retired
nondom	+	+ +	+ +	+ +	o	+	Work compensation
nondom	o	+	+ +	+	+ +	o	Housewife
nondom	+	+	+	o	o	o	Voluntary work
nondom	+ +	+	+ +	+	+	o	Working (parttime)

Current treatment is classified as: N = no treatment anymore, Yther = yes; therapeutic treatment either acupuncture, physical, manual or occupational therapy, Yphar = yes; pharmacological treatment, including analgetics and peripheral vasodilators, Yboth = yes; both pharmacological and therapeutic. Presence and severeness momentary pain, pain after strain, Active Range of Motion (AROM) of wrist & the two most impaired fingers, grip strength, temperature of the dorsal aspect and volume of the hand were determined. For AROM, strength, temperature and volume, intra individual comparisons of the involved and non-involved sides determined presence or absence. These signs and symptoms were classified as follows: o = absence, + = mild presence, + + = clear presence. Temperature and volume symptoms were indicated as positive (higher temperature and presence of oedema of the involved side) or negative (lower temperature and presence of tissue atrophy of the involved side).

Upper Limb-Activity Monitor

The technique of ambulatory accelerometry is based on long-term monitoring of signals from body-fixed acceleration sensors. Information on general mobility can be obtained by determining which mobility-related activities (body positions, body motions and transitions between positions) are performed, when, how often, and for how long [30]. Studies using video recordings as a reference method have shown that these mobility-related activities can be validly quantified [26-30] and that differences in everyday physical activities between groups can be detected [38, 39], which supports the validity and usability of such a technique in clinical research.

Figure 5.1: An example of 80 s of several signals and the automatically detected output of mobility-related activities and upper limb (in-)activity of the dominant and non-dominant forearms of a control subject. ULAM outcome measures are composed of the signals of the mobility-related activities and the forearms signals.



The ULAM allows to obtain information on upper limb activity of both upper limbs in relation to mobility-related activities [31]. Uni-axial piezoresistive acceleration sensors (Analog Devices, ADXL201) were used (size 1x1x0.5 cm). The raw acceleration signals are expressed in g (9.81 ms $^{-2}$) and are a combination of two components: gravitational acceleration and accelerations due to activity [30, 40]. The magnitude of these components depends on the extent and direction of the accelerations with regard to the sensitive direction. To detect mobility-related activities, one sensor was placed lateral on the right thigh halfway between the spina iliaca anterior superior and upper side of the patella (sensitive direction in sagital plane) and two sensors on the sternum (sensitive direction in sagital and longitudinal plane). To detect upper limb activity, two sensors were attached on each forearm just proximal from the wrist joint (sensitive direction in sagital plane being in the anatomical position). The sensors were attached to Rolian Kushionflex^{TM} or silicon based stickers (Schwamedico) with double-sided tape; both materials can be fixed directly on the skin. The raw acceleration signals were stored digitally on a 40 MB PCMCIA flash card (Sandisk, USA) with a sample frequency of 32 Hertz. After the measurements, the raw data were downloaded onto a PC for analysis.

Detection of mobility-related activities and upper limb activity was done by automatic kinematic analysis based on signal processing and inferencing language (SPIL) routines, yielding 'C'-code [41]. For detection, three feature signals are derived from each raw accelaration signal: the angular, motility and frequency feature, each with a time resolution of 1 s. The subsequent steps of analysis (activity detection and postprocessing) have been described previously [26-28, 30, 38, 39]. Briefly, for each activity and for each feature signal, a maximum and minimum value is pre-set. Each second, the 'distance' from the actual feature signal value to the pre-set range is calculated for each feature signal from each sensor. The mobility-related activity with the lowest total distance is detected. During post-processing, wrongly detected mobility-related activities (e.g. time spent with transport is currently not 100% well-detected) may be edited using SPIL routines to unobtrusively detect the outcome measures of interest.

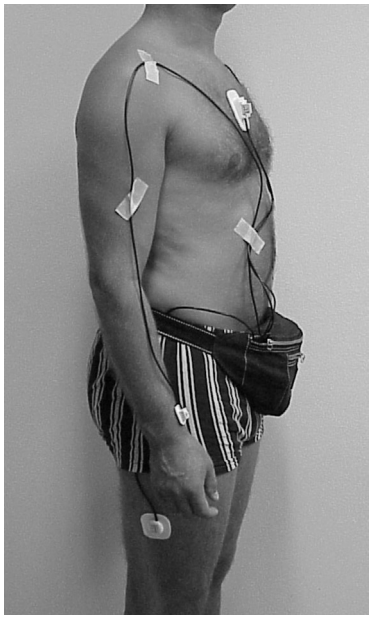
To detect upper limb activity, one of the three features i.e. the motility feature was used. This motility feature is created after zero-phase finite impulse response high pass filtering (0.3-16 Hz) of the raw acceleration signal, rectifying and averaging over 1 second. The value of this signal depends on the variability of the raw signal around the mean and is also expressed in g (9.81 ms^{-1}). The variability of the raw upper limb acceleration signal can be regarded as a measure for upper limb activity; the more the value is varied, the higher the motility value, the more the upper limb activity. To determine whether an upper limb was active, it was automatically determined (each second) whether the motility values of an upper limb sensor exceeded a preset threshold assigned to the mobility-related activity that was performed during that second [31]. Each second the motility values exceeded the threshold, the ULAM signal for the upper limb forearm was positive, indicating upper limb activity (figure 5.1).

Each second the motility value did not exceed the threshold, the ULAM signal for the upper limb forearm was zero, indicating upper limb inactivity.

Protocol

Subjects were measured during a 24-hour period during one randomly selected weekday (and night). Patient and control were measured within 3 weeks to avoid the possible effect of season. To minimize interference with normal everyday activity patterns, the ULAM was fitted at home (figure 5.2). Subjects were instructed to continue their ordinary everyday physical activities, but were not allowed to swim, take a bath or shower while monitored. To avoid bias, initially the exact technique of the ULAM was not explained. After the measurements, the subjects were visited again to remove the device, to determine several patient characteristics, to make an inquiry about which activities were performed during the last 24 h and about convenience of wearing the ULAM. Furthermore, complete information was given about what the ULAM exactly measures and, of course, the reason for not having given that information before. All subjects agreed with this procedure.

Figure 5.2: A subject wearing the Upper Limb-Activity Monitor.



Outcome measures

To obtain information about the impact on performing mobility-related activities, the following general mobility outcome measures were used:

- Percentages spent in body positions (lying, sitting, standing) and body motions (walking, cycling, general non-cyclic movement) expressed as percentages of the 24-hour measurement period,
- Number of transitions between body positions,
- Number of walking periods (> 10 seconds),
- Mean intensity of body activity (in g), expressed as the mean value of the motility signals of the trunk and leg sensors. This mean value over the 24-hour period (excluding time spent with transportation, because of external vibrations) can be regarded as a general measure for the intensity of everyday physical activity.

To determine the impact of CRPSI on upper limb activity in relation to mobility-related activities the following upper limb usage outcome measures were used:

- Mean intensity of upper limb activity during sitting and standing, expressed as the mean motility value of an upper limb during the time that a subject was sitting and standing. Upper limb activity during standing and sitting were considered most important, because, in our opinion, limitations in upper limb usage as a consequence of upper limb disorders are mainly expressed in everyday life during these body positions.
- Percentage of upper limb activity of the upper limbs during sitting and standing, expressed as percentage of the time the upper limbs were active (exceeding the motility threshold) while the subjects were sitting and standing,
- Proportion of upper limb activity of one side relative to the other side during sitting and standing, expressed a ratio: the percentage of activity of the non-dominant upper limb relative to the percentage of activity of the dominant upper limb. For subjects with dominant side involvement a ratio higher than the controls indicated more limitations. For subjects with non-dominant side involvement a ratio lower than the controls indicated more limitations. A ratio of exactly one meant equal activity of both upper limbs.

To determine whether the impact depends on dominant or non-dominant side involvement, the outcome measures described above were also analyzed for both patient subgroups compared to their controls. In the results section, the total group of CRPSI patients will be referred to as "Pnt_{tot}" and the total group of control subjects will be referred to as "Crl_{tot}". Patients with the dominant side involved will be designated the "Pnt_{dom}" group and patients with the non-dominant side involved will be designated the "$Pnt_{non\text{-}dom}$" group. The respective control subgroups will be referred to as "$Crl_{(dom)}$" and "$Crl_{(non\text{-}dom)}$" (with indicated between parentheses to which patient subgroup these controls were compared). The upper limbs of the CRPSI

patients are described as “involved” and “non-involved” side and the upper limbs of the controls are described as “dominant” and “non-dominant” side.

Statistics
Differences between CRPSI patients and controls for the general mobility outcome measures were tested with the Mann-Whitney *U* test. The Kruskal-Wallis test was used to determine whether there were differences between the four upper limb sides. Differences between the separate upper limbs (involved, non-involved; dominant and non-dominant side) for upper limb usage outcome measures were also tested with the Mann-Whitney *U* test.

5.4 Results

Patient characteristics
Mean duration of CRPSI since the preceding event was 44.7 months in the Pnt_{tot} group (52.4 months in Pnt_{dom} and 37.0 months in $Pnt_{non\text{-}dom}$ group) (table 5.1). The mean duration of CRPSI since diagnosis was 41.4 months (46.9 months in Pnt_{dom} and 35.8 months in $Pnt_{non\text{-}dom}$ group). No significant rank correlations were found between duration of CRPSI and the upper limb activity outcome measures. All patients showed CRPSI-related signs and symptoms at the moment of measurement, and the majority currently had treatment, either pharmacological or therapeutic.

General mobility
There were no significant differences for the general mobility outcome measures between the Pnt_{tot} and the $Pnt_{non\text{-}dom}$ groups and their respective controls (table 5.2). The Pnt_{dom} group was significantly less active (percentages spent in body positions and body motions) compared to their controls ($p=0.028$). Although no significant differences were found for the number of transitions and walking periods, there was a tendency for patients to be less active (especially the Pnt_{dom} group). There was a significant difference in 24-hour mean body activity intensity between the Pnt_{dom} group and their controls ($p=0.047$). There were no significant differences in any of the outcome measures for general mobility between both groups of control subjects ($Crl_{(dom)}$ and $Crl_{(non\text{-}dom)}$).

Table 5.2: Outcome measures for mobility-related activities in ten upper limb CRPSI patients and ten controls. Data are presented as mean (standard deviation) [ranges between brackets] for the Pnt_{tot} group, the Pnt_{dom} group and the $Pnt_{non\text{-}dom}$ group, each with their controls. Because body positions and body motions together comprise the total 24-hour measurement period, p-values with respect to difference between patients and controls are the same.

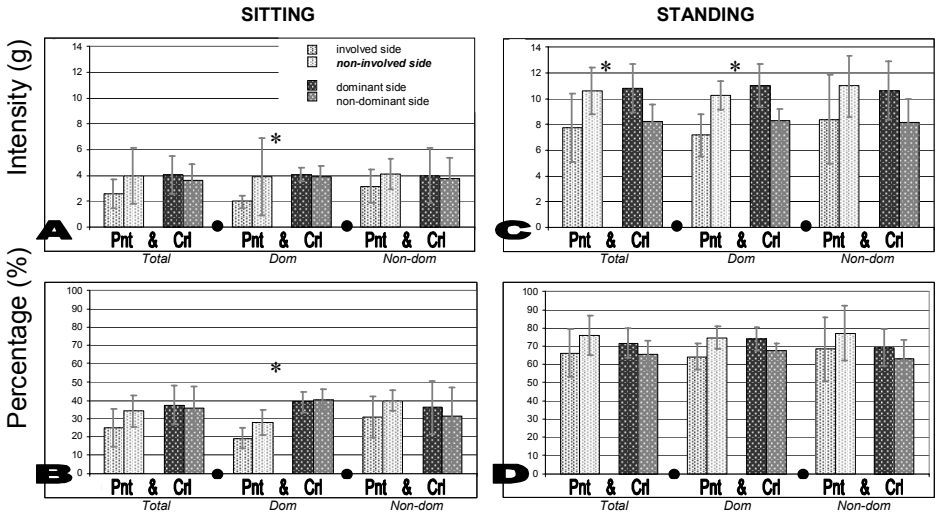
Outcome measure	Pnt_{tot} (n=10)	Crl_{tot} (n=10)	P-value	Pnt_{dom} (n=5)	$Crl_{(dom)}$ (n=5)	P-value	$Pnt_{non\text{-}dom}$ (n=5)	$Crl_{(non\text{-}dom)}$ (n=5)	P-value
Percentage body positions	89.2 (5.7) [76.0 - 93.9]	88.4 (2.3) [84.8 - 91.4]	0.199	92.0 (1.7) [90.2 - 93.8]	87.3 (2.7) [84.8 - 91.1]	0.028 *	86.4 (7.1) [76.0 - 93.9]	89.5 (1.1) [88.3 - 91.4]	0.602
Percentage body motions	10.8 (5.7) [6.1 - 24.0]	11.6 (2.3) [8.6 - 15.2]	0.199	8.0 (1.7) [6.2 - 9.8]	12.7 (2.7) [8.9 - 15.2]	0.028 *	13.6 (7.1) [6.1 - 24]	10.5 (1.1) [8.6 - 11.7]	0.602
Number transitions	124 (21) [96 - 167]	146 (53) [80 - 253]	0.326	119 (13) [103 - 137]	156 (64) [80 - 253]	0.175	129 (28) [96 - 167]	136 (46) [104 - 216]	0.917
Number walking periods (> 10 seconds)	213 (89) [92 - 371]	221 (54) [131 - 290]	0.570	169 (38) [107 - 199]	231 (61) [131 - 290]	0.075	255 (109) [92 - 371]	210 (50) [142 - 275]	0.347
Body activity intensity (during transport not included)	2.08 (0.70) [1.41 - 3.32]	2.41 (0.50) [1.51 - 3.35]	0.174	1.74 (0.28) [1.41 - 2.06]	2.63 (0.55) [1.80 - 3.35]	0.047 *	2.43 (0.86) [1.56 - 3.32]	2.18 (0.38) [1.51 - 2.40]	0.347

Upper limb usage

During sitting, a significant difference between mean activity intensity of the different upper limbs of the Pnt_{dom} group and $Crl_{(dom)}$ subjects was found (p=0.014) (figure 5.3A). Mean activity intensity of the involved limb in the Pnt_{dom} group was significantly less than the other limbs. Overall, the involved limbs of the CRPSI patients were less intensely active than the non-involved limbs and the upper limbs of the controls.

The percentage of upper limb activity of the different upper limbs during sitting was not significantly different for the four sides in the Pnt_{tot} and Crl_{tot} groups, nor for the $Pnt_{non\text{-}dom}$ and $Crl_{(non\text{-}dom)}$ groups. However, there was a significant difference between percentage of upper limb activity of the upper limbs of the Pnt_{dom} group and $Crl_{(dom)}$ subjects (p=0.004) during sitting (figure 5.3B).

*Figure 5.3: Mean activity intensity (expressed in g) and percentage of upper limb activity of the upper limbs of CRPSI patients and controls. From left to right in each graph, results are shown for the Pnt $_{tot}$ group, the Pnt$_{dom}$ group, the Pnt$_{non\text{-}dom}$ group and the limbs of the corresponding controls. Graphs A and B represent upper limb activity during sitting and graphs C and D represent upper limb activity during standing. * Indicates a significant difference between of the four upper limbs.*



During standing, a significant difference between mean activity intensity of the different upper limbs of the Pnt$_{tot}$ group and Ctl$_{tot}$ subjects (p=0.004) was found (figure 5.3C). Also, a significant difference was found between mean activity intensity of the different upper limbs of the Pnt$_{dom}$ group and Ctl$_{(dom)}$ subjects (p=0.004). The percentage of upper limb activity of the different upper limbs during standing showed no significant differences in any of the three groups (figure 5.3D).

Mean intensity and percentage of upper limb activity of the involved side of CRPSI patients were compared with the mean intensity and percentage of activity of the other limbs (i.e. the non-involved, dominant and non-dominant sides). It appeared that the mean intensity and percentage of activity of the involved limb were always less than the mean intensity and percentage of upper limb activity of the other limbs during sitting in the Pnt$_{tot}$ group (table 5.3).

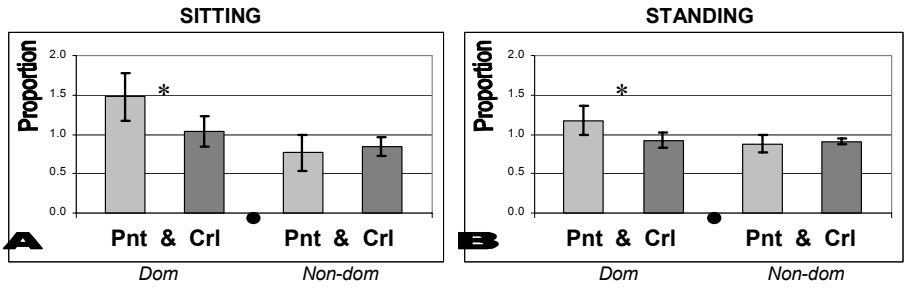
*Table 5.3: Overview of the mean intensity and percentage of upper limb activity: the involved side of the CRPSI patients were compared with the non-involved side of the patients and the dominant and non-dominant sides of the controls using Mann-Whitney U Tests. Each time, it is tested whether the involved limb of the CRPSI patients is significantly less used than the other limbs. Data are presented for the Pnt_{tot} and Crl_{tot} group, the Pnt_{dom} and $Crl_{(dom)}$ group and the $Pnt_{non\text{-}dom}$ and $Crl_{(non\text{-}dom)}$ group, respectively, each for sitting and standing. * $p \leq 0.05$, ** $p \leq 0.01$, ^{ns} not significant.*

	Pnt_{tot} & Crl_{tot} (n=20)		Pnt_{dom} & $Crl_{(dom)}$ (n=10)		$Pnt_{non\text{-}dom}$ & $Crl_{(non\text{-}dom)}$ (n=10)	
	Sitting	Standing	Sitting	Standing	Sitting	Standing
Intensity Inv < Non-inv	*	*	ns	*	ns	ns
Intensity Inv < Dom	*	**	**	*	ns	ns
Intensity Inv < Non-dom	*	ns	**	ns	ns	ns
Percentage Inv < Non-inv	*	ns	ns	*	ns	ns
Percentage Inv < Dom	*	ns	**	ns	ns	ns
Percentage Inv < Non-dom	*	ns	**	ns	ns	ns

As stated, the Pnt_{tot} and the Crl_{tot} groups could not be compared with respect to the proportion of upper limb activity because a high ratio indicated more limited in dominant side involvement and a low ratio indicated more limited in non-dominant side involvement. The proportion of upper limb activity during sitting was significantly higher in the Pnt_{dom} than in the $Crl_{(dom)}$ group ($p=0.032$), indicating limitations (figure 5.4A). This proportion during sitting in the $Pnt_{non\text{-}dom}$ was lower than the proportion in the $Crl_{(non\text{-}dom)}$ group, indicating limitations, but this difference was not significant.

Similar results were found with respect to the proportion during standing (figure 5.4B); the ratio was significantly higher in the Pnt_{dom} than in the $Crl_{(dom)}$ group ($p=0.016$). Finally, none of the outcome measures for upper limb usage during sitting and standing differed significantly between both control groups ($Crl_{(dom)}$ and $Crl_{(non\text{-}dom)}$).

*Figure 5.4: The proportion of upper limb activity during sitting (A) and standing (B). For dominant side involvement a high ratio indicated more limitated. For non-dominant side involvement a low ratio indicated more limited. Results are shown for the Pnt_{dom} group, the $Pnt_{non-dom}$ group and their respective controls. * Indicates a significant difference between the proportion of upper limb activity in patients and controls.*



5.5 Discussion

Impact of upper limb CRPSI on everyday life

With respect to the mobility-related outcome measures, the subjects with dominant side involvement showed significantly lower percentages spent in body motions (higher percentages of body positions) and a decreased mean body activity intensity. But overall, CRPSI in one upper limb did not have a large impact on performance of mobility-related activities during everyday life. The impact on general mobility may be more obvious in patients with acute CRPSI, when signs and symptoms are usually more severe and may more markedly affect activity levels (e.g. afraid to knock the involved limb). In later stages, signs and symptoms may have decreased and strategies may be developed for participation in everyday life (despite remaining signs & symptoms). Finding such compensatory strategies is presumably easier with non-dominant than with dominant side involvement, which may explain the different impact on general mobility in both patient subgroups.

Although the impact of CRPSI on general mobility was modest, there was a clear impact on upper limb activity. The mean intensity and percentage of activity of the involved limb and the proportion of upper limb activity of the patients differed considerably from the controls, and again especially when the dominant side was involved. Upper limb CRPSI had greater impact on upper limb activity during sitting than during standing, which cannot easily be explained, especially because of the small sample size. Inactivity of an involved upper limb could be real disuse, i.e. just not using the limb, or conscious protection (which cannot be distinguished with the ULAM). However, because of the intuitively higher risk of bumping an involved upper limb during standing than during sitting, a patient may be more inclined to protect the

involved limb during standing. This makes it tempting to state that inactivity during sitting was probably more due to disuse and less to protection, which may explain (together with compensatory strategies in chronic CRPSI) why the long-term impact on upper limb activity was more obvious during sitting.

We realize that our findings may be no surprise at all to clinicians and just confirm the supposition of disuse and protection in CRPSI. However, the objectively measured ULAM findings were not in concordance with subjective patient findings (who reported having limitations in both general mobility and upper limb usage). The surplus value of the ULAM is that it enables to study discrepancies between objective and subjective findings, which are more regularly present than one often thinks. Such a study is currently performed in a larger population of CRPSI patients. Objective determination of treatment effect on the activity level may also be performed in future studies.

Pain behavior and the ULAM

Pain is most frequently used as outcome measure in CRPSI research [12] and is often described as the most unpleasant feature [2, 5, 16, 19, 20, 22, 42]. However, a problem with pain measurement is its variability during the day, and between patients [22]. Also, acute pain in early stages of CRPSI usually changes to chronic pain at later stages. Acute and chronic pain are different clinical entities [43], which may involve different dimensions [44]. Questionnaires for pain rely on self-reports and are thus subject to biases that may result in inappropriate assumptions and decisions [45]. In a study of the "Pain-Behavior Construct" Turk and colleges [45] considered the idea of Fordyce [46] that there is a vicious circle of pain behavior, because pain behavior is subject to operant conditioning. Pain behavior is observable and consequently measurable [45, 47-49], therefore pain behaviors can be considered an objective way of assessing pain (level). We consider the ULAM outcome measures valid operationalizations of the behavioral dimension of pain behavior as described by Fordyce et al. [50]. However, because the ULAM does not allow measurement of all aspects of pain behavior, the ULAM should be viewed within a broad context of pain evaluation.

Practical and methodological aspects

One may wonder whether wearing the ULAM possibly affected what subjects actually did and whether 24-h measurement periods were too short. First, longer periods (up to 72 h) were technically possible and desirable, but it was the first time the ULAM was used in an ambulatory situation and little was known about (dis)comfort of sensors on the (involved) upper limbs. Second, we do not imply that 24-h activity patterns were representative of habitual activities of CRPSI patients. The aim was to get insight into the extent of the impact of CRPSI on general mobility and upper limb usage compared to a group of healthy controls. Third, the subjects were carefully instructed to continue their ordinary everyday physical activities while monitored. Most subjects reported that they had to get used to wearing the device the first few minutes and again when they went to sleep. Nobody considered the ULAM

uncomfortable or too heavy (weight ≈ 500 grams), although two subjects had some aesthetic problems (i.e. 'tourist' look).

Because of an allergy to all normally used fixatives, a special bandage was used for thigh and forearms in one subject and the trunk sensors were attached to her bra (which she kept on for one night), which caused no discomfort and had no effect on data acquisition. Although one patient showed hyperalgesia and allodynia in two fingers, all the subjects could bear sensors attached to their forearms, indicating absence of allodynia or hyperalgesia at sites of sensor attachement. All subjects wore the ULAM for the total 24-h measurement period, there was no non-compliance.

The small sample size prevented us from correlating patient characteristics with the ULAM activity outcome measures, which is currently studied in a larger patient group. Even though statistical power was low, a large number of statistically significant differences were found between patients and controls. Although, the $CrI_{(non\text{-}dom)}$ group was somewhat less active than $CrI_{(dom)}$ group, no significant differences were found, which might have influenced activity levels.

5.6 Conclusion

In conclusion, CRPSI in one of the upper limbs does not appear to have a large impact on mobility-related activities in everyday life. However, there is a clear impact on the mean intensity, percentage and proportion of upper limb activity of these upper limb CRPSI patients, especially during sitting. The impact of CRPSI was greater when the dominant side was involved.

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6 Impairments and activity limitations in subjects with chronic upper limb complex regional pain syndrome type I

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6.1 Abstract

Objective: Complex Regional Pain Syndrome type I (CRPSI) is a symptom complex comprised of several impairments, which may lead to activity limitations. Our aim was to determine the degree of impairments and activity limitations and their inter-relationship. **Design:** Cross-sectional study inter-relating impairments and objectively measured activity limitations. **Setting:** Ambulatory/home environment. **Patients:** Thirty non-acute upper limb CRPSI subjects. **Main outcome measure(s):** Sensory, motor and autonomic impairments, as well as activity limitation outcome measures. The latter were objectively measured with a novel Upper Limb-Activity Monitor (based on ambulatory accelerometry). **Results:** All subjects were impaired to some degree but with a large variability with respect to magnitude. Regarding activity limitations, the involved upper limb was clearly less active (lower intensity and percentage of activity) than the non-involved side. Impaired active range of motion (adjusted R^2 18-39%) and grip strength (adjusted R^2 12-45%) were the most important factors explaining variance in activity limitations. **Conclusions:** All subjects were still impaired nearly three years after the causative event. The involved upper limb was also clearly less active than the non-involved side, especially when the subjects were sitting and when the dominant side was involved. The more impairments a subject had, especially motor impairments, the more activity limitations were present.

6.2 Introduction

Complex Regional Pain Syndrome type I (CRPSI; also known as reflex sympathetic dystrophy) remains a poorly understood and variously defined symptom complex [1-9]. When CRPSI occurs, it usually follows surgery or trauma and it is generally expressed in the extremities. Its course shows large variability, which makes diagnosis and interpretation of clinical findings and research data difficult. Uncertainty surrounding the disorder is also reflected by the wide variety of treatments and, consequently, the numerous measures used to determine treatment outcome [9-12]. Sensory, autonomic, trophic and motor impairments may be found in CRPSI [10, 13, 14]. Furthermore, activity limitations during normal daily life including occupation [8, 15-24] and participation problems such as social functioning and role fulfillment have been reported [25, 26]. These studies show that CRPSI encompasses impairments, activity limitations and partictipation problems as described in the International Classification of Functioning (ICF, $ICIDH_2$) [27-30]. However, most outcome measures used in CRPSI research concentrate on impairments [10, 31]. Up to now, there has been a lack of appropriate instruments to objectively determine activity limitations of subjects with upper limb CRPSI [10]. The small number of instruments used in CRPSI research to determine activity limitations were retrospective scales and questionnaires.

From a rehabilitation viewpoint, it is important to analyse the relationship between impairments and activity limitations in order to address such questions as: 'does an impairment always lead to activity limitations?', 'should treatment or prevention focus on impairment or activity limitations?' [16] and 'which impairment mainly affects activities?'. However, only two studies have investigated the relationship between impairment-activity limitations relationship in CRPSI [16, 25]. In both these studies scales and questionnaires were used to determine activity limitations; a Visual Analogue Scale for perceived activity limitations (VAS-ADL) and the Groningen Activity Restrictions Scale for activity limitations (GARS) [16, 25].

For this reason, an Upper Limb-Activity Monitor (ULAM) was developed, which allows objective measurement and quantification of upper limb activity while a subject is functioning during normal daily life [32]. The ULAM has proven its ability to noninvasively detect limitations in upper limb activity in chronic upper limb CRPSI subjects [33]. The advantages of the ULAM over scales and questionnaires are, for example, that it is more extensive than a VAS-ADL and, more importantly, it provides objective outcome measures for activity limitations that allows quantification of what subjects actually do in normal daily life and not what they report they are capable of.
Our aim was to analyse the relationship between impairments and objectively measured activity limitations in upper limb CRPSI subjects. This will be the first study to determine how impairments and objectively measured activity limitations are inter-related in upper limb CRPSI.

The research questions were:

- What is the degree of impairments and activity limitations?
- What is the relationship between impairments and activity limitations?
- Which impairment(s) mainly explain(s) activity limitations?
- Do other variables influence the relationship between impairment-activity limitations?

6.3 Methods

Design and subjects

Thirty subjects with CRPSI in one upper limb volunteered for this cross-sectional study inter-relating impairments and objectively measured activity limitations. In 15 subjects the dominant side was involved and in the other 15 the non-dominant side. Only 1 subject was male; the average age was 55.1 (sd ± 14.9, range 20-81) years. Mean duration of CRPSI was 33 months (table 6.1). Inclusion criteria were: 1) presence of Veldman´s criteria [13] at diagnosis and 2) ongoing CRPSI-related complaints at enrollment into the study. The criteria of Veldman were a) four or five of the following: unexplained diffuse pain, different skin color relative to other side, diffuse edema, different skin temperature relative to other side, limited active range of motion, b) occurrence or increase of signs and symptoms after use, and c) presence of signs and symptoms in an area larger than was initially involved, including the area distal to primary injury. These criteria do not substantially differ from the IASP criteria [3, 34]. Subjects were excluded if co-morbidities affecting upper limb usage or general mobility were present. Informed consent was obtained from all subjects and the study was approved by the Medical Ethics Committee of Erasmus MC.

Impairment outcome measures

The 'Impairment level Sum Score' (ISS) [11], a validated set of five items (temperature, VAS-pain, McGill-pain, AROM, volume) especially developed for upper limb CRPSI, was used to determine the degree of impairment. However, because the ISS, as most other sum scores [4, 11, 16, 35-37], is based on diagnostic criteria, it was considered incomplete to study the present population. Since it has recently been recognised that motor impairments are not only prominent in chronic CRSPI [8, 13, 18, 19, 38-42] but are also a distinct component to be incorporated in the IASP criteria for CRPSI [4], loss of grip strength was chosen as an additional item:

- *ISS-Temperature*
  An infrared thermometer [a] was used (measurement range 0–42.2ºC, accuracy ± 0.2 ºC). Temperature can be reliably measured dorsally perpendicular to the middle of the hand after 10-15 minutes acclimatisation [43]. Normal temperature difference between both hands was set at ≤ 0.3 ºC [11].
- *ISS-VAS*
  Pain resulting from effort was measured with a Visual Analogue Scale (VAS)

indicated on a 100-mm long horizontal line. This is a reliable and valid instrument to measure intensity of pain [44].

- *ISS-McGill*
  The McGill Pain Questionnaire (MPQ) is often used in CRPSI research [45-47]. The total number of words chosen from the list of sensory, affective and evaluative pain words from the reliable [48] Dutch language version (MPQ-DLV) was used to assess pain during the previous week.
- *ISS-AROM*
  Maximum active range of motion (AROM) within pain threshold was measured. Percentages of normal AROM (involved versus non-involved side) were determined for the wrist (dorsal/palmar flexion) and MCP and PIP (flexion/extension) of the two most impaired digits. Each joint movement was measured three times and averaged [11, 49, 50].
- *ISS-Volume*
  Volumetric measurements of the hands were taken with a volumeter [b] which determines fluid overflow. The difference in volume between both hands was considered in relation to the volume of the unimpaired hand. A difference in volume up to 3.5% was considered normal [11].
- *Strength*
  A portable hand-held dynamometer [c] was used, which allows quantification and, if performed in a standardized manner, reproducible and reliable [51] determination of grip strength. Only four-point grip strength was measured because several forms of grip strength were well correlated in CRPSI subjects [25]. Subjects were instructed to squeeze as hard as possible with hands in the ´lumbrical´ grip (thumb at bottom and digits II-IV on top of the device). Strength was measured three times after one practice and the average was calculated for both the involved and non-involved side.

Oerlemans et al. converted the ISS impairment items to a range of 1-10 (based on intra-individual comparisons for AROM, volume and temperature of both hands) [11]. A score of 1 was interpreted as absence of that impairment. In the present study, to make grip strength comparable with ISS scores, intra-individual comparisons for grip strength were also ascribed scores of 1 to 10 (if strength of the involved side was > 90% of the non-involved side then the score was 1, if strength of the involved side is 0-10% then 10 was scored, the intermediate strength differences were ascribed scores 2-9). This score was added to the five ISS scores to create the Total Impairment Score ranging from 6-60, with a higher score indicating more severe impairment.

Activity Limitations outcome measures

The Upper Limb-Activity Monitor (ULAM) is an extended version of the ´classic´ Activity Monitor (AM) which has been developed and validated in our department [52-57]. The AM allows objective measurement of mobility-related activities such as lying, sitting, standing, walking, cycling and general movement. This portable device enables detailed long-term ambulatory measurement of what subjects actually do

during normal daily life and can therefore be used to determine activity level and, if present, activity limitations. The ULAM was developed to determine activity limitations of subjects with disorders related to the upper limbs. It enables one to determine whether or not the upper limbs are active when a subject is performing one of the mobility-related activities [32]. The combination of mobility-related activities and upper limb activity allows one to obtain more specific information than with less advanced techniques, such as a wrist actigraph or actometer [58-62].

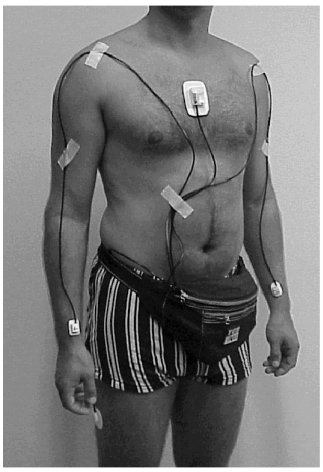
Uni-axial piezoresistive acceleration sensors [d] attached to thighs (sensitive direction in sagital plane), trunk (sensitive direction in sagital and longitudinal plane) and forearms (sensitive direction in sagital plane being in the anatomical position) are connected to a small recorder [e] that is worn around the waist (figure 6.1). The raw acceleration signals are expressed in g (9.81 ms $^{-2}$) and are a combination of two components: gravitational acceleration and accelerations due to activity [57, 63]. The raw data was stored digitally on a PCMCIA flash card with a sample frequency of 32 Hertz downloaded onto a PC for subsequent analysis.

Automatic detection of mobility-related activities and upper limb activity was done by kinematic analysis based on Signal Processing and Inferencing Language (SPIL) routines, yielding 'C'-code [64]. For detection, three feature signals are derived from each raw accelaration signal: the angular, motility and frequency feature (time resolution 1 second). The subsequent steps of analysis have been described previously [53-55, 57, 65, 66]. To detect upper limb activity, the motility feature (Finite Impulse Response filter 0.3-16 Hz, envelope of the AC component of the acceleration signal), which is the variability around the mean in the raw acceleration signal expressed in g (9.81 ms^{-1}), is used. This variability can be considered as a measure for the intensity of upper limb activity: the more intensely active, the higher the motility value. For a more technical description of the detection method we refer to other studies [32, 57]. Based on previous research [33, 56] the following outcome measures were used:

- *Mean intensity of upper limb activity of the involved side during sitting and standing*
  The mean intensity of upper limb activity of the involved side was expressed in mean (scaled) motility values during the time the involved upper limb was active while the subjects were sitting and standing. The lower the mean intensity of upper limb activity the more limited the activity.
- *Percentage of upper limb activity of the involved side during sitting and standing*
  The percentage of upper limb activity of the involved side was expressed as the percentage of the time that the involved upper limb was active (i.e. exceeding a threshold in the motility value) while the subjects were sitting and standing. The lower the percentage of upper limb activity the more limited the activity.

- *Proportion of activity between both upper limbs during sitting and standing*
  The proportion of activity of one upper limb relative to the other upper limb was expressed as a ratio: the percentage of activity of the non-dominant side relative to the percentage of activity of the dominant side. These ratios were normalised based on a reference value derived from ten healthy subjects in an earlier study [33]. For subjects with dominant side involvement, a ratio higher than 1 was associated with activity limitations. For subjects with non-dominant side involvement, a ratio lower than 1 was associated with activity limitations. The higher/lower these respective ratios, the more limited the activity.
- *Percentage of dynamic mobility-related activities*
  In addition to outcome measures related to the upper limbs, the percentage of the measurement period during which dynamic mobility-related activities (i.e. walking, cycling and general non-cyclic activity) were performed was also used as activity limitation outcome measure. The lower the percentage of dynamic mobility-related activities, the more limited the activity.

Figure 6.1: A subject wearing the Upper Limb-Activity Monitor



Other variables

Some demographic variables, such as age, gender, marital status and employment status, may influence the relationship between impairments and activity (limitations). Duration of CRSPI, time between onset and diagnosis and whether or not receiving therapy/medication may also influence this relationship. Involvement of dominant or non-dominant side should also be taken into account, because the inter-relation between impairment and activity may differ depending on whether or not the dominant side is involved.

Protocol
To reduce interference with normal daily life, the ULAM was fitted at home and worn for 24 hours. Subjects were instructed to continue their ordinary activities, except for swimming, bathing or showering. To avoid bias, initially, the exact technique and output parameters were not explained: the subjects were just told that the sensors detect movement of body parts to which they were attached. After 24 hours, the device was removed, subject characteristics and activities performed were noted and the six impairments were measured. At this stage, complete information was given about what the ULAM actually measures: a 24-hour activity pattern of whether the upper limbs are active or not plus which mobility-related activity was performed. All subjects agreed with this protocol. Measurements on the second day took approximately 1.5 hours; the order of measurement was the same for each subject with grip strength being measured last to avoid provoking physical complaints (e.g. pain) or increasing temperature.

Statistics
Non-parametric statistical methods were used: Spearman rank coefficients were used to describe correlations between outcome measures and other variables, the Wilcoxon signed rank test was used to determine whether outcome measures differed between involved and non-involved sides, and the Mann-Whitney test was used to determine whether activity limitation outcome measures differed between subjects with dominant and non-dominant side involvement.
After confirmation that linear regression was allowed to analyse the relationship between impairment-activity limitations, simple linear regression was carried out for each dependent variable with impairment outcome measures as independent variables. Statistically significant ($p \leq 0.05$) impairments that explained 10% or more of the variance in the simple models were included in the multiple models. Separate regression models were made for the two subgroups for the proportion of activity between both upper limbs during sitting and standing. SPSS for Windows (version 10.0) statistical package was used for data analysis.

6.4 Results

Subject characteristics
Most subjects were aged 40-70 years (table 6.1). Only one man participated, and overall the main precipitating event was one or more fracture(s). Most subjects had CRPSI for more than 1 year, with a mean duration of 32.8 months (sd 31.3 months, range 4-143 months). In about one third, the time between onset and diagnosis was more than 2 months (range 3-33 months).

Table 6.1: Several characteristics of the thirty subjects with upper limb CRPSI. n = number of subjects, % = percentage of subjects.

Subject characteristics	n	%
Age (years)		
20-30	2	6.7
31-40	3	10.0
41-50	5	16.7
51-60	10	33.3
61-70	5	16.7
71-80	3	10.0
80+	2	6.7
Gender		
Male	1	3.3
Female	29	96.7
Causative event		
Fracture	15	50.0
Other	11	36.7
Idiopathic	4	13.3
Time since onset (months)		
0-3	0	0
3-12	9	30
12+	21	70
Duration between onset & diagnosis		
≤ 2 months	19	63.3
> 2 months	11	36.7
Employment		
Yes, part time	7	23.3
No, retired	4	13.3
No, work compensation	10	33.3
No, housewife	9	30.0

Impairments

Impairment scores ranged considerably (table 6.2): nearly all possible values were present for each outcome measure. Median scores for ISS-AROM, Strength, ISS-McGill and ISS-VAS were higher than for ISS-Volume and ISS-Temperature. The only impairment that was present to a some degree in all subjects was impaired AROM. None of the subjects was completely unimpaired as indicated by the minimum Total Impairment Score of 13. Total Impairment Scores were not related to any of the other variables such as age or other demographic variables, duration of CRPSI, time between onset and diagnosis and having therapy or not. No significant differences were found between those with dominant side and those with non-

dominant side involvement with respect to impairment outcome measures or any other variables. ISS-VAS did not correlate well with ISS-McGill (r_s=0.21). Momentary pain (additionally measured with a VAS) ranged from 0-70 mm (median 13 mm) and was significantly correlated with ISS-VAS pain resulting from effort (r_s=0.71, p= 0.000). Momentary pain was significantly less than pain resulting from effort (p= 0.000).

Table 6.2: Descriptive statistics (median scores and range) for the impairment outcome measures.

Impairment (possible range)	Median [range]
ISS-VAS (1-10)	5 [1-10]
ISS-McGill (1-10)	6 [1-10]
ISS-AROM (1-10)	7 [3-10]
ISS-Volume (1-10)	2 [1-10]
ISS-Temperature (1-10)	3 [1-10]
Strength (1-10)	6 [1-10]
Total Impairment Score (6-60)	31.5 [13-52]

Activity limitations

The mean intensity and percentage of upper limb activity of the involved side were significantly less than the non-involved side, during both sitting and standing (upper part table 6.3). The percentage of dynamic mobility-related activities did not differ significantly between subjects with dominant side involvement and those with non-dominant side involvement (lower part table 6.3); also, between these two subgroups there were no significant differences for the mean intensity and percentage of upper limb activity of the involved sides. Compared to the mean activity intensity of the dominant (4.04 g) and non-dominant (3.66 g) side of 10 healthy subjects during sitting [33], in these CRPSI subjects the activity of the involved side was low (3.10 g). This is also true for the percentage of upper limb activity during sitting (healthy subjects: dominant side 37.5%, non-dominant side 35.6%).

Table 6.3: Activity Limitation outcome measures (I)
*Descriptive statistics (mean and standard deviation; SD) for the mean intensity of upper limb activity (expressed as scaled (*100) motility values) and the percentage of upper limb activity (expressed as % of the time the limb was active during a specific mobility-related activity). The upper part presents within subject comparisons between involved and non-involved side (Wilcoxon signed rank). The lower part presents between subject comparisons between subjects with dominant and non-dominant side involvement (Mann-Whitney). n = number of subjects.*

Activity limitations	Mean	SD	Mean	SD	p-value
Within subject comparison:	*Involved side (n=30)*		*Non-involved side (n=30)*		*(Wilcoxon)*
Intensity sitting (g *100)	3.10	± 0.99	4.17	± 1.66	0.001
Intensity standing (g *100)	9.96	± 3.16	12.88	± 3.38	0.001
Percentage sitting (%)	29.20	± 8.54	34.64	± 9.96	0.008
Percentage standing (%)	72.96	± 10.85	78.66	± 10.06	0.002
Between group comparison:	*Dominant involvement (n=15)*		*Non-dominant involvement (n=15)*		*(Mann-Whitney)*
Percentage of dynamic mobility-related activities (%)	10.32	± 4.04	12.22	± 5.68	0.604
Involved side:					
Intensity sitting (g *100)	2.98	± 1.08	3.21	± 0.91	0.455
Intensity standing (g *100)	10.82	± 3.72	9.11	± 2.30	0.254
Involved side:					
Percentage sitting (%)	27.76	± 9.56	30.63	± 7.42	0.237
Percentage standing (%)	72.69	± 10.66	73.23	± 11.4	0.820

Table 6.4 gives data on the proportion of activity between both upper limbs during sitting and standing separately for both subgroups. Not all subjects were limited with respect to these outcome measures, as indicated by the fact that most interquartile ranges included the reference value: seven subjects (23%) were classified as limited. After subsequent analysis of the percentages of activity of both upper limbs of the individual subjects, it appeared that for the subjects with dominant side involvement, limitations in the proportion of upper limb activity during sitting were due to a decreased percentage of upper limb activity of the involved dominant side; during standing, the activity of the non-involved (non-dominant) upper limb was increased. Unlike the subjects with dominant side involvement, there were no such patterns with respect to increase and/or decrease of percentage of upper limb activity in those with non-dominant side involvement.

Table 6.4: Activity Limitation outcome measures (II)
Median scores [and interquartile range] for the normalised ratios for the proportion of activity between both upper limbs during sitting and standing for both subgroups. For dominant side involvement, a ratio higher than 1 was associated with activity limitations. For non-dominant side involvement, a ratio lower than 1 was associated with activity limitations. The higher/lower these respective ratios, the more limited a subject was.

Proportion of upper limb activity		
non-dominant : dominant side	During sitting	During standing
	Median [interquartile range]	*Median [interquartile range]*
Dominant involvement (n=15)	1.20 [0.85 – 1.61]	1.13 [1.05 – 1.19]
Non-dominant involvement (n=15)	0.88 [0.74 – 0.98]	0.98 [0.96 – 1.01]

Impairment-activity limitations relationship
The Total Impairment Score, ISS-AROM and Strength were significant in each simple model for the mean intensity and percentage of activity of the involved upper limb during sitting and standing (table 6.5). In addition, ISS-VAS and ISS-Temperature were significant in both the simple models during sitting. Since age was considered as a potential confounder for activity (i.e. the older, the less active), it was always included in the multiple models. In the multiple models AROM (p=0.009) and age (p=0.001) were significant contributors to the percentage of upper limb activity during standing. The variability in upper limb outcome measures explained by impairments and age ranged from 24% to 52%. Because the percentage of dynamic mobility-related activities (average 11.3%) performed by CRPSI subjects did not differ from earlier findings in healthy subjects [65, 66], indicating that the CRPSI subjects were not limited with respect to mobility, it was decided not to make regression models for this ULAM outcome measure.
Regarding the proportion of activity between both upper limbs during sitting and standing, ISS-AROM and the Total Impairment Score were significant in three of the four simple regression models made for both subgroups (table 6.6). Strength was significant in each simple model. The multiple regression models for the two subgroups explained variances ranging from 34-57%.

Table 6.5: Impairment-activity limitation relationship (I)
*Simple and multiple regression models with activity limitation outcome measures (mean intensity and percentage of upper limb activity during sitting and standing) as dependent variables and impairment outcome measures as independent variables. For the simple models, the adjusted R squares are shown. For the multiple models, the standardized beta regression coefficients and the total adjusted R square are shown for impaiments that were significant in the simple regression models (and age). Intensity sitting and standing = Mean intensity of upper limb activity of the involved upper limb during sitting and standing seperately, Percentage sitting and standing = Percentage of upper limb activity of the involved upper limb during sitting and standing respectively, - not significant in the simple model and therefore not included in the multiple model, *** p≤ 0.001, ** p≤ 0.001, *p≤ 0.05.*

Impairment	Intensity sitting		Intensity standing		Percentage sitting		Percentage standing	
	β	Adj. R sq.	β	Adj. R sq.	β	Adj. R sq.	β	Adj. R sq.
Simple models:								
ISS-VAS		0.12*		0.00		0.12*		0.00
ISS-McGill		0.00		0.00		0.00		0.00
ISS-AROM		0.24**		0.23**		0.18**		0.29***
ISS-Volume		0.04		0.06		0.07		0.00
ISS-Temperature		0.12*		0.00		0.04		0.00
Strength		0.34***		0.15*		0.31***		0.12*
Total Impairment Score		0.36***		0.14*		0.31***		0.14*
Multiple models:								
Age	0.21		0.22		0.14		0.50	***
ISS-VAS	0.03		-		-0.04		-	
ISS-AROM	-0.23		-0.40		-0.17		-0.47	**
ISS-Temperature	-0.31		-		-		-	
Strength	-0.35		-0.12		-0.41		-0.03	
Total Adjusted R sq.		0.39**		0.24*		0.27*		0.52***

Other variables
The relative temperature score (the degree to which the involved side is colder or warmer than the non-involved side) was significantly correlated with the percentage of upper limb activity (r_s= 0.38, p=0.037): the colder the hand, the less the percentage of activity. Also, the involved side of subjects having CRPSI for longer than 12 months was significantly colder compared to those with CRPSI of shorter duration (p=0.02). Duration of CRPSI, time between onset and diagnosis, employment status, marital status and level of education were not related to the upper limb activity outcome measures.

Table 6.6: Impairment-activity limitation relationship (II)
*Simple and multiple regression models with activity limitation outcome measures (proportion of upper limb activity during sitting and standing) as dependent variables and impairment outcome measures as independent variables, for both subgroups separately. For the simple models, the adjusted R squares are shown. For the multiple models, the standardized beta regression coefficients and the total adjusted R square are shown for impaiments that were significant in the simple regression models (and age). Proportion sitting = Proportion of upper limb activity of the non-dominant side relative to dominant side during sitting, Proportion standing = Proportion of upper limb activity of the non-dominant side relative to dominant side during standing, - not significant in the simple model and therefore not included in the multiple model, *** p≤ 0.001, ** p≤ 0.001, *p≤ 0.05.*

	Dominant side involvement (n=15)				Non-dominant side involvement (n=15)			
Impairment	**Proportion sitting**		**Proportion standing**		**Proportion sitting**		**Proportion standing**	
	β	Adj. R sq.	β	Adj. R sq.	β	Adj. R sq.	β	Adj. R sq.
Simple models:								
ISS-VAS		0.13		0.02		0.08		0.00
ISS-McGill		0.00		0.00		0.00		0.00
ISS-AROM		0.38 **		0.39 **		0.08		0.29 *
ISS-Volume		0.07		0.08		0.00		0.00
ISS-Temperature		0.00		0.00		0.06		0.14
Strength		0.45 **		0.26 *		0.31 *		0.35 *
Total Impairment Score		0.21 *		0.14		0.46 **		0.38 **
Multiple models:								
Age	0.41		0.36		0.28		0.14	
ISS-AROM	-0.31		-0.57		-		-0.37	
Strength	-0.30		-0.01		-0.56		-0.42	
Total Adjusted R sq.		0.57**		0.43*		0.34*		0.37*

6.5 Discussion

Impairments
There was large intersubject variability in magnitude of impairments, which is in accordance with other studies [11, 13]. The mutual impairment correlations did not differ from the findings of Oerlemans et al. [11] in more acute CRPSI, with the exception of the present significant correlations between VAS-AROM (r_s=0.50) and VAS-Volume (r_s=0.37). None of the impairments was related to duration of CRPSI. In our chronic population, impaired strength, AROM and pain were most prominent, which supports earlier findings that motor impairments become more important as the complicated syndrome becomes chronic [8, 13, 18, 19, 38-42].

AROM was most impaired in our group of subjects, but did not differ between subjects with multiple fractures or another causative event. In contrast to other motor impairments, because AROM and strength are relatively constant throughout the day, they were considered more suitable as outcome measures. The problem remains, however, that although rigidly standardized in every aspect, AROM and grip strength measurements may be subject to considerable systematic and random variation [49, 51], which was anticipated by determining average scores of three movements per joint. Geertzen et al.[49] also reported AROM differences between involved and non-involved side in shoulder, elbow and wrist, but considered these differences not clinically relevant because AROM was within the range needed for normal daily life. Since small reductions in mobility of especially the hand are thought to predominantly affect fine motor skills [11], we considered AROM of wrist and fingers more important outcome measures than AROM of shoulder and elbow. We did not notice other motor impairments such as tremors, spasms or dystonia during the measurements on the second day. These latter impairments have been reported in small patient groups with more generalized and severe CRPSI [8, 13, 40-42, 67], but are not common [16, 41, 42, 68, 69]. Also, their underlying mechanism is unclear [19, 40, 41, 70].

Temperature and volume appeared least impaired. Regarding skin temperature, Oerlemans et al. [11] pointed out that unequivocal measurement is difficult, because temperature may change with time in CRPSI [11, 13, 71] and may be higher or lower than on the contralateral side [72, 73]. Moreover, objective and subjective temperature measurements do not always correspond in CRPSI [74]. To partly overcome such validity problems, we differentiated between a warmer or colder involved side compared to the non-involved side. The finding that the involved sides were significantly colder in CRPSI of longer duration was in accordance with findings from advanced techniques measuring the vascular reflex response during a complete thermoregulatory cycle [75]. No subjects was in the ´acute phase´ (< 3 months), so we could not contribute to the discussion about subsequent stages in CRPSI [13, 68, 75-80].

ISS-McGill was poorly correlated with other impairments both in our study and in that of Oerlemans et al [11]. The McGill Pain Questionnaire (MPQ) assesses sensory, affective and evaluative aspects of pain [81] and, for this reason, measures beyond impairment level [11]. Our data were in accordance with the finding that chronic pain patients such as in CRPSI choose affective and especially evaluative aspects with greater frequency than acute patients [74, 82]. Sensory indicators tingling, stiff and nagging, affective indicator tiring and evaluative indicators tolerable/bearable and annoying (Dutch Language Version) were indicated most often. ISS-VAS was more strongly correlated with ISS-McGill´s affective and evaluative aspects than with its sensory aspects; although a VAS is intended to measure pain intensity, chronic CRPSI subjects may indeed use it to reflect affective and evaluative aspects of pain [11, 83]. Because acute pain becomes chronic pain as the CRPSI syndrome continues, the MPQ is important to monitor changes over time. Although not all CRPSI patients have pain [8, 13], it is too important an aspect to quantify using only a simple VAS [25].

Activity limitations

Although our subjects with dominant side involvement were somewhat less active, in general, CRPSI in one upper limb does not appear to limit general mobility. The involved side was on average significantly ´disused´ or 'spared/protected', both during sitting and standing. Unfortunately, it was not possible to detect to what degree disuse and/or sparing/protecting were responsible for this inactivity [32]. Moreover, because upper limb activity during standing in our CRPSI group did not differ from healthy subjects, upper limb activity during sitting seems to be the most important aspect when determining activity limitations resulting from an upper limb disorder.

In our study, the lack of significant differences for mean intensity and percentage of activity of the involved upper limb between both subgroups (table 6.4) seems to indicate that both subgroups were equally limited; however, dominant side involved subjects were more limited. With respect to intensity and percentage of upper limb activity, equal absolute values of the dominant and non-dominant involved sides are due to a relatively larger decrease in activity of the dominant involved side than of the non-dominant involved side; in 'healthy' upper limb activity the dominant side is more active than the non-dominant side [84, 85]. Since our two subgroups were similar with respect to duration of CRPSI, impairment outcome measure scores and a number of other relevant variables, it can be concluded that the impact on normal daily life of CRPSI in the dominant side is larger than when the non-dominant side is involved. This is in accordance with earlier findings and supports the intuitive idea that a dominant upper limb involvement generally has greater impact than non-dominant involvement.

Subjects with dominant side involvement who were classified as limited showed a clearly decreased percentage of activity of the involved dominant side during sitting and a clearly increased percentage of activity of the non-involved (non-dominant) side during standing. It may be relatively easier to activate the non-involved (non-dominant) upper limb to compensate for decreased activity of the involved limb during standing in order to do what one wants to do. However, since upper limb activity during sitting requires more precision skills (fine motor skills, manipulative upper limb usage) [32], compensating decreased activity of the involved limb with the non-involved (non-dominant) limb may be more difficult during sitting. It was difficult to compare our findings with other studies reporting 77% [24], 62% [16] and 78% [20] of the subjects with chronic CRPSI being limited because the ULAM measurement technique we used was not used in these other studies.

Relationship between impairments and activity limitations

Impaired AROM and grip strength and to a lesser extent pain resulting from effort were the most important factors explaining variance in activity limitations in normal daily life in chronic upper limb CRPSI. The fact that the Total Impairment Score was significant in each simple regression model underlines the fact that heterogeneous presence of impairments is a complicating factor when studying the ´impairment-activity limitation´-relationship in CRPSI [11]. In our opinion, however, it would have been inadequate to take only one or a few impairments into account.

In the studies by Geertzen et al. [16, 25], a VAS for perceived activity limitations (VAS-ADL) and two subscores of the Groningen Activity Restrictions Scale (GARS), performance of activities of daily life (ADL) and instrumental activities of daily life (IADL), were used as outcome measures for activity limitations. Pain appeared to be the most important impairment limiting activity [16, 25], which is in contrast to the present findings and may have been due to different operationalisation of pain degree.

One may hypothesize that the ULAM is inherently more related to motor impairments since it measures only activity limitations and not other limitations (e.g. situational or communicational limitations), thereby being more associated with pain resulting from effort (‘activity’) than with momentary pain. However, the items assessed with the GARS and VAS-ADL were also solely activity limitations. Therefore, it was considered unlikely that different operationalisations explain why pain was less important than motor impairments. Moreover, since our data on momentary pain did not differ from Geertzen et al. (range 0-80 mm, mean 12 mm) we think this excludes volunteer/selection bias with respect to pain. The different results with respect to pain may have been due to different characteristics of the instruments used to determine activity limitations: the ULAM is a non-retrospective, objective outcome measure to quantify what subjects actually do and did not quantify perceived or self-reported limitations as did the VAS-ADL and GARS.

The importance of motor impairments in chronic CRPSI was stressed by Geertzen et al. and others [11, 16, 19, 25]. Clinically, this may indicate that increasing AROM and grip strength as early as possible is as (or even more) important than pain management when treating CRPSI in order to prevent or reduce CRPSI-related complaints. Our aim was to find out which impairment(s) were most prominent and least variable among 30 subjects with chronic upper limb CRPSI as well as which impairment(s) explained most of the variability at the ICF activity level. It appeared that motor and sensory impairments were most prominent and equally variable. However, impaired AROM and grip strength clearly explained a higher percentage of the variability in activity limitations.

Therefore we conclude that the more impaired a subject was, the more activity limitations were present. It should be noted, however, that caution is needed when

relating quantified impairment to quantified activity limitations [86]. This cross-sectional study does not allow us to conclude that an impairment always leads to activity limitations; linear regression analysis does not say anything about causality between variables. For example, it cannot be said that the percentage of activity was less because a hand was colder, or the other way around (i.e. because of a lower activity percentage, a hand becomes colder). This may also partly explain why the relationship between the ICF consequences of a disease is often found to be ambiguous [16, 86, 87]. It was our intention to determine which impairment(s) explained most of the variability in activity limitations.

Other variables

There was no relationship between the duration of CRPSI and either of the outcome measures, which was probably due to large intersubject variability in the presence and severeness of impairments and activity limitations. Age was always included in the regression models, although it was not always significantly related to the activity limitation outcome measures. The present subjects were representative of the CRPSI population with respect to age [13, 16, 24]. Although CRPSI affects predominantly women [13], men were clearly underrepresented in this study. This homogeneity with respect to gender should be taken into account when findings are extrapolated to the male CRPSI population. This study clearly demonstrates the important influence of the involved side (dominant or non-dominant) on the degree of activity limitations.

Similar to Geertzen et al.[16], we found no evidence that early diagnosis and subsequently early initiation of therapy might give better long-term outcome [88]. As stated, causative event, employment status, marital status and level of education were not related to any of the upper limb activity outcome measures; this might be due to the relatively small number of subjects or possible selection bias. Finally, it can not be excluded that factors other than those examined in the present study need consideration. Other impairments such as hyperhydrosis, discoloration, dystonia, tremor or psychosocial factors such as motivation, kinesiophobia, presence of social life events may also explain some of the variance in the activity limitation outcome measures, but were not assessed in this study.

Practical and methodological issues

Our aim was to use outcome measures that were workable and allowed quantification. In addition, the outcome measures had to be as far as possible objective, reliable and valid to factually describe the 'impairment-activity limitation' relationship in subjects with chronic upper limb CRPSI. A potential limitation of this study, however, was its cross-sectional nature. Since CRPSI is a chronic disease with exacerbations and remissions even throughout the same day [11], this may hamper reliable measurement of some of the outcome measures. Despite this, the fact that the ULAM outcome measures were relatively comprehensive, plus the small group of subjects and resulting potential lack of explanatory power and biological variance in daily activity, the explained variances in the multiple models were not low.

Linear regression was used because there was no co-linearity between impairment variables. Because of the subject-to-variable ratio, no independent variables other than impairment and age were included in the multiple models.

With a novel device like the ULAM, activity limitations of subjects with an upper limb disorder can be viewed from a perspective other than the usual one. The additional value of the ULAM is that it allows objective and ambulatory determination of (in-)activity of both upper limbs while a subject is performing specific mobility-related activities. This technique also enables differentiation between the impact of dominant side or non-dominant side involvement on activity during normal daily life, a topic that has not yet been investigated. Of course, a new technique also has some disadvantages [57]. The recorder and sensor could be smaller and lighter, little is known about between-day variability in activity patterns of subjects, and fitting the ULAM at home to reduce interference with normal life is time-consuming. In addition, manipulative/fine upper limb activity, holding of objects and leaning are currently not 100% well detected with the ULAM [32]. Since a large number of upper limb CRPSI subjects also experience problems with these forms of upper limb usage in addition to decreased gross motor activity, the explained variances from the regression models probably would have been higher had we been able to detect all forms of upper limb usage 100% correctly. Fortunately, development of instruments, such as the ULAM, is an ongoing process of extending possibilities and optimizing current properties.

6.6 Conclusion

These thirty subjects with chronic upper limb CRPSI showed large variability with respect to magnitude of impairments. All subjects were impaired to some degree, but AROM, strength and pain were far more severe than impaired volume or temperature. Subjects with dominant and non-dominant side involvement were equally impaired and both subgroups were also comparable with respect to other relevant variables. With respect to activity limitations, the involved upper limbs were all less active for the mean intensity and percentage of upper limb activity; the subjects clearly spared or protected their involved side during normal daily life. This impact of upper limb CRPSI was more obvious during sitting than during standing. As measured with the ULAM, subjects with dominant side involvement had more activity limitations than subjects with non-dominant side involvement.
Analysis of the relationship between impairment-activity limitation showed that impairments associated with upper limb CRPSI are not related to the percentage of dynamic mobility-related activities performed. However, impaired AROM and grip strength, and to a lesser extent pain resulting from effort, were the most important factors explaining variance in activity limitations in normal daily life in these 30 subjects with chronic CRPSI of one upper limb. Thus the more impaired a subject was, the more activity limitations were present.

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Suppliers
[a] Braun Pro 3000 Type 6014, Kronberg, Germany
[b] Volumeters Unlimited, Idywild, USA
[c] Microfet, Force Evaluating and Testing System, Hoggan Health Industries Inc., Draper, USA
[d] Analog Devices, ADXL201 (size 1x1x0.5 cm)
[e] TEMEC Instruments BV, Kerkrade, the Netherlands

6.7 References

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7 Comparison of five instruments including a novel Upper Limb-Activity Monitor to determine functioning in complex regional pain syndrome type I

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Submitted for publication

7.1 Abstract

Objective: To study how five instruments that measure the functional consequences of diseases are related to each other in subjects with upper limb complex regional pain syndrome type I (CRPSI), with emphasis on a novel Upper Limb-Activity Monitor (ULAM). **Design:** Cross-sectional comparison study. **Setting:** Home environment. **Subjects:** Thirty patients with chronic CRPSI in one of the upper limbs. **Main measures:** The ULAM, which is based on ambulatory accelerometry. Two generic questionnaires; the 68-item Sickness Impact Profile (SIP68) and the RAND 36-item Health Survey (RAND36). Two body-part specific questionnaires; the Disabilities of Arm Shoulder and Hand questionnaire (DASH) and the Radboud Skills Questionnaire (RASQ). Statistics: Spearman rank correlations. **Results:** Of the inter-questionnaire correlations 87% were significant, whereas 39% of the correlations calculated between the ULAM and the questionnaires were significant. The number and strength of the correlations between the ULAM and questionnaires was dependent on the degree to which the same aspects of functioning were measured. **Conclusion:** All five instruments measure similar aspects of functioning to a certain extent; on the other hand, the ambiguous pattern of correlations demonstrates that the ULAM measures considerably different aspects of functioning than the questionnaires. It is concluded that the ULAM has a distinct place in the field of outcome assessment; it offers an alternative but important insight into the impact a disorder may have on a subject's functioning.

7.2 Introduction

For many medical disciplines, particularly for rehabilitation medicine, preferably objective instruments and quantifiable outcome measures that focus on the functional consequences of diseases are essential [1, 2]. In the International Classification of Functioning (ICF), activity limitations and participation restrictions are classified as two possible disease consequences on everyday life at the level of the person and society, respectively [3]. These functional consequences can be measured in different ways [4] but, until recently, objective, reliable and valid instruments were lacking [5]. To objectively measure activity limitations of subjects with upper limb disorders, an Upper Limb-Activity Monitor (ULAM) has been developed [6], based on a previously developed Activity Monitor (AM) that allows valid determination of limitations related to mobility [7-10]. The ULAM is based on long-term ambulatory monitoring and consists of body-fixed acceleration sensors connected to a recorder. Ambulatory accelerometry enables measurement of mobility-related activities and activity of upper limbs. The ULAM mainly measures at the ICF activity level, but some aspects of participation are also measured because what subjects actually do during everyday life in society is also determined. The ULAM has proven its ability to detect limitations of upper limb activity of subjects with upper limb complex regional pain syndrome type I (CRPSI) when compared to healthy subjects [11].

CRPSI is a disorder that may comprise sensory, trophic, autonomic and motor impairments. When it occurs, it usually follows surgery or trauma and is generally expressed in the limbs [12]. The pathophysiology of CRPSI remains controversial [13-16] and it may lead to activity limitations and participation restrictions [17-33]. Up to now, only scales and questionnaires (both generic and body-part specific) have been applied to determine functioning in CRPSI [34]. Knowledge of the relationships between the ULAM and these other instruments, and mutual relationships between questionnaires and scales, is important in the assessment of the characteristics and added value of both the ULAM and other instruments. On the one hand, relationships can be expected because all these instruments generally aim at measuring the same functional levels or concepts; on the other hand, differences (related to characteristics of the technique, the aspects that are measured, and methodological quality) will also exist [4]. For example, questionnaires measure functioning as perceived and recalled by the subjects, whereas the ULAM measures what subjects actually do; questionnaires have standardised response options and retrospective data collection, whereas the ULAM measures *during* everyday life. Within the “same functional level” two or more sub-levels can be distinguished, and instruments may differ in their sub-levels. In addition, questionnaires sometimes measure a mixture of aspects (i.e. both capacity and performance items, or both simple skills and complex motor tasks). Furthermore, instruments will differ in displaying ceiling or floor effects, or in their reliability and validity. Thus, these differences may affect the strength of relationships or may even result in an absence of relationships.

Therefore this study aimed to explore and describe how instruments with outcome measures at functional levels were inter-related in upper limb CRPSI, with emphasis on the ULAM. To structure the study, two main assumptions were made. First, we assumed that some relationship will exist between ULAM outcome measures and questionnaires, but this relationship will be weak, and certainly weaker than the mutual relationships between the questionnaires. Second, we assumed that the relationships will be stronger between outcome measures that are aimed at the same aspect of activity limitations or participation restrictions.

7.3 Methods

Design and subjects

Thirty subjects with CRPSI in one upper limb volunteered for this cross-sectional comparison study. Their average age was 55.1 (sd ± 14.9, range 20-81) years and the majority was female (n= 29). In 15 subjects the dominant side was involved and in the other 15 the non-dominant side was involved. Mean duration of CRPSI was 33 months. Inclusion criteria were: 1) presence of Veldman´s criteria [35] at diagnosis, which do not substantially differ from the official IASP criteria [12, 16] and 2) presence of CRPSI-related complaints at enrolment. Subjects were excluded if they had co-morbidities that might influence functioning.

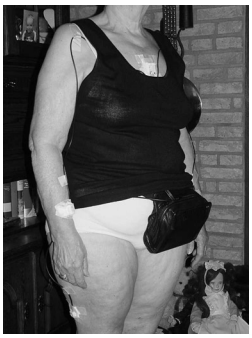
Instruments and outcome measures

Two generic questionnaires, two body-part specific questionnaires, and the ULAM were used. The generic Sickness Impact Profile (SIP) measures the impact of a disease on everyday functioning [36]. The SIP68 is a reliable and valid short version [37, 38] of the original SIP; both have been applied in CRPSI [39-42]. The body-part specific Radboud Skills Questionnaire (RASQ) [19] reliably scores the effort certain activities cost compared to pre-CRPSI; it has only been used in upper limb CRPSI [41]. The body-part specific Disabilities of Arm Shoulder and Hand Questionnaire (DASH) has been developed to determine limitations of the entire upper limb [43, 44]; the Dutch version [45] has not been used in CRPSI. The generic RAND36 Health Survey [46] is a valid Dutch version of the Short Form 36 [47, 48] but with different scoring rules [49]; the RAND36 has been used in CRPSI research [21, 22].

The ULAM consists of acceleration sensors (Analog devices, ADXL202, uni-axial piezo-resistive, size 1x1x0.5cm) on forearms, thighs and trunk connected to a waist-worn recorder (TEMEC Instruments BV, Kerkrade, the Netherlands, see Figure 7.1). The raw signals are a combination of gravitational acceleration and accelerations due to activity [50]. Data were stored on a PCMCIA card and downloaded onto a PC for automatic post-measurement kinematic analysis using signal processing and inferencing language (SPIL) routines [51]. Briefly, the accelerometer signals from the thighs and the trunk allow mobility-related activities (such as lying, sitting, standing, walking, cycling and general movement) to be automatically detected. Two of the generic ULAM outcome measures used in the present study were the percentage of

the measurement period that a person was “dynamic” (i.e. walked, walked stairs, cycled, moved without cyclic movements) (ULAM-%dyn), and body motility (the intensity of body movement measured with accelerometry) (ULAM-body). The addition of accelerometers on the forearms allowed to calculate four body-part specific ULAM measures: the intensity of upper limb movement during sitting (ULAM-isit) and during standing (ULAM-istand), and the percentage of the time that the upper limb was used during sitting (ULAM-%sit) and during standing (ULAM-%stand). A more extensive description is given in earlier studies [6-9, 11, 52].

Figure 7.1: A woman wearing the ULAM that was fitted in her home environment.



Instruments can be assessed according to measurement technique, type of instrument, health related quality of life domain, ICF level, performance of capacity aspect, and on their possibility to compare populations with upper limb disorders (table 7.1). Although specific terminology is not consciously applied in literature [44], we consider capacity to be a subject’s capability, ability or potential to carry out activities (can do), and performance to be a subject’s actual execution of activities (do do). Concerning the possibility to compare upper limb populations, intra-subject comparability refers to the possibility to compare the activity of one upper limb relative to the activity of the other upper limb in one subject (e.g. involved side relative to non-involved side for a patient). Inter-subject comparability refers to the possibility to compare outcome measures between subjects across one population. Intra-group comparability refers to comparison of outcome measures between one or more subgroups within one specific population (e.g. comparing scores between the subgroup with dominant side involvement and the subgroup with non-dominant side involvement, or between chronic and acute subgroups). Inter-group comparability refers to the possibility to compare outcome measures between various populations (e.g. comparing scores between CRPSI and other patient groups or a healthy population). Finally, norm score comparison refers to whether population norm scores were available.

Table 7. 1: Overview of several characteristics of the ULAM and four questionnaires. If an instrument partly measured other aspects in addition to the main aspect, this is indicated by 'partly' between brackets. It was not possible to classify ULAM outcome measures according to health-related quality of life (HRQoL) domains because these domains represent functioning as subjectively perceived by the study population.

Characteristic / Instrument	ULAM	RASQ	DASH	RAND-36	SIP-68
Measurement technique	Ambulatory monitoring	Questionnaire	Questionnaire	Questionnaire	Questionnaire
Type of instrument: Generic (G), body-part specific (BPS), condition specific (CS)	G, BPS	BPS, CS (partly)	BPS, G (partly) CS (partly)	G, BPS (partly)	G, BPS (partly)
Health-related quality of life (HRQoL) domain: physical & occupational function (POF), psychological state (PS), social interaction (SI), somatic sensation (SS)	POF, SI (partly)	POF	POF, PS (partly), SI (partly), SS (partly)	POF, PS, SI, SS	POF, PS, SI
International Classification of Functioning (ICF) level: function & structure (FS), activity (A), participation (P)	A, P (partly)	A	A, FS (partly), P (partly)	A, P, FS (partly)	A, P
Performance (P), capacity (C)	P	P, C (partly)	C	C, P (partly)	P, C (partly)
Possibility to compare in upper limb population: intrasubject (intraS), intersubject (interS) intragroup (intraG), intergroup (interG), norm scores (Nscores)	intraS, interS, intraG, interG, Nscores	InterS, intraG	interS, intraG, interG	interS, intraG, interG, Nscores	interS, intraG, interG

Protocol

The study was approved by the local Ethical Committee and all subjects gave informed consent. All measurements took place in the subjects' home environment. On the first day, the ULAM was fitted and subsequently worn for 24 hours. Subjects were instructed to continue their usual everyday life, but not to swim, bath or shower. The next day, the ULAM was removed and the exact measurement technique was explained. Then, the four questionnaires were administered.

Data-analysis and statistics

Descriptive statistics and Spearman rank correlations were calculated (significance level $p \leq 0.05$). First, correlations were calculated between the ULAM outcome measures and the questionnaire sum and total scores to determine the degree of relationship between the instruments. Then, inter-questionnaire correlations were calculated between the mutual questionnaire sum and total scores to determine the relationship between the four questionnaires. In addition, correlations between the mutual ULAM outcome measures were calculated. Finally, because the ULAM mainly measures at the ICF activity level, the questionnaire outcome measures were classified according to the ICF level and correlations were calculated between these classified questionnaire outcome measures and the ULAM outcome measures to establish whether relationships differed depending on the ICF level.

7.4 Results

Descriptive statistics (table 7.2) showed that the results of the generic questionnaires tended to show better functioning (i.e. absence of activity limitations and participation restrictions) rather than worse functioning. The body-part specific questionnaire scores indicated worse functioning than the generic questionnaires. The RASQ-ra, RASQ-w and RASQ-da, RAND36-prl, RAND36-bp and RAND36-pf, SIP68-mc and SIP68-sb scores were the worst. The SIP68-psss sum score expressed worse functioning than the SIP68-phss sum score.

Table 7.2: Descriptive statistics for all five instruments and their outcome measures.

*^ The possible range is not specified for ULAM scores because the theoretical range for outcome measures involving percentages is from 100 to 0%, whereas this range is from ∞ to 0 g for outcome measures involving intensity. For each ULAM outcome measure, a higher score refers to better functioning. # An unweighted mean across all eight RAND36 outcome measure scores was used as additional outcome measure. However, the RAND36 'change in health' score was not taken into account in this chronic CRPSI population which explains the 35 items for RAND36-tot. * These are the population mean norm scores of a Dutch population for the RAND36 outcome measures [58].*

Instrument & Outcome measures (number of items)		Abbreviation	Possible range [best – worst functioning]	Mean score	Actual range
RASQ					
RASQ-total (45)		RASQ-tot	1-5	2.8	1.7-4.0
Personal care (13)		RASQ-pc	1-5	2.3	1.0-3.5
Domestic activities (19)		RASQ-da	1-5	3.2	1.8-4.2
Recreational activities (2)		RASQ-ra	1-5	4.1	1.0-5.0
Social activities (3)		RASQ-sa	1-5	2.4	1.0-5.0
Other items (7)		RASQ-oi	1-5	2.6	1.0-4.7
Work (1)		RASQ-w	1-5	3.8	2.0-5.0
DASH					
Function Symptoms Score (30)		DASH-fss	0-100	43.3	16.7-68.3
RAND-36 / SF-36					
RAND-36 total score (35#)	Nscores: *	RAND36-tot	100-0	67.2	95.3-34.9
Physical functioning (10)	81.9	RAND36-pf	100-0	67.7	90.0-20.0
Social functioning (2)	86.9	RAND36-sf	100-0	85.0	100.0-25.0
Physical role limitations (4)	79.4	RAND36-prl	100-0	32.5	100.0-0.0
Emotional role limitations (3)	84.1	RAND36-erl	100-0	81.1	100.0-0.0
Mental health (5)	76.8	RAND36-mh	100-0	79.6	100.0-36.0
Vitality (4)	67.4	RAND36-vit	100-0	68.8	100.0-10.0
Bodily Pain (2)	79.5	RAND36-bp	100-0	54.5	100.0-22.4
General health perception (5)	72.7	RAND36-ghp	100-0	68.7	90.0-20.0
SIP68					
SIP68-total (68)		SIP68-tot	0-68	9.1	1-22
Somatic autonomy (17)		SIP68-sa	0-17	0.8	0-5
Mobility control (12)		SIP68-mc	0-12	2.8	1-8
Psychological autonomy and communication (11)		SIP68-pa	0-11	1.1	0-10
Social behaviour (12)		SIP68-sb	0-12	3.2	0-7
Emotional stability (6)		SIP68-es	0-6	0.7	0-4
Mobility range (10)		SIP68-mr	0-10	0.6	0-4
Physical sum score (39)		SIP68-phss	0-39	4.1	1-14
Psychosocial sum score (29)		SIP68-psss	0-29	5.0	0-17
ULAM					
Percentage spent in dynamic mobility-related activities		ULAM-%dyn	^	11.3	3.1-24.0
Mean intensity of body activity		ULAM-body	^	2.3	0.8-4.5
Mean activity intensity involved limb during sitting		ULAM-isit	^	3.1	1.5-5.2
Mean activity intensity involved limb during standing		ULAM-istand	^	10.0	4.5-17.4
Percentage of activity involved limb during sitting		ULAM-%sit	^	29.2	13.3-46.6
Percentage of activity involved limb during standing		ULAM-%stand	^	73.0	40.1-89.1

Appendix for Table 7.2:

ULAM:

The generic ULAM outcome measure ULAM-%dyn represents the percentage of the 24-hour measurement period spent in dynamic mobility-related activities (i.e. walking, cycling, general non-cyclic movement) and ULAM-body describes the mean intensity of body activity (in g, ms^{-2}), which can be regarded as a general measure for the intensity of everyday physical activity. The body-part specific ULAM outcome measures ULAM-isit and ULAM-istand represent the mean intensity of upper limb activity of the involved side, expressed in mean (scaled) motility values during the time the involved upper limb was active while the subjects were sitting and standing, respectively. ULAM-%sit and ULAM-%stand represent the percentage of upper limb activity of the involved side, expressed as the percentage of the time that the involved upper limb was active (i.e. exceeding a certain threshold in the motility value) while the subjects were sitting and standing, respectively. The lower the scores, the worse the functioning.

RASQ:

The RASQ outcome measure RASQ-pc describes items related to personal hygiene, getting dressed and eating/drinking [19]. RASQ-da describes items related to housekeeping, meal preparation and taking care of clothes. RASQ-ra contains items related to sports and hobbies and RASQ-sa items related to going out, on holiday/vacation and playing with children or pets. The RASQ-oi score describes items related to communication (e.g. writing and typing) and transportation (bicycle, car, public). The RASQ-w score refers to performing occupation (excluding household activities). For each item, subjects score from 1 (normal) to 5 (not done anymore) and for each outcome measure a mean across the various items is calculated, with a lower mean score representing better functioning.

DASH:

The DASH function symptoms score (DASH-fss) includes 21 activity items (e.g. prepare a meal, lock a door, similar to RASQ items), 6 body structure and function items (e.g. pain, tingling) and 3 participation items (e.g. undertaking activities with friends and family) [48]. Scores are transformed into a score ranging from 0-100, with a lower score indicating better functioning.

RAND36:

The RAND36-pf score contains items such as walking (stairs), washing up, getting dressed, lifting a heavy bag. The RAND36-sf score describes the influence of physical and/or emotional problems on undertaking activities with friends and family. The RAND36-prl score refers to whether physical problems interfere with the amount of time spent with (specific kinds of) work or other engagements, satisfaction with what is accomplished and the effort it costs, while the RAND36-erl score refers to whether emotional problems due to the disorder interfere with the amount of time spent with and careful execution of work or other engagements, and satisfaction with what is accomplished [58]. Each outcome measure is expressed as a score ranging from 100-0, with a higher score representing better functioning.

SIP68:

The SIP68-sa score describes the level at which an individual is autonomous in his or her basic somatic functioning (getting dressed, standing, walking, eating and the fact that help is needed). SIP68-mc describes behaviour related to the level to which an individual has control over his or her body (walking and arm-hand control). SIP68-pa describes behaviour associated with the level to which an individual is able to function without help of others in areas of mental functioning (including communication). SIP68-sb describes a persons´ functioning in relation to other persons (sexual activity, visiting friends and activities in groups of people among others). SIP68-es assesses the effect health status has on the emotional status of a subject

(irritability and acting disagreeably). SIP68-mr describes the influence of health status on a number of usual tasks like shopping, housecleaning and taking care of personal affairs (the range of actions to which a subject has limited disposition). The physical sum score SIP68-phss consists of SIP68-sa, SIP68-mc and SIP68-mr and the psychosocial sum score SIP68-psss consists of SIP68-pa, SIP68-es and SIP68-sb [68]. To calculate the SIP68 score, only those items that a subject was sure to describe the current health situation were added up, with a higher score indicating worst functioning.

Fourteen of the 36 correlations (14/36, 39%) calculated between the ULAM outcome measures and the sum and total scores of the questionnaires (table 7.3) were significant. One correlation coefficient exceeded 0.6 (3%). The body-part specific ULAM outcome measures related to activity of the involved upper limb during sitting were most often (8/12, 67%) significantly related to the questionnaire sum and total scores, whereas the same measures during standing (1/12, 8%) were less often related. Of the questionnaire outcome measures, the DASH-fss was most often significantly related to the generic and specific ULAM outcome measures.

Table 7.3: Significant Spearman rank correlations between ULAM outcome measures and the sum and total scores of the questionnaires. Please note that the absolute values of the significant correlations are shown.

		Generic		Body-part specific			
		ULAM-%dyn	ULAM-body	ULAM-isit	ULAM-%sit	ULAM-istand	ULAM-%stand
Body-part specific total scores	RASQ-tot	-	-	0.48	0.41	-	-
	DASH-fss	0.41	0.36	0.48	0.45	-	-
Generic sum and total scores	RAND36-tot	-	-	0.57	0.53	0.43	-
	SIP68-phss	0.69	0.60	-	-	-	-
	SIP68-psss	-	-	0.39	-	-	-
	SIP68-tot	0.38	-	0.38	-	-	-

Thirteen of the 15 inter-questionnaire correlations (13/15, 87%) were significant (table 7.4); 7 of these 15 (47%) had a correlation coefficient higher than 0.6.The RAND36-tot – RASQ-tot and SIP68-psss – SIP68-phss correlations were not significant (R_s=0.36, p=0.053 and R_s=0.36 p=0.052, respectively). The two ULAM generic outcome measures were significantly inter-related (R_s=0.92, p=0.000), as were the four ULAM body-part specific outcome measures ($0.53<R_s<0.93$). The correlations between the ULAM generic and ULAM body-part specific outcome measures were not significant ($0.03<R_s<0.26$).

Table 7.4: Significant Spearman rank inter-questionnaire correlations between the sum and total scores and respective p-values. Please note that the absolute values of the correlation coefficients are shown.

Spearman R_s x p-value		Body-part specific		Generic			
		RASQ-tot	DASH-fss	RAND36-tot	SIP68-tot	SIP68-phss	SIP68-psss
Sum and total scores	RASQ-tot	x	0.74	-	0.53	0.48	0.52
	DASH-fss	0.000	x	0.43	0.68	0.55	0.68
	RAND36-tot	-	0.018	x	0.64	0.49	0.61
	SIP68-tot	0.003	0.000	0.000	x	0.72	0.87
	SIP68-phss	0.007	0.000	0.006	0.000	x	-
	SIP68-psss	0.003	0.002	0.000	0.000	-	x

Seventeen of the 42 correlations (40%, 5% of these had a R_s>0.6) between ULAM outcome measures and the questionnaire outcome measures at the ICF activity level were significant (table 7.5, Part A). There were more significant correlations between generic ULAM outcome measures and the questionnaire outcome measures at this ICF activity level (9/14, 64%) than between body-part specific ULAM outcome measures and these questionnaire outcome measures (8/28, 29%). Again, the questionnaire outcome measures at this ICF level were more often significantly related to ULAM body-part specific outcome measures during sitting (7/14, 50%) than during standing (1/14, 7%). The RASQ-tot and SIP68-sb scores were not related to the two generic ULAM outcome measures and the RAND36-pf, SIP68-mc and SIP68-mr scores were not related to any of the four body-part specific ULAM outcome measures.

Fourteen of the 42 correlations (33%) between ULAM outcome measures and the questionnaire outcome measures at the ICF participation level were significant (table 7.5, Part B). There were far less significant correlations between generic ULAM outcome measures and the questionnaire outcome measures at this ICF participation level (1/14, 7%) than between body-part specific ULAM outcome measures and these questionnaire outcome measures (13/28, 46%). The RAND36-prl and SIP68-es scores were not related to any of the ULAM outcome measures, whereas the RAND36-sf and RAND36-vit scores were significantly related to each of the four body-part specific ULAM outcome measures. In contrast with the results of table 7.3 and table 7.5A, no relevant differences between sitting and standing were found with respect to the number of significant correlations between the questionnaire outcome measures and the ULAM body-part specific outcome measures.

Table 7.5: Significant Spearman rank correlations between ULAM outcome measures and the questionnaire outcome measures that measure at the ICF activity level (Part A) and between ULAM outcome measures and the questionnaire outcome measures that measure at the ICF participation level (Part B). Outcome measures that mainly contained items beyond activity and participation levels were not classified. Please note that the absolute values of the significant correlations are shown.

		Generic		Body-part specific			
		ULAM-%dyn	ULAM-body	ULAM-isit	ULAM-%sit	ULAM-istand	ULAM-%stand
ICF activity level *Part A*	RASQ-tot	-	-	0.48	0.41	-	-
	DASH-fss	0.41	0.36	0.48	0.45	-	-
	RAND36-pf	0.41	-	-	-	-	-
	SIP68-sa	0.48	0.46	0.38	0.41	-	-
	SIP68-mc	0.68	0.59	-	-	-	-
	SIP68-sb	-	-	0.45	-	0.40	-
	SIP68-mr	0.61	0.55	-	-	-	-
ICF participation level *Part B*	RAND36-sf	-	-	0.60	0.64	0.57	0.45
	RAND36-prl	-	-	-	-	-	-
	RAND36-erl	-	-	-	-	0.53	-
	RAND36-mh	0.40	-	0.43	0.39	-	-
	RAND36-vit	-	-	0.69	0.68	0.48	0.41
	SIP68-sb	-	-	0.45	-	0.40	-
	SIP68-es	-	-	-	-	-	-

7.5 Discussion

Although the body-part specific questionnaires indicated worse problems with functioning than the generic questionnaires, these 30 chronic upper limb CRPSI subjects did not generally perceive their functioning as very limited or restricted. Descriptive statistics were in accordance with other studies [21, 22, 40]; most SIP68 outcome measures had little value in upper limb CRPSI and only a few RAND36 outcome measures were worse than the Dutch norm population [53].

The structure of this study was based on two main assumptions; first, ULAM measures will be related to scores from questionnaires, but this relationship will be weak, and weaker than the mutual relationships between questionnaires. Second, relationships will be stronger between outcome measures that are aimed at the same aspects of functioning. Because the ULAM aims at measuring roughly the same concept as the questionnaires (i.e. functioning), but is at the same time different in many aspects, we expected no ($p > 0.05$) or weak ($R_s < 0.5$) relationships. Because the difference between questionnaires is smaller than the difference between ULAM

and questionnaires, we expected stronger and more significant relationships between questionnaires. We realise that especially our “correlation threshold” of 0.5 is arbitrary, but regarded from the percentage of the variability that is ‘explained’ by the relationship between two outcome measures ($100r^2$) we consider this choice to be reasonable. For example, the significant correlation between ULAM-isit and RASQ-tot (R_s=0.48, p=0.008) implies that only about 23% of the variability may be explained by this relationship. Furthermore, the level of the threshold does not influence the conclusions drawn from this study. The data clearly support the first assumption: generally the relationships between ULAM measures and questionnaire scores were non-significant or weak, whereas significant and stronger relationships were more often found between questionnaire scores. This supports our hypothesis that the ULAM significantly differs from questionnaires, with the difference between actual behaviour and perceived functioning probably being the most important. The difference or discrepancy between these two aspects of functioning is described in literature: e.g. health care professionals do not always agree with patients when it concerns their self-perceived functioning [54, 55].

From the second assumption it was expected that ULAM measures and scores from questionnaires focused on the same aspect(s) of functioning would have stronger relationships than measures and scores focused on different aspects. Therefore, it was expected that mutual correlations between generic outcome measures would be relatively strong. This was indeed true for ULAM correlations with SIP68-phss, but not for ULAM correlations with SIP68-psss and RAND36-tot. One of the factors that may explain this finding is that the ULAM differs considerably from the SIP68-psss and RAND36-tot in other aspects. For example, there is more similarity with respect to HRQoL domains between SIP68-phss and ULAM than between ULAM and SIP68-psss or RAND36-tot. Furthermore, the RAND36-tot and SIP68-psss are generally aimed more at measuring ICF participation level (and beyond) than activity level. Finally, both ULAM and SIP68 score the subject’s performance rather than their capacity, whereas the RAND-36 clearly stresses capacity. Apparently, the more characteristics generic questionnaires have in common with the ULAM, the stronger the correlations, which supported the second assumption. This conclusion is additionally supported by significant correlations between the generic items containing DASH-fss and the two generic ULAM outcome measures versus the lack of significant correlations between the plain body-part specific RASQ-tot and these ULAM outcome measures.

With the same type of reasoning it was expected that the DASH-fss would be more strongly correlated with body-part specific ULAM outcome measures than with generic ULAM outcome measures. This was true, but only for the ULAM body-part specific outcome measures during sitting. Since subjects with upper limb CRPSI were investigated, the correlations between mutual body-part specific outcome measures were of primary importance and expected to be significant. Hence, it was striking that the correlations between body-part specific questionnaire outcome

measures were all significant with the ULAM outcome measures during sitting, whereas none was significant during standing. This unexpected finding was reinforced by the proportion of questionnaire items; far more items describe upper limb activity during standing than during sitting, which would lead one to expect opposite results. Although it has been shown that the impact of upper limb CRPSI on ULAM outcome measures was somewhat greater during sitting than during standing [11], unfortunately this cannot adequately explain the present findings.

An important factor still to be discussed is the ICF level. Classification of questionnaire outcome measures according to the ICF resulted in a remarkable pattern of correlations between the ULAM and questionnaires. The lack of significant correlations between generic ULAM outcome measures and questionnaire outcome measures at the participation level is most probably due to differences in ICF level; the ULAM mainly measures activity, whereas these generic questionnaire outcome measures mainly measure participation. The strikingly large number of significant correlations between questionnaire participation outcome measures and ULAM outcome measures *during standing* was difficult to explain because both groups of outcome measures have major differences with regard to type of instrument, ICF level, and problems with functioning (ULAM is body-part specific, at activity level and shown to be limited in CRPSI [11], whereas questionnaires were generic, at participation level, and not perceived as limited). It may be that when subjects are questioned about their functioning, aspects of activity and of participation and even beyond (i.e. HRQoL) are taken into account, whether subjects realise this or not. Such latter aspects can of course not be measured with the ULAM, but may perhaps to some degree be reflected in its outcome measures. The concept activity is generally less broadly defined than the concept participation [56, 57], which was also confirmed by the present inter-questionnaire correlations. Questionnaire outcome measures at the activity level were more often significantly inter-related than the questionnaire outcome measures at the participation level.

It should be noted that the ULAM also has some limitations that may affect methodological quality [6, 11, 52, 58]. For example, the current ULAM does not validly measure fine motor skills and holding of objects and is therefore a rather rough outcome measure. Another possible limitation related to (test-retest-)reliability is the 'between-day variance of upper limb activity'. Unfortunately, this measure for biological variability of upper limb usage has not yet been fully studied because only 24-hour measurements have so far been performed. However, previous 48-hour measurements with the ULAM´s `older brother` the AM [59, 60] have shown that between-day variance for (ULAM-)%dyn and (ULAM-)body was small and not significantly different between the first and second 24 hours, both in patients and in healthy subjects. But this is of course no guarantee for biological variability of upper limb usage. Although there certainly are some differences in methodological quality (reliability and validity aspects) between the presently used questionnaires, it is clear that their methodological strengths and weaknesses can be compared. In contrast,

the aspects of methodological quality of the ULAM are less easily applicable to questionnaires and the ULAM can therefore only in part be compared with the questionnaires, which may also explain the ambiguous relationships between ULAM and questionnaire outcome measures.

Finally, it is important to realise that the present findings should not be confused with the idea that the ULAM is a new reference method and that measurement of what a person really does during everyday life is most important. The ULAM should be regarded as a relevant and valuable addition to other techniques; however, we agree with others [61-63] that the choice for an instrument should always depend on a complexity of factors, including clinical problem, research question and study design, activity aspects of interest, and cost and availability of instruments [4].

7.6 Conclusion

Generally the relationships between ULAM measures and questionnaire scores were non-significant or weak, whereas more often significant and stronger relationships were found between questionnaire scores. This supports our hypothesis that the ULAM measures similar aspects of functioning only to a certain extent. It also appeared that the more characteristics the instruments and outcome measures had in common, the stronger and more often significant the correlations were. From the findings it may be concluded that the ULAM has a distinct place in the field of outcome assessment; it offers an alternative but important insight into the impact a disorder may have on a subject's functioning.

7.7 References

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8 Upper limb activity over time of subjects with complex regional pain syndrome type I as objectively measured with an Upper Limb-Activity Monitor; a multiple case study

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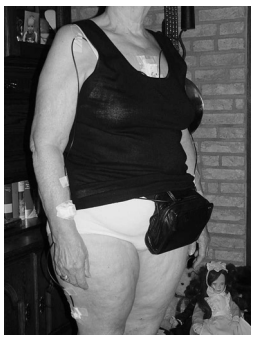
8.1 Abstract

Background: Recently, an Upper Limb-Activity Monitor (ULAM) has been developed to detemine activity limitations of subjects limb Complex Regional Pain Syndrome type I (CRPSI). The ULAM is based on long-term ambulatory monitoring of signals from body-fixed sensors and allows valid and objective quantification of mobility-related activities and upper limb activity during everyday life. **Aims:** To explore upper limb activity over time in subjects with acute upper limb CRPSI as measured with this novel ULAM, and to compare the upper limb activity time course to the time course of other measures at the level of activity and impairment. **Method:** Four subjects with acute upper limb CRPSI were measured at four relatively fixed moments in time during a treatment protocol. Several ULAM outcome measures related to upper limb usage and mobility were used. Furthermore, we used three questionnaires at the activity level (RASQ, DASH, RAND36) and six impairment outcome indicators (VAS-moment, VAS-effort, volume, temperature, AROM, strength). **Results:** Objectively measured upper limb activity often improved; improvements of >5% were found for the majority (63%) of ULAM upper limb outcome measures at final assessment. The ULAM outcome measures had a time course more similar to the body-part specific questionnaire RASQ than the other two questionnaires. The time course of impaired temperature was most often in accordance with changes over time as measured with the ULAM: volume, AROM and strength were less frequently in accordance with the ULAM outcome measures, and both VAS scores showed least accordance. **Conclusion:** Clear changes in upper limb activity over time as measured with the ULAM were found. The relationships between the time courses of the ULAM outcome measures and other outcome measures for activity limitations and impairments were explainable. The current ULAM therefore has the potential to validly assess upper limb activity over time in upper limb CRPSI.

8.2 Introduction

Complex Regional Pain Syndrome type I (CRPSI) comprises a combination of impairments [1, 2] and usually leads to activity limitations in everyday life [2-9]. Until recently, most CRPSI research concentrated on impairments, and when activity limitations were quantified merely scales and questionnaires were used [10]. This lack of instruments that allow objective measurement of activity limitations, together with the recently stressed importance of objective outcome measures for CRPSI [11], and recent developments in the field of ambulatory accelerometry [12] formed the basis of a novel Upper Limb-Activity Monitor (ULAM). This ULAM is based on long-term ambulatory monitoring of signals from body-fixed sensors and allows detailed objective quantification of mobility-related activities and upper limb activity during everyday life [13]. It is an extension of a validated Activity Monitor (AM) [14-18] and consists of acceleration sensors on forearms, thighs and trunk, connected to a waist-worn recorder (figure 8.1). The ULAM has proven its ability to detect limitations in the mean intensity, percentage and proportion of upper limb activity in chronic upper limb CRPSI patients when compared to healthy subjects [19]. Impaired active range of motion of wrist and digits, and grip strength were the most important factors explaining variability in activity limitations in chronic upper limb CRPSI as measured with the ULAM [20]. A cross-sectional comparison study of the relationship between ULAM and questionnaires in chronic upper limb CRPSI demonstrated the ULAM´s distinct place in the field of outcome assessment [21]; it offers an alternative but important insight into limitations of everyday functioning.

Figure 8.1: A subject wearing the ULAM in her home environment.



The ULAM has proven to be feasible and valid in transversal studies in chronic upper limb CRPSI [13,19], but upper limb activity over time as measured with the ULAM has not yet been explored in a longitudinal setting. There is also no knowledge of whether changes in objectively measured upper limb activity are related to changes over time as measured with other instruments. This is an important methodological issue that has to be studied if the ULAM is to be used to monitor functioning of individuals or

groups over time in future (intervention) studies. Therefore, the research questions were:

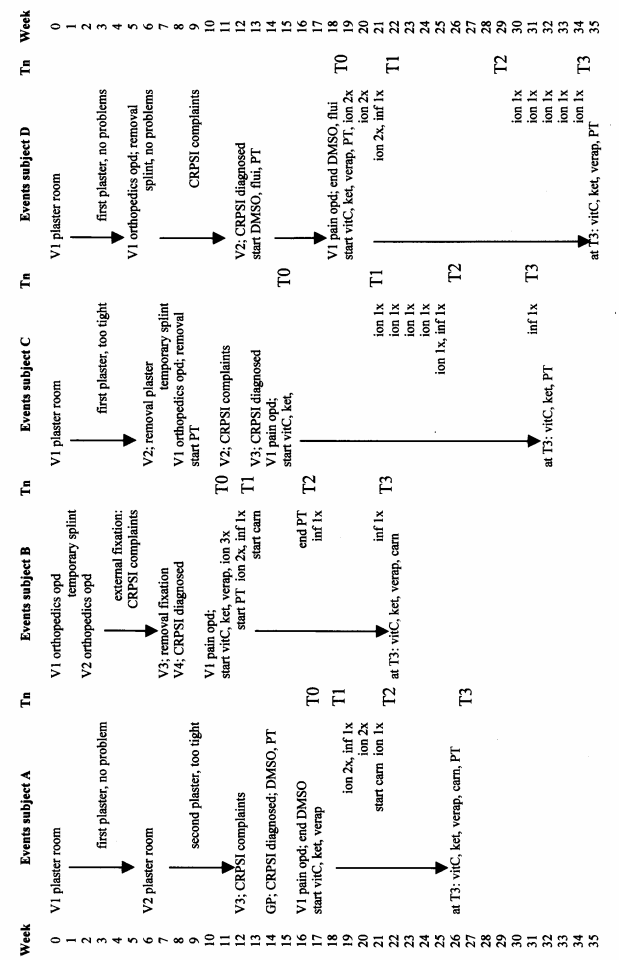
- What is the time course of upper limb activity as objectively measured with the ULAM in acute upper limb CRPSI?
- Is the time course of upper limb activity as measured with the ULAM related to the time course of other instruments and outcome measures at the activity and impairment levels?

8.3 Method

Design, subjects and treatment regimen

Because changes in upper limb activity are more likely in acute than in chronic upper limb CRPSI, subjects having CRPSI-related complaints for less than 10 weeks were recuited from the outpatient pain department (H.J.K.) for this multiple case study. Four subjects with fractures as causative event volunteered and were assessed four times during a treatment regimen. CRPSI was diagnosed according to Veldman´s criteria [22] that are similar to those of the International Association for the Study of Pain [23, 24]. Subject A was a 48-year old man with non-dominant side CRPSI who worked with the police detective force, was divorced and lived with his two children. Subject B was a 58-year old man with non-dominant side CRPSI, worked as a mechanic, was married and lived with his wife and child. Subject C was a 71-year old woman with non-dominant side CRPSI, was married and lived with husband. Subject D was a 52-year old man with dominant side CRPSI, worked as a night-watchman, was married and lived with his wife and two children. Unfortunately, there still is no well accepted evidence based treatment algorithm for CRPSI [11, 25, 26]. Moreover, treatment efficacy to reduce impairments (i.e.mainly pain) has scarcely been demonstrated with methodologically sound studies [27], let alone treatment efficacy to reduce activity limitations [10, 25, 28]. Therefore, a reasonably standardized treatment regimen [b] was used that aimed at improving activity and everyday functioning, in addition to reducing impairments. For a chronological overview of the subjects´ CRPSI history see figure 8.2.

Figure 8.2: Chronological overview of the patients´ CRPSI history from the causative event in week 0 up to final assessment at T3, including treatment parameters.



Abbreviations and content / function of treatment parameters:

CRPSI = Complex Regional Pain Syndrome type I, GP = general practitioner, PT = physical therapy / physical exercises and connective tissue massage with some pain allowed aimed at functioning, MT = manual therapy /segmental approach and physical exercises with some pain allowed aimed at functioning, Vn= n^{th} visit department, Tn = Outcome measurement 0-3, vitC = vitamin C / radical scavenger, ket = ketanserin / vasodilator capillaries, verap = verapamil / vasodilator large vessels, carn = carnitine / stimulator aerobe metabolism when perfusion is normalized and reduction of free radicals, ion nx = iontoforesis n times that week with ketanserin , inf = infusion n times that week with carnitine, DMSO = di-methyl sulfoxide / radical scavenger, flui = fluimecil, radical scavenger, opd = hospital outpatient department

Instruments and outcome measures

The ULAM enables objective determination of whether or not the upper limbs are active when a subject is performing one of these mobility-related activities: lying, sitting, standing, walking, climbing stairs, cycling and general movement [13]. Based on this information and 'feature' signals derived from the raw acceleration signals, several ULAM outcome measures can be calculated. Because extensive descriptions of measurement technique and automated signal analysis have been provided previously we would like to refer to these studies [12, 13, 15-18, 29, 30]. The following ULAM outcome measures, with lower scores indicating more limited activity, were used:

- *%dyn*; the percentage of the measurement period that dynamic mobility-related activities (i.e. the body motions walking, climbing stairs, cycling and general non-cyclic activity) were performed,
- *intsit & intstand*; the mean intensity of upper limb activity of the involved side while the subjects were sitting and standing, expressed in g (9.81 ms^{-2}),
- *%sit & %stand*; the percentage of the time that the involved upper limb was active while the subjects were sitting and standing,
- *propsit & propstand*; the proportion of the intensity of activity of the upper limb of one upper limb relative to the intensity of activity of the other upper limb, expressed as a ratio [19, 20].

Because there was no guaranteed treatment effect and no ´gold standard´ for objective measurement of changes in activity limitations over time, the time course of the ULAM outcome measures was compared to the course of questionnaires. Three questionnaires were used that also aimed at measuring limitations of everyday functioning, but with other measuring techniques and different operationalisations of the concept functioning than the ULAM. We assumed that if functioning changed over time, this had to be reflected to a lesser or greater extent in both ULAM and questionnaires, depending on the strength of the conceptual relationships between the instruments and similarities regarding instrument characteristics. The following questionnaires were used:

- *RAND36 Health Survey*; the RAND36 [31] is a generic questionnaire that has been used in CRPSI research [32, 33]. Although it was most responsive of five generic questionnaires [34], it was less responsive for upper limb disorders [35] because of ceiling- and floor-effects,
- *Radboud Skills Questionnaire (RASQ)*; the RASQ is a reliable body-part specific questionnaire [36] especially developed for subjects with upper limb CRPSI that compares the current effort certain activities cost to pre-CRPSI [21, 28]. Its responsiveness has not been studied specifically,
- *Disabilities of Arm Shoulder and Hand Questionnaire (DASH);* the DASH function and symptom score is a 30-item body-part specific questionnaire that mainly measures limitations of everyday activity of subjects with upper limb disorders [37-39] but also contains some impairment items. Except for our study [21], it has not been used in CRPSI but responsiveness was sufficient after carpal tunnel release [40].

The time course of several impairment outcome indicators was also explored. Most of these impairments have been described as a responsive multi-component score for (acute) upper limb CRPSI [28, 41];

- *VAS-effort*; pain intensity resulting from effort as measured with a visual analogue scale,
- *VAS-moment*; momentary pain intensity as measured with a visual analogue scale
- *Volume*; the difference in volumetric measurements (oedema, atrophy) between both hands in relation to the volume of the non-involved side as measured with a fluid overflow volumeter,
- *Temperature*; temperature of the dorsal side of the involved hand relative to the non-involved side as measured with an infrared thermometer,
- *AROM*; maximum active range of motion (AROM) within pain threshold of the wrist and two most impaired fingers of the involved hand relative to the non-involved side as measured with a goniometer,
- *Strength*; four point grip strength of the involved hand relative to the non-involved side as measured with a portable hand-held dynamometer.

Impairments were converted to a range of 1-10 with a score of 1 to be interpreted as absence of that impairment and 10 as severely impaired. For a more information we would like to refer to other studies [20, 41].

Protocol

All assessments were in the subjects' home environment. Informed consent was signed, the ULAM was fitted and information regarding treatment was obtained. The subjects were instructed to continue everyday activities while wearing the ULAM, except for swimming, bathing or showering. To avoid fatiguing the subjects and to assess wearing comfort, the ULAM was worn for 24 hours although 48-h measurements are technically possible. After removing the ULAM, it was asked whether the wearing period was representative for the rest of the days of that week, a gross overview of activities performed was noted to support data interpretation, and questionnaire and impairment scores were obtained. The exact ULAM measurement technique and output parameters were not explained until final assessment. All subjects agreed with this protocol, which was approved by the local medical ethical committees.

Data-analysis

To determine the time course of objectively measured upper limb activity, the absolute values of the ULAM outcome measure scores were analysed at assessments t0 to t3. Changes in the absolute values of all outcome measures at t1, t2 and t3 compared to baseline (t0) were subsequently normalized to visualise their course in time. The maximum change compared to baseline (either positive or negative, either for time interval t1-t0, t2-t0 or t3-t0) was set at 100% (or -100% in case of a negative change). These normalized change scores were shown in bar graphs for both the individual subjects and the group (n=4). A from a clinical

viewpoint 'ideal pattern' for the outcome measures would be that the normalized time interval for t3-t0 was at +100%, whereas the t2-t0 and t1-t0 intervals were both at repectively lower percentages. Such a pattern meant that the more time had passed, the more a subject's functioning had improved (irrespective of whether positive changes in functioning were due to treatment or natural recovery). It has to be noticed such figures do not display the magnitude of changes between different outcome measures but only the direction of changes over time. To compare the time courses, we calculated how often changes over time between consecutive follow-up assessments (t1-t0, t2-t1 and t3-t2) as measured with the ULAM outcome measures were in the same direction as changes over time as measured with other outcome measures. For each combination of two outcome measures twelve delta pairs (4 assessments, so 3 deltas for each of the 4 subjects) were analysed. The higher the number of changes in the same direction for two outcome measures (either in a positive or in a negative direction), the more similar the time course between these outcome measures.

8.4 Results

The subjects did not report any problems wearing the ULAM although they had to get used to it for a few minutes each time it was fitted. The ULAM outcome measures propsit and propstand were missing at three assessments due to technical problem with the sensor on the non-involved forearm. These outcome measures were only presented in table 8.1 and not further analysed.

Time course of upper limb activity
The ULAM outcome measure %dyn fluctuated over time in subject A, whereas the absolute values of its outcome measures related to upper limb usage indicated clearly improved functioning between t0 and t1 (table 8.1). The apparent stabilisation of upper limb outcome measures at t2 and t3 was probably due to 24-h ULAM wearing periods that were not representative (i.e. inactive) for other days of that week. Nevertheless, all ULAM outcome measures demonstrated improvements at the end of the 3-months period compared to baseline; intsit +24%, %sit +28%, intstand +25% and %stand +7%. The three questionnaires also indicated improved functioning at t3 compared to baseline. The impairment outcome indicators AROM and strength had clearly improved ($\geq$ 2 points) and temperature had clearly worsened after 3 months. At final assessment, subject A was working full-time and started jogging again.

Subject B's upper limb activity as measured with the ULAM had not changed much at the end of the 3-month measurement period compared to baseline (intsit +7%, %sit -2%, intstand +4%, %stand +1%, propsit +18% and propstand +1%); improved propsit was mainly due to decreased activity of the non-involved side (table 8.1). Although the 24-h ULAM wearing period was representative for that week at t3, it was unrepresentative for previous assessments because the family-dog had died; the

percentage and intensity of upper limb activity were worse which may have been due to less petting. The questionnaire scores had not changed much at the end of the 3-month period. At final assessment, only both VAS scores had worsened and the other impairments had hardly changed compared to baseline. So subject B´s overall functioning did not appear to change much during the measurement period. It has to be noted, however, that his treatment did not pass problemless with a delayed start and premature ending of physical therapy in addition to an unintentional initially too small dose of medication.

*Table 8.1: Overview of absolute values for the ULAM outcome measures, the questionnaire outcome measures and the impairment outcome indicators of the four individual subjects and the group. - unrepresentative 'inactive' 24 hours with the ULAM, o representative day for the rest of the days of that week, + unrepresentative 'overactive' 24 hours, * could not be computed due to a technical problem*

	Subject A				Subject B				Subject C				Subject D				Group n=4			
	t_0	t_1	t_2	t_3	t_0	t_1	t_2	t_3	t_0	t_1	t_2	t_3	t_0	t_1	t_2	t_3	t_0	t_1	t_2	t_3
ULAM activity outcome measures (representative 24 hrs -, o, +)		o	o	o	o	o	o	-	o	-	o	o	+	o	o	-				
The higher the score, the better the functioning																				
%dyn	9,8	10,1	11,8	10,6	11,8	16,6	10,3	11,8	7,0	6,8	7,0	8,4	19,5	12,3	17,4	13,8	12,0 (5,4)	11,5 (4,1)	11,6 (4,3)	11,4 (1,9)
intsit	2,8	4,0	4,1	3,5	3,4	2,8	3,7	3,6	1,9	5,1	5,2	4,9	2,4	1,9	2,6	2,4	2,6 (0,6)	3,4 (1,4)	3,9 (1,1)	3,6 (1,0)
%sit	27,6	40,4	35,3	35,2	37,1	31,0	39,1	36,4	20,3	51,4	45,4	45,1	23,0	19,5	26,6	22,2	27,0 (7,4)	35,6 (13,6)	36,6 (7,9)	34,8 (9,4)
intstand	6,3	7,1	7,8	7,9	8,0	8,3	9,7	8,3	9,1	10,7	11,0	11,3	6,8	8,4	8,7	9,0	7,5 (1,3)	8,6 (1,5)	9,3 (1,4)	9,1 (1,5)
%stand	53,7	56,1	55,9	57,4	73,8	73,6	78,5	74,7	79,0	82,4	77,9	80,2	68,3	81,9	76,6	74,4	68,7 (10,9)	73,5 (12,3)	72,2 (10,9)	71,7 (9,9)
propsit	0,94	0,97	*	*	0,76	*	0,62	0,90	0,93	0,87	0,94	0,96	0,83	0,83	0,84	0,82	0,86 (0,10)	*	*	*
propstand	0,92	0,94	*	*	0,71	*	0,71	0,72	0,90	1,01	0,88	1,03	0,84	0,90	0,73	0,72	0,79 (0,10)	*	*	*
Questionnaire activity outcome measures and impairment outcome measures																				
The higher the score, the better the functioning																				
RAND36 (0-100)	62	88	71	79	61	51	59	61	33	40	56	49	69	65	62	70	58 (16)	56 (13)	62 (7)	65 (13)
The lower the score, the better the functioning																				
RASQ (1-5)	2,5	1,8	1,3	1,2	2,8	2,7	2,3	2,4	3,8	2,7	2,3	2,0	2,9	2,4	2,1	1,6	3,0 (0,6)	2,4 (0,4)	2,0 (0,5)	1,8 (0,5)
DASH (0-100)	41	44	24	15	42	39	50	41	67	56	50	50	57	50	41	34	51 (13)	47 (7)	41 (12)	35 (15)
VASeffort (1-10)	2	3	1	1	2	5	5	4	4	4	4	3	7	3	4	2	3,8 (2,4)	3,8 (1,0)	3,5 (1,7)	2,5 (1,3)
VASmoment (1-10)	1	1	1	1	1	2	5	4	3	2	3	3	2	2	2	1	1,8 (1,0)	1,8 (0,5)	2,8 (1,7)	2,3 (1,5)
volume (1-10)	5	4	4	4	1	1	1	1	6	4	1	2	5	3	1	1	4,3 (2,2)	3,0 (1,4)	1,8 (1,5)	2,0 (1,4)
temperature (1-10)	2	5	3	4	2	3	5	3	4	2	1	3	4	1	1	2	3,0 (1,2)	2,8 (1,7)	2,5 (1,9)	3,0 (0,8)
AROM (1-10)	7	7	6	5	3	2	2	2	8	6	6	5	6	3	2	2	6,0 (2,2)	4,5 (2,4)	4,0 (2,3)	3,5 (1,7)
strength (1-10)	6	4	3	3	6	4	4	5	7	7	5	5	6	4	5	4	6,3 (0,5)	4,8 (1,5)	4,3 (1,0)	4,3 (1,0)

The %dyn performed by subject C was lower than the other subjects (table 8.1). Despite an unrepresentative inactive 24-h ULAM period at t1, the majority of ULAM upper limb outcome measures clearly indicated improved functioning between t0 and t1 (except for propsit), and was relatively stable at t2 and t3 (except for propstand at t2). The worsened propsit and propstand scores were due to less increased activity of the involved side compared to increase activity of the non-involved side. At the end of the 4-month period, all ULAM outcome measures indicated improved functioning; intsit +158%, %sit 123%, intstand +25%, %stand +2%, propsit +3% and propstand +14%. All questionnaires also indicated improved functioning after 4 months, also with major improvements between t0 and t1. After 4 months, volume, AROM and strength were clearly improved (≥ 2 points) and no impairment had worsened.

The ULAM outcome measure %dyn varied over time in subject D and was generally high (table 8.1). The unrepresentativeness of two 24-hour ULAM periods (i.e. overactive t0 and inactive t3) was reflected in %dyn and in upper limb activity during sitting. After 4-months, the upper limb activity outcome measures during sitting had hardly changed compared to baseline (intsit +1%, %sit -4%, and propsit -1%), whereas the two outcome measures during standing indicated improved functioning despite unfavourable unrepresentativeness (intstand +32%, %stand +9%, and propstand +13%). The questionnaires RASQ and DASH showed (continuous) improvements over time compared to baseline, whereas the RAND36 scores slightly varied but had not changed after 4 months. All impairments had improved after 4 months, except for VAS-moment that was already least impaired in subject D.

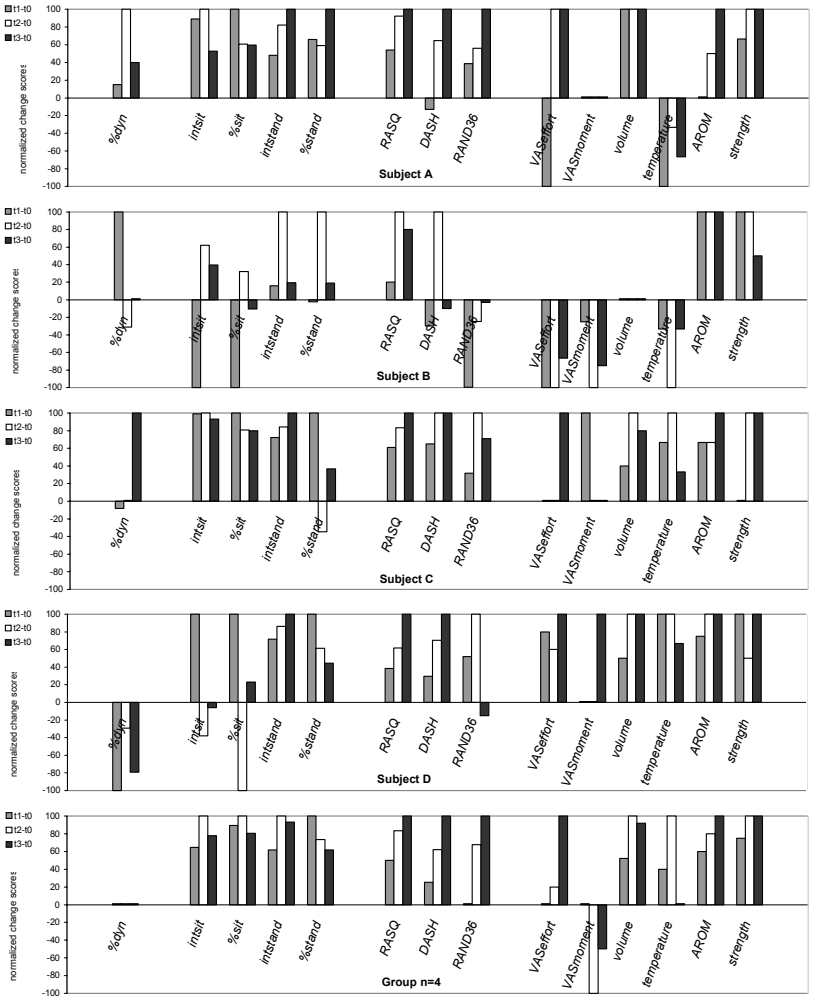
At the group level, %dyn was relatively constant ranging between 11.4-12.0% (table 8.1). At the end of the on average 3½ months period, the four ULAM upper limb outcome measures all indicated improved functioning: intsit +38%, %sit +29%, intstand +21% and %stand +4. The questionnaire scores also indicated improved functioning for the group over 3½ months time. Because the magnitude and moments of changes in impairments varied between individual subjects, only volume, AROM and strength had clearly improved compared to baseline at the end of the measurement period.

Time course of normalized change scores

The patterns of normalized change scores were 'clinically ideal' only for a few outcome measures (figure 8.3, see also method section); actually primarily for the ULAM outcome measure intstand, the RASQ questionnaire, and the impairment outcome indicator AROM. Questionnaires more often displayed such a pattern than the ULAM outcome measures that, in turn, more often displayed such a pattern than the impairment outcome indicators. Not one 'clinically ideal' pattern was found for subject B. For subjects A, C and D, the majority of questionnaire and impairment outcome measures displayed their maximum normalized positive change (+100%) for the t3-t0 time interval, which was not true for the ULAM outcome measures. Outcome measures that displayed a maximum normalized negative change (-100%) or did not

change during two or more of the time intervals were mainly at the impairment level, and mainly for subject B. Overall, the ULAM outcome measure %dyn appeared dissimilar to the other ULAM outcome measures. The normalized change scores of subject B were clearly divergent from the other subjects.

Figure 8.3: Overview of normalized change scores of all outcome measures for three delta scores (t1-t0, t2-t1, t3-t2), for both the individual subjects and the average score of these subjects as a small group. The maximum change compared to baseline (either positive or negative, either for time interval t1-t0, t2-t0 or t3-t0) was set at 100% (or -100% in case of a negative change).



Time course ULAM outcome measures in relation to other outcome measures
Calculations of how often changes over time between consecutive assessments (t1-t0, t2-t1 and t3-t2) were in the same direction (table 8.2) showed that the time course of ULAM outcome measures was most often in the same direction with the RASQ. The changes in functioning as measured with the RAND36 and DASH were less often in the same direction as the ULAM outcome measures. The DASH showed a number of changes in the same direction as the ULAM outcome measures about equal to the impairment outcome indicators volume, temperature, AROM and strength; both VAS scores clearly had lower numbers. Of the ULAM outcome measures, the time course of intstand was best related to the time course of both the questionnaire and impairment outcome measures.

Table 8.2: The time course of the five ULAM outcome measures in relation to the time course of the questionnaire and impairment outcome measures. It was calculated how often changes over time between follow-up assessments and baseline assessment (t1-t0, t2-t1 and t3-t2) as measured with the ULAM outcome measure were in the same direction as changes over time as measured with the other outcome measures.

	RAND36	RASQ	DASH	VAS effort	VAS moment	volume	tempera-ture	AROM	strength	*Sum*
%dyn	5	6	6	3	2	3	6	4	4	*39*
intsit	8	7	4	2	2	5	7	3	4	*42*
%sit	6	5	2	1	3	4	5	2	2	*30*
intstand	7	12	8	5	2	5	4	7	7	*57*
%stand	6	7	3	5	3	3	4	4	4	*39*
Sum	*32*	*37*	*23*	*16*	*12*	*20*	*26*	*20*	*21*	
Sum - %dyn	*27*	*31*	*17*	*13*	*10*	*17*	*20*	*16*	*17*	

8.5 Discussion

When the absolute values of the ULAM outcome measures at final assessment were compared to baseline, objectively measured upper limb activity of these four subjects with acute upper limb CRPSI often improved. Improvements of >5% were found for the majority of ULAM upper limb outcome measures (10/16, 63%), despite actually unchanged functioning in subject B and the sometimes very short time intervals

between assessments. Because we had no idea as to how limited the subjects would be or how fast changes over time would occur, small time frames were considered appropriate for the present study, however. Although these four subjects showed more limited upper limb activity than thirty subjects with chronic CRPSI as previously measured with the ULAM [19, 20], this should not be interpreted as a confirmation of the supposition that functioning is generally more limited in acute than in chronic CRPSI. CRPSI clearly is a syndrome and usually varies enormously between subjects with respect to type and magnitude of impairments and activity limitations, as well as the duration of these consequences of the syndrome.

The finding that the body-part specific RASQ had a time course more similar to the ULAM than the RAND36 and DASH was probably due to more similarities with respect to operationalisation of functioning and other instrument characteristics, as was also found in chronic CRPSI [21]. Changes over time as measured with the impairment outcome indicators were less well related to changes as measured with the ULAM than the questionnaires were, which was already expected because impairments are operationalisations of functioning at a different level than ULAM and questionnaires (i.e. body impairments versus a person's activity). Among the impairments, the time course of volume, temperature, AROM and strength were more frequently in accordance with the ULAM outcome measures than the VAS pain scores, which was not really surprising because, especially in acute CRPSI, pain can vary widely during the day [41]. It has to be noticed that the present VAS scores were not very high; the four subjects may therefore not have been representative for acute CRPSI with respect to pain intensity. The divergent time course of %dyn was also not unexpected considering the population studied; the present subjects had an upper limb disorder and were not limited with respect to mobility at the group level, which was also found in chronic upper limb CRPSI [19]. The present 11-12 %dyn did not differ from chronic upper limb CRPSI or healthy subjects [19, 12, 13, 15-18, 29, 30].

The present results, in our opinion, demonstrate that the current ULAM outcome measures have the potential to validly assess changes in upper limb activity over time of subjects with upper limb CRPSI in future longitudinal studies. Although the ULAM is considered potentially sensitive for changes in upper limb activity, some aspects will have to be studied before definite conclusions can be drawn, however. An important methodological issue of a ULAM measurement is between-measurement variability. Variability between measurements can be the result of several factors. First, everyone’s level of everyday physical activity will vary, even within 'representative days', and thus the level of upper limb activity in CRPS patients will also vary. The intra-individual biological variability of upper limb activity as measured with the ULAM could not be investigated as yet because we have only performed 24-h measurements. Between-day-variability for %dyn has been studied in 48-h measurements with the ULAM´s older sibling AM [29, 30], however, and appeared to be 1.1% and 1.3% in two different patient groups and 0.8% in healthy subjects. Some between-day variability for upper limb activity will not be problematic as long as

it is relatively small compared to actual changes in upper limb activity. However, intra- and inter-individual between-day variability have to be studied for both patients and healthy subjects to determine to which degree changed upper limb activity as measured with the ULAM falls under biological variability and above which threshold changed upper limb activity can be considered as clinically relevant. Such a study may lead to an advice about the number of monitoring days that is needed. Moreover, related to the number of monitoring days, knowledge of biological variability is also important to determine the required sample size for future intervention studies.

Second, besides the random fluctuation within a probably limited range, some days may clearly be different from “regular” days. For example, in the current study 6 of the 12 measurement days were not representative according to the patient’s own opinion. This was due to unusual overactivity such as organising a barbeque party, or unusual inactivity such as going to a lecture, take an unexpected day of from work or hot humid wheather. Such unrepresentativeness of the 24 hours was logically not (or less) reflected in the questionnaire scores because questionnaires measure a perceived average score over the last few days whereas the ULAM measured what subjects actually did during that specific 24-hour period. Concerning the possible negative effects of unrepresentativeness of the measurement day on validity, it will stay important to ask a patient about this matter. Possibly, measurement days that are not representative should not be included in the analysis in future studies. Moreover, increasing the number of measurement days will also address this problem.

Finally, the instrument itself can be a source of within-measurement variability. It has to be noticed that the ULAM upper limb outcome measures are rather rough; the ULAM detects upper limb activity but does not yet allow valid measurement of every aspect of upper limb usage as a consequence of the measurement technique [13]. However, due to our experiences and data from previous studies we think that this latter point is less important than the issue of between-day variability in everyday physical activity. Nevertheless, improving the reliability and validity of the ULAM itself will remain an ongoing issue.

8.6 Conclusion

In general, clear changes were found in upper limb activity over time as objectively measured with the ULAM. The relationships between the time course of the ULAM outcome measures and the time course of other outcome measures for activity limitations and impairments appeared to be logical and explainable. It was therefore concluded that the current ULAM outcome measures have the potential to validly assess changes in upper limb activity over time of subjects with upper limb CRPSI. However, the issue of between-day variability needs further study in a larger population during a longer time period.

8.7 References

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9 General discussion

In the previous chapters several issues on various topics have already been discussed. The aim of this chapter is to bring some of these issues together to discuss them from a more general viewpoint and to introduce some new issues.

Health-related classifications

In this thesis, several names are used for the classification currently known as the International Classification of Functioning (ICF). Our studies were performed during the time that the changeover from ICIDH, via ICIDH-2, to ICF was ongoing, which may have led to some confusion. The ICF is one of the health-related classifications of the World Health Organisation (WHO) which was originally set up as the International Classification of Impairments, Disabilities and Handicaps (ICIDH) in 1980 [1] as a response to problems with evaluating health care at that time [2]. The ICIDH was developed because the even older International Classification of Diseases (ICD, first published in 1893) could not meet the need to describe medical outcome for chronic conditions. This ICIDH went beyond morbidity and mortality because it described the *consequences* of diseases and disorders. It recently underwent some revisions, which resulted in the ICIDH-2 in 2000 and the ICF in 2001 with an altered framework and terminology [3, 4]. General shortcomings of the ICIDH were insufficient attention to the role of the environment, overlap between dimensions and lack of clarity about causal and temporal relationships [2]. In the ICF positive counterparts of the ICIDH terminology are used; deviations or loss in body structures and functions are referred to as impaired body function and structure, difficulties with performing an activity are referred to as activity limitations (and not disabilities), and problems with participation or involvement in life situations are referred to as participation restrictions (and not handicaps). The current ICF terminology fits the ULAM better than the ICIDH terminology because the ULAM outcome measures are also positively expressed.

Health outcomes research

The changing view on health and health care has not only led to the development and revision of the WHO classifications, but also contributed to the rising of health outcome research. Within this discipline, it was increasingly acknowledged that methods and measures of activity (limitations) are very important indicators of human functioning and determinants of treatment effect [5-9]. Despite this, very limited attention is paid to devices like the ULAM and AM when it comes to reviews of methods and measures for health outcomes research. Scales and questionnaires are discussed extensively, whereas the technique of ambulatory monitoring is hardly ever mentioned although it comes up to a substantial number of requirements and criteria that are often formulated [9-11]. This may be due to the fact that ambulatory monitoring of activities is a relatively new technique that is still unknown to many and therefore not widely accepted. It may also be so that there is no notion of its numerous possibilities as yet because the technique goes beyond the general way of thinking about health outcome research. Hopefully, future technical developments and the increasing number of international publications involving ambulatory monitoring

devices such as the AM and ULAM will underline that ambulatory monitoring of activities is a relevant and valuable addition to the field of health outcomes research that can no longer be denied. It is important to realise, however, that this remark should not be confused with the idea that ambulatory monitoring is a new reference method and that measurement of what a person really does during everyday life is most important. As described several times in this thesis, the choice for an instrument should always depend on a complexity of factors.

Terminology for CRPSI

The results from the different application studies [12-15] showed that relatively large inter-individual differences with respect to the impact of upper limb CRPSI on everyday functioning exist. Such large inter-individual differences in presence, magnitude (and recovery) of limited upper limb activity as measured with the ULAM was also shown for impairments in upper limb CRPSI [13, 16, 17] and can be considered typical for disorders referred to as a syndrome. Regarding this heterogeneity in several aspects of the disorder, the 1994 decision of the International Association for the Study of Pain (IASP) to rename the 'disorder-with-an-ever-changing-name' to complex regional pain *syndrome* [18, 19] is considered appropriate. However, pain was not the most prominent impairment and neither did pain explain most of the variability in activity limitations in the studies described in this thesis. We therefore agree with vanderLaan et al [20], who suggested that it may be more appropriate to change the term pain to dysfunction, as in complex regional dysfunction syndrome type I (CRDSI). CRDSI is, in our opinion, also more appropriate with respect to the International Classification of Functioning (ICF) terminology because the consequences of this syndrome encompass all three levels of the ICF. The term dysfunction in CRDS can refer to consequences at all ICF levels whereas the term pain in CRPSI refers to only one of these levels.

Upper limb usage definition and framework

Our definition of upper limb usage as active movement(s) of (parts of) the upper limb(s) in relation to proximal parts, holding objects and/or leaning appeared to be workable when used together with the framework we compiled. Since developing and validating a novel device like the ULAM already is an innovative, and by that complex and time-consuming process, and because we did not know what the wearing comfort of the ULAM would be, particularly with sensors in the involved area, we wanted to limit the number and type of sensors in the first instance. In the framework used up till now, some sub-forms of upper limb usage were taken together because from a technical point of view, there are no real differences between for example leaning and holding, or between gesticulating, operating, handling and manipulating. As we also knew in advance that not all forms of upper limb usage could be equally well detected with the ULAM as a consequence of its technique, we made the assumption that a relationship exists between different forms of upper limb usage. Since leaning, holding and manipulating are usually preceded and followed by active upper limb movements to bring the limb in the right position to lean, hold or

manipulate in normal upper limb usage, a subject with an upper limb disorder will also perform less leaning, holding and manipulating with the involved side. Thus the assumption was that limitations of leaning, holding and manipulating are (indirectly) expressed in the amount of number of upper limb activity. This assumption and the technical-anatomical approach were, in our opinion, necessary for the developmental- and initial application-phase of the ULAM. Considering the results described in this thesis, sole usage of accelerometers can be sufficient to satisfactorily explore limitations of subjects with upper limb CRPSI. The ULAM outcome measures that have been used up to now were carefully formulated on the basis of those forms of upper limb usage from the framework that were best detected, as well as clinical considerations with respect to activity limitations in CRPSI. A more clinical definition of upper limb usage that may be worthwhile for further development and future applications, however, is active and purpose-directed usage of the upper limb (i.e. arm, including hand) to perform or carry out functional activities during everyday life. Using such a definition will result in a more extensive framework, which may also have consequences for ULAM requirements and the number and type of sensors and outcome measures. For example, if activity limitations of subjects who mainly have problems with manipulative upper limb usage (i.e. fine motor skills) have to be determined, the present ULAM outcome measures are too rough, and it may become necessary to distinguish between the sub-forms of primary functional upper limb usage gesticulating, positioning, handling and manipulating upper limb movements. Preliminary results with additional electromyography (EMG) sensors on the forearms to improve detection of these forms of upper limb usage have shown that there is some profit to gain [21, 22]. The development and validation of devices like the ULAM and its outcome measures clearly is an ongoing process of extending possibilities, optimising properties and enhancing interpretation.

Methodological considerations

Because the ULAM is, in fact, an extension of the AM, several limitations or issues that have already been discussed with respect to the AM [23] also apply to the ULAM. One of these issues is intra-subject variability of everyday activity, which refers to biological or natural differences in activity patterns of any given person between workdays, weekend days or irregular activities [24-26]. Between-day variability of upper limb activity may depend on the type of population that is studied; healthy subjects or subjects with a mild upper limb disorder may have a greater range of upper limb activity during everyday life than subjects with a severely limiting upper limb disorder. Second, between-day variability of upper limb activity may also depend on whether a disorder is acute or chronic. And third, between-day variability may differ depending on the outcome measures that are used. There may be differences regarding between-day variability between the intensity of upper limb activity and the percentage of upper limb activity or between the percentage of upper limb activity during sitting and the percentage of body motions that are performed (i.e. the ULAM outcome measure %dyn). From the viewpoint of novelty and patient burden (not

bathing, swimming etc) we chose to only perform 24-hour week-day measurements with the ULAM at first instance. However, it appeared that neither chronic nor acute CRPSI subjects had major problems with wearing the device for 24-hours. Retrospectively, it would have been interesting (or maybe even better) if we had performed some 48-hour measurements to have some indication of between-day variability of upper limb activity in CPRSI. Obtaining 'norm-values' for healthy upper limb activity and its between day between-day variability are also particularly important for future use as reference values to classify a subject with an upper limb disorder as limited or not.

Two other timely issues related to intra-subject variability of everyday activity are the impact of external factors and the ´reactivity-´ or ´perturbation-effect´. When performing a cross-sectional (comparison) study or longitudinal study with the ULAM, external factors possibly influencing activity patterns and upper limb activity, such as time of the year / season or family / living situation, should always be considered, because these factors may have an impact on validity of the results [27]. These factors are similar to the factor unrepresentativeness of the ULAM measurement period as already extensively discussed in chapter 8. This factor should also be taken into account during time management and planning of studies, selection of control groups and data-analysis. The second issue is the ´reactivity-´ or ´perturbation-effect´, which refers to the possibility that the ULAM influences the activity pattern of subjects because they are aware that they are measured [27]. Such an effect can also be due to wearing the instrument itself (i.e. a subject does not perform usual sports or therapeutic exercises while monitored). To avoid bias with this respect, instructions given to the subjects is of major importance as already explained in chapters 5 and 6. Another option to avoid some bias is to measure for more than one day and not use the data of the first day. Since it is questionable whether a subject is able to consciously adapt his or her activity pattern throughout the measurement, however, this option is probably unnecessary provided that it is always stressed that a subject's performance is not tested.

Last but not least, it has to be mentioned that ethical considerations of the ULAM are equal to those of the AM [23]. Just like all medical research, research the ULAM is subject to Medical Ethical Committee guidelines: the subjects can not be forced to participate and have to be well informed about the study including the consequences of participating. Measurement results may also not necessarily have consequences for their treatment, and it should be clear that measurements are not a test of a patient's capacity. It should be noted that the output of the ULAM is no more and no less than a specific set of outcome measures related to upper limb activity and mobility-related activities.

Practical aspects

Of the available methods for fixation of the acceleration sensors on the skin, Rolian Kushionflex™ or silicone-based stickers (Schwamedico) in combination with double-sided tape between these materials and the sensors appeared to be best, although this is still not optimal. To ensure that the sensors will remain fixed throughout the measurement period, mostly, additional skin friendly tape (Durapore™) was used on top the sensors and other fixatives. This was particularly important for the sensors on the forearm because sensors and cables at this location are more sensitive to bumping, getting wet and getting caught in objects. Moreover, since excessive sweating in the involved hand or arm may also be a problem in CRPSI, an extra roll of skin friendly tape was left behind for each subject if sensors and fixatives were in danger of getting loose. In two subjects that were studied in this thesis, a bandage was used for sensor fixation, however, because of allergy to all normally used fixatives and (rightly or wrongly) uneasiness about negative effects of taking off the fixatives. Because changes in sensor position during the measurement period are not desirable and should be kept to a minimum [23], subjects were instructed to check every now and then whether the sensors were still properly fixed. In case of (unexpected) problems of any kind, for instance with sensor attachment or fixation, ULAM power supply or recorder errors, the subjects were instructed to phone the researcher at any time during the measurement period, even in the middle of the night. Fortunately, this never happened.

Measurements with the ULAM may cause some discomfort because the system can not be used in a wet environment, which means that subjects can not shower or take a bath during the 24-hour measurement period. Cables or the recorder may disturb sleeping or (un)dressing, especially the cables of the ULAM forearm sensors that go up the sleeves and then down again to the recorder. For proper attachment of trunk and leg sensors with the AM, as well as with the ULAM, it was / is sometimes necessary to shave chest- or leg-hair, which did not cause difficulties. As for attachment of the ULAM forearm sensors, however, shaving may very well bring about objections. Fortunately, the majority of the subjects that have been studied so far was female, and the male subjects were either not very hairy or did not raise objections. Although some subjects disliked the ´tourist look´ and it sometimes appeared as though the weight of the recorder increased at the end of the measurement period, none of the subjects had insuperable problems with wearing the ULAM for 24-hours. Even though most subjects reported that they had to get used to wearing the device the first few minutes and again when they went to sleep, nobody found the ULAM uncomfortable to wear. So we do not think that wearing the ULAM influenced the subjects' activity. However, user-friendliness can and should always be subject to improvement. Especially if measurement periods for longer than 24 hours are desirable further technical developments such as a smaller, waterproof and lighter data logger, as well as (preferably wire-less) waterproof sensors are necessary.

Future applications and clinical implications

The work described in this thesis concerned the development, validation and application of the ULAM to determine activity limitations in subjects with upper limb CRPSI. The four application studies (chapters 5-8) have provided much information about the potential of this novel device. An important finding is that the consequences of upper limb CRPSI on everyday functioning are not restricted to impairments: clear limitations of upper limb activity were found. A clinical implication for medical practice therefore is the apparent importance to prevent upper limb CRPSI from becoming chronic because objectively measured limitations of the intensity, percentage and proportion of upper limb activity were found at on average 3.7 years after the causative event. It may be worthwhile to aim at reducing impaired AROM and strength in subjects with acute upper limb CRPSI because these impairments were the more important factors explaining variance in activity limitations in chronic CRPSI. However, this will have to be supported by further research. In a recent paper that described a positive effect of mono-disciplinary physical therapy to reduce impairments in acute upper limb CRPSI [17, 28-30], it was recommended that specific instruments suitable to measure activity limitations and participation problems need to be developed. In our opinion, the ULAM definitely meets this need. It has to be noticed, however, that only a subgroup within the CRPSI population was studied. Although the present population did not have severe uncommon motor impairments such as tremor, spasms or dystonia, one has to be very careful with generalising the present results to the total population with unilateral (or bilateral) upper limb CRPSI. Let alone to the total CRPSI population that consists for about 50% of lower limb CRPSI subjects. There may very well be discrepancies between other CRPSI subgroups or other upper limb disorders with respect to limitations of upper limb activity or the relationship between upper limb activity as measured with the ULAM and activity or impairment as measured with other instruments and their outcome measures. Such discrepancies and similarities may on the other hand also provide meaningful information for clinicians. Despite some limitations and some aspects that need further study, the ULAM has numerous possibilities for future applications in both the CRPSI population and other populations with upper limb disorders, such as repetitive strain injury, carpal tunnel syndrome, rheumatoid arthritis or after stroke.

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Summary

Complex Regional Pain Syndrome type I (CRPSI) is a far from fully understood symptom complex that, when it occurs, usually follows surgery or trauma. The syndrome is expressed in the upper limbs in about 50% of the total CRPSI population, and may cause impaired body functions and structures, activity limitations during everyday life (including occupation) and participation problems such as social functioning and role fulfilment. The course of CRPSI shows large variability, both between and within subjects, which makes interpretation of clinical findings and research data difficult. As described in the general introduction of this thesis ***(chapter 1)***, CRPSI is increasingly investigated from various perspectives all over the world, including from the perspective of rehabilitation medicine.

The goal of rehabilitation medicine is regaining and/or maintaining functionality by decreasing the consequences of diseases or disorders. For this reason, feasible, reliable, valid and preferably also objective instruments that measure everyday functioning are of fundamental importance to provide insight into activity limitations. To determine the availability of such instruments for CRPSI, we performed a literature review and studied a large number of instruments and outcome measures that have been used in CRPSI research ***(chapter 2)***. All these outcome measures were classified as either measuring impairments, activity limitations or participation restrictions. Also, for each outcome measure, a description of the concept that was measured, the operationalisation of this concept into variables (≈ how the concept is measurable), and the actual instrument was also given. It appeared that most of the outcome measures for CRPSI were concentrated on impairments, whereas measures concentrating on activity limitations and participation restrictions, which are most relevant for rehabilitation medicine, were mentioned in very few studies and were measured with scales and questionnaires which are liable to subjective influences. Objective outcome measures were merely found for impairments; there clearly was a need for relevant outcome measures that can objectively measure activity limitations and participation restrictions in CRPSI.

The above study provided the starting point of developing a novel Upper Limb-Activity Monitor (ULAM). Due to developments in data recording and sensor technology, advanced ambulatory systems that measure aspects of human functioning during everyday life have gradually become available over the past years. One such ambulatory system is the ULAM which allows objective measurement of activity limitations of subjects with CRPSI in one upper limb. The ULAM is an extended version of its ´older brother´ the Activity Monitor (AM). Both instruments are based on ambulatory accelerometry and aim at long-term assessment of body postures (lying, sitting, standing) and body motions (walking, going up/down the stairs, cycling, general non-cyclic movement). In case of the ULAM also activity of the upper limbs while a subject is performing these body postures and motions can be assessed. Signals from body-fixed acceleration sensors are recorded for a period of

at least 24 hours in a subject's home environment and continuously stored in a digital portable recorder. During post-measurement analysis, body postures, body motions and upper limb activity performed by the subject are detected by means of custom-made software programs ***(chapters 3 and 4)***. In a feasibility study, the ability of the ULAM to discriminate between upper limb usage and non-usage in healthy and disabled subjects during normal daily life was assessed. Based on our definition of upper limb usage (i.e. active movement of (parts of) the upper limb(s) in relation to proximal parts, holding and leaning) and a framework of different forms of upper limb usage, an activity protocol was compiled that represented normal daily life upper limb usage or non-usage. Video recordings were used as a reference method and agreement scores between ULAM data and videotape recordings were calculated. The ULAM data of special interest for rehabilitation medicine were detected satisfactorily (overall agreement 83.9%). There were no systematic differences in the agreement percentages between healthy and disabled subjects for the different forms of upper limb usage or non-usage. Although the ULAM did not allow valid measurement of every aspect of upper limb (non-)usage, its use was considered feasible for future application studies on activity limitations in upper limb CRPSI.

In the first clinical application study, the long-term impact of upper limb CRPSI on general mobility and upper limb usage during everyday life, as measured with the ULAM, was determined ***(chapter 5)***. In ten female chronic CRPSI patients (on average 3.7 years after the causative event) and ten healthy control subjects, 24-hour activity patterns were measured with the ULAM. Several ULAM outcome measures related to general mobility and upper limb usage were compared between the CRPSI patients and the controls. It appeared that the general mobility of subjects with CRPSI in their non-dominant upper limb was not affected by CRPSI. However, CRPSI in the dominant upper limb had modest impact on general mobility; i.e. on the percentages spent in body positions and body motions and on mean intensity of body activity. Furthermore, for the ULAM outcome measures related to upper limb usage there were marked differences between the ten CRPSI patients and the healthy control subjects, although less obvious during standing than during sitting. Especially the patients with dominant side involvement clearly showed less activity of their involved limb during sitting. This was indicated by significant differences for the mean intensity, percentage and proportion of upper limb activity. Even though the statistical power was low because of the small sample size, it can be concluded that chronic CRPSI patients still have objectively measurable limitations in upper limb usage during everyday life.

CRPSI really is a syndrome: sensory, autonomic, trophic and motor impairments may be found. From a rehabilitation point of view it is important to analyse the relationship between impairments and activity limitations to address questions as: ´does an impairment always lead to activity limitations?´ and ´which impairment particularly affects everyday activity?´. Because the impairment-activity limitations relationship in CRPSI had only been studied using questionnaires to measure the degree of activity

limitations, the aim of the second clinical application study ***(chapter 6)*** was to determine the degree of impairments, the degree of activity limitations as objectively measured with the ULAM in the subjects home environment, and the relationship between impairments and activity limitations. Thirty chronic upper limb CRPSI subjects volunteered to participate.
Several instruments were used to measure the following impairments; an infrared thermometer was used to determine temperature differences between both hands, a visual analogue scale (VAS, 100 mm long horizontal line) was used to measure pain resulting from effort, the number of pain words from the McGill Pain Questionnaire was used to assess pain during the previous days, a goniometer was used to determine differences in maximum active range of motion (AROM) within pain threshold of the wrist and fingers between both hands, volumeter fluid overflow was used as a means to determine volume differences between both hands, and a portable hand-held dynamometer was used to assess differences in grip strength between both upper limbs were determined with. The main ULAM outcome measures were the intensity, percentage and proportion of upper limb activity while the subjects were sitting and standing. It was found that all thirty CRPSI subjects were impaired to some degree but with a large variability with respect to magnitude. Moreover, the involved upper limb was clearly less active (lower intensity and percentage of activity) than the non-involved side. These activity limitations were more prominent when the subjects were sitting than when the subjects were standing and when the dominant side was involved. As for the relationship between impairments and activity limitations, impaired active range of motion, grip strength, and to a lesser extent pain resulting from effort were the most important impairments explaining variance in activity limitations. It was concluded that all subjects were still impaired nearly three years after the causative event and that the involved upper limb was clearly less active than the non-involved side. It also became clear that the more impairments a subject had, and especially motor impairments, the more activity limitations were present.

Because the ULAM is relatively new and its measurement technique clearly differs from what is commonly used in research and clinic with respect to several methodological and practical criteria, we studied how the ULAM outcome measures were related to four questionnaires that also aim to assess the functional consequences of diseases ***(chapter 7)***. In a cross sectional comparison study, thirty patients with chronic CRPSI in one of the upper limbs were measured with the ULAM in their home environment and after this completed four questionnaires including two generic questionnaires, the 68-item Sickness Impact Profile (SIP68) and the RAND 36-item Health Survey (RAND36), and two body-part specific questionnaires, the Disabilities of Arm Shoulder and Hand questionnaire (DASH) and the Radboud Skills Questionnaire (RASQ). Spearman rank correlations were calculated between the outcome measures. It appeared that 87% of the inter-questionnaire correlations were significant, whereas 39% of the correlations calculated between the ULAM and the questionnaires were significant. It was also shown that the number and strength of

the correlations between the ULAM and questionnaires was dependent on the degree to which the same aspects of functioning were measured. In summary, all five instruments measured similar aspects of functioning to a certain extent; but on the other hand, the ambiguous pattern of correlations demonstrated that the ULAM measured considerably different aspects of functioning than the questionnaires. It was concluded that the ULAM has a distinct place in the field of outcome assessment; it offers an alternative but important insight into the impact a disorder may have on a subject's functioning.

In addition to the chronic CRPSI subjects that were studied in the previous application studies, we also explored upper limb activity over time in four subjects with acute CRPSI in one of the upper limbs ***(chapter 8)***. In this study, we compared the upper limb activity time course as measured with the ULAM to the time course of other outcome measures for activity (limitations) and impairments. The subjects were measured at four moments in time during a treatment protocol. Several of the ULAM outcome measures related to upper limb usage and mobility were assessed. Furthermore, three questionnaires at the activity level (RASQ, DASH, RAND36) and six impairment outcome indicators (VAS-momentary pain, VAS-pain resulting from effort, volume, temperature, AROM, strength) were used. The results indicated that the objectively measured upper limb activity often improved; improvements of >5% were found for the majority (63%) of ULAM upper limb outcome measures at final assessment. In comparison with the three questionnaires, the time course of the ULAM was most similar to that of the body-specific questionnaire RASQ. With respect to the observed time course of the measured impairments, the time course of impaired temperature was most often in accordance with changes over time as measured with the ULAM. Volume, AROM and strength were less frequently in accordance with the ULAM outcome measures, and both VAS scores showed least accordance. In conclusion, we were able to detect clear changes in upper limb activity over time as measured with the ULAM. Furthermore, relationships between the time courses of the ULAM outcome measures and other outcome measures for activity limitations and impairments were explainable. It was therefore concluded that the current ULAM has the potential to validly assess upper limb activity over time in upper limb CRPSI.

Finally, in the general discussion ***(chapter 9)***, some of the issues already discussed were brought together and considered from a more general viewpoint and some new issues were introduced.

Samenvatting

Complex Regionaal Pijn Syndroom type I (CRPSI) is een verre van volledig begrepen complex van symptomen. Wanneer CRPSI ontstaat is dit meestal het gevolg van een operatie of andersoortig trauma. Het syndroom treft bij ongeveer 50% van de totale CRPSI populatie de bovenste extremiteit (arm en/of hand) en kan voor de desbetreffende persoon verscheidene gevolgen hebben: stoornissen in de structuren en functies van het lichaam, beperkingen in het uitvoeren van dagelijkse activiteiten (inclusief beroep) en participatie problemen zoals het sociaal functioneren en de rolvervulling. Het verloop van CRPSI is erg variabel, hetgeen de interpretatie van klinische bevindingen en onderzoeksgegevens bemoeilijkt. Zoals beschreven in de algemene introductie van dit proefschrift ***(hoofdstuk 1)*** wordt CRPSI in toenemende mate onderzocht en wel vanuit verschillende vakgebieden, waaronder de revalidatiegeneeskunde.

Het doel van revalidatiegeneeskunde is het herwinnen en/of handhaven van functionaliteit van personen door het verminderen van de gevolgen van aandoeningen of ziekten. Gezien dit doel zijn bruikbare, betrouwbare, valide en zo mogelijk objectieve meetinstrumenten die het dagelijks functioneren van personen kunnen meten van fundamenteel belang omdat zulke instrumenten inzicht verschaffen in beperkingen in activiteiten. Om de beschikbaarheid van dergelijke meetinstrumenten voor CRPSI te bepalen hebben we een literatuur studie uitgevoerd ***(hoofdstuk 2)***. Een groot aantal uitkomstmaten die in eerder CRPSI onderzoek beschreven werden zijn geclassificeerd naar wat ze beogen te meten; stoornissen in structuren of functies, beperkingen van activiteiten, of participatie problemen. Vervolgens werd voor elke van de uitkomstmaten uit de literatuur aangegeven welk concept (wat) ze beogen te meten, met behulp van welke variabelen dit concept geoperationaliseerd (≈ meetbaar gemaakt) werd, en met welk instrument (hoe) die variabelen gemeten werden. Het bleek dat de meeste uitkomstmaten in de CRPSI onderzoeken zich richten op stoornissen in de structuren en functies van het lichaam. Daarentegen werden de voor revalidatiegeneeskunde meest relevante uitkomstmaten, te weten beperkingen in activiteiten en participatie problemen, maar in enkele studies genoemd. Voor beperkingen van activiteiten of participatie problemen waren geen objectieve uitkomstmaten beschreven; alleen stoornissen in structuren of functies werden objectief gemeten. Er was duidelijk een gebrek / behoefte aan objectieve uitkomstmaten om beperkingen in activiteiten en participatie problemen te meten.

Bovenstaande literatuur studie was de aanleiding voor het ontwikkelen van de ´Upper Limb-Activity Monitor´ (ULAM). Door recente ontwikkelingen in data opslag en sensor technologie zijn de laatste jaren geavanceerde systemen om ambulant en in de natuurlijke leefsituatie verschillende aspecten van het menselijk functioneren te meten beschikbaar gekomen. Een dergelijk ambulant systeem is de ULAM. Dit instrument maakt het mogelijk om beperkingen in activiteiten van patiënten met

CRPSI in één arm en / of hand objectief te meten. De ULAM is een uitgebreide versie van zijn ´oudere broer´ de Activiteiten Monitor (AM). Beide instrumenten zijn gebaseerd op ambulante accelerometrie en kunnen gedurende een lange periode lichaamshoudingen (liggen, zitten, staan) en lichaamsactiviteiten (lopen, traplopen, fietsen, niet cyclische algemene activiteit) meten. Bovendien is het met de ULAM mogelijk om ook (beiderzijds) arm-hand activiteit te meten terwijl personen deze lichaamshoudingen en activiteiten uitvoeren. Met de ULAM kan een 24-uurs activiteiten profiel van een persoon worden verkregen ***(hoofdstukken 3 en 4)***. Hiervoor draagt een persoon de ULAM gedurende 24 uur. Terwijl de persoon in zijn natuurlijke omgeving alledaagse activiteiten uitvoert, worden signalen van op het lichaam bevestigde versnellingssensoren (op romp, bovenbenen en onderarmen) opgeslagen in een digitale draagbare recorder. In de analyse na de 24-uurs metingen worden lichaamshoudingen, lichaamsactiviteiten en arm/hand activiteit van beide bovenste extremiteiten gedetecteerd door middel van speciaal voor de ULAM ontwikkelde software. In een haalbaarheidstudie is het vermogen van de ULAM om bij zowel gezonde personen als (merendeels CRPSI) patiënten met een beperking in één arm of hand onderscheid te kunnen maken tussen arm-hand gebruik en geen arm-hand gebruik. Op basis van de volgende definitie van arm-hand gebruik ´actieve bewegingen van (delen van) de bovenste extremiteit(en) in relatie tot proximale delen, steunen en vasthouden´ en een zogenaamd framework waarin verschillende vormen van arm-hand gebruik en geen arm-hand gebruik beschreven zijn werd een activiteiten protocol opgesteld. In dit protocol waren alle vormen van arm-hand gebruik in het dagelijks functioneren vertegenwoordigd. Als referentie werden video opnames gebruikt waarmee het percentage overeenkomst met de ULAM output werd uitgerekend. De voor revalidatie geneeskunde meest belangrijke ULAM output werd naar tevredenheid gedetecteerd (totaal percentage overeenkomst 83.9%). Er waren bovendien geen systematische verschillen in de percentages overeenkomst tussen de CRPSI patiënten en de gezonde proefpersonen voor wat betreft de verschillende vormen van arm-hand gebruik of geen arm-hand gebruik. Alhoewel er rekening mee moet worden gehouden dat de ULAM niet alle vormen van (geen) arm-hand gebruik valide kan meten, concludeerden we dat het instrument geschikt is om beperkingen in activiteiten van patiënten met CRPSI in een arm of hand te bepalen.

In de eerste klinische studie werd met de ULAM de lange termijn invloed van CRPSI op de algemene mobiliteit en het arm-hand gebruik tijdens het dagelijks functioneren bepaald ***(hoofdstuk 5)***. Tien vrouwen met chronische CRPSI in één arm of hand (gemiddeld 3.7 jaren na de oorzakelijke gebeurtenis) en tien gezonde controle personen die vergelijkbaar waren met de CRPSI patiënten voor wat betreft geslacht, leeftijd en woonsituatie droegen de ULAM gedurende 24 uren in hun thuissituatie. Verschillende ULAM uitkomstmaten gerelateerd aan algemene mobiliteit en arm-hand gebruik werden vergeleken tussen de CRPSI patiënten en de controle personen. Het bleek dat de algemene mobiliteit van de vijf patiënten met CRPSI in hun niet-dominante zijde niet beïnvloed werd door CRPSI. De vijf patiënten met CRPSI in de dominante zijde (de arm/hand waarmee men schrijft) ondervonden wel

enige invloed van CRPSI op de algemene mobiliteit. Deze patiënten brachten een significant hoger percentage van de 24 uur door in lichaamshoudingen (liggen, zitten en staan) dan de gezonde personen. Daarnaast was de gemiddelde intensiteit van de lichaamsactiviteit van deze patiënten significant lager. De ULAM uitkomstmaten gerelateerd aan arm-hand gebruik verschilden wel duidelijk tussen de tien patiënten en tien controle personen. De verschillen waren in het algemeen duidelijk voor arm-hand gebruik tijdens zitten dan tijdens staan. Met name de subgroep van patiënten met CRPSI in de dominante zijde liet minder activiteit zien van de aangedane zijde: er waren significante verschillen voor wat betreft de intensiteit en het percentage van arm-hand activiteit tijdens zitten, en ook de verhouding tussen arm-hand activiteit van beide zijden tijdens zitten en staan verschilde significant met de gezonden. Er kan geconcludeerd worden dat personen met chronische CRPSI na lange tijd nog steeds invloed ondervinden van deze aandoening gezien de objectief gemeten beperkingen in arm-hand gebruik in hun dagelijks leven.

CRSPI is een echt syndroom: patiënten met CRPSI hebben in meer of mindere mate stoornissen in de sensoriek (o.a. pijn & tast), autonome functies (o.a. bloedvoorziening weefsel, rood/blauwkleuring huid, volumeveranderingen), trofiek (o.a. voedingstoestand weefsel, veranderde bot en haargroei) en motoriek (o.a. beweeglijkheid gewrichten, spierkracht, stijfheid, contractuur bindweefsel). Vanuit het oogpunt van de revalidatie geneeskunde is het belangrijk om de relatie tussen stoornissen en beperkingen in activiteiten te analyseren om vragen te beantwoorden als: ´leidt een stoornis altijd tot beperkingen in activiteiten in CRPSI?´en ´welke stoornis beperkt met name activiteiten van het dagelijks leven in CRPSI?´. Omdat de stoornis-beperking relatie in CRPSI voorheen alleen met vragenlijsten naar beperkingen in activiteiten onderzocht was, was het doel van de tweede klinische studie ***(hoofdstuk 6)*** om de mate van stoornissen en objectief met de ULAM gemeten beperkingen te bepalen bij patiënten met CRPSI in een arm of hand. Centraal stond hierbij de relatie tussen stoornissen en beperkingen in activiteiten. Dertig patiënten met chronische CRPSI in één arm of hand deden vrijwillig mee aan het onderzoek. Meerdere instrumenten werden gebruikt om de volgende stoornissen te meten: een infrarood thermometer om het temperatuur verschil tussen beide handen te meten, een visueel analoge schaal (VAS, 100 mm horizontale lijn) om de pijn intensiteit na inspanning te meten, de McGill Pain Questionnaire welke bestaat uit een aantal sensorische, affectieve en evaluatieve ´pijnwoorden´ om pijn gedurende de laatste paar dagen te meten, een goniometer werd gebruikt om het verschil tussen de pols en vingergewrichten van beide handen voor wat betreft het maximaal actief bewegingsbereik binnen de pijngrens (AROM) te bepalen, een volumeter waarmee de mate van overstroming uit een speciaal gevormde bak met water kan worden vastgesteld werd gebruikt om volumeverschillen tussen beide handen te meten, en tot slot werd een draagbare handkrachtmeter gebruikt om verschillen in knijpkracht tussen de handen te bepalen. De belangrijkste ULAM uitkomstmaten waren wederom de intensiteit, het percentage en de verhouding/proportie van arm-hand activiteit tijdens zitten en staan. Het resultaat van

deze studie was dat bij alle dertig CRPSI patiënten stoornissen aanwezig waren, maar er was grote variabiliteit in de ernst van deze stoornissen. Voor wat betreft de met de ULAM gemeten beperkingen in activiteiten bleek dat de aangedane zijde duidelijk minder actief / meer beperkt was (lagere intensiteit en lager percentage arm-hand activiteit) dan de niet aangedane zijde. Dit was met name te zien was tijdens arm-hand activiteit tijdens zitten en bij de subgroep van vijftien patiënten met CRPSI in de dominante zijde. Analyse van de relatie tussen stoornissen en beperkingen in CRPSI liet zien dat stoornissen in het actief bewegingsbereik en knijpkracht, en in mindere mate pijn na inspanning, het meest verklarend waren voor hoe beperkt iemand was in zijn of haar arm-hand activiteit tijdens het dagelijks leven. Er kon geconcludeerd worden dat, gemiddeld bijna 3 jaar na het ontstaan van CRPSI, bij alle patiënten nog in meer of mindere mate stoornissen aanwezig waren en dat de aangedane zijde nog duidelijk minder actief is (cq gebruikt werd) dan de niet aangedane zijde. De belangrijkste conclusie was dat hoe meer stoornissen een persoon heeft, en dan vooral hoe meer motorische stoornissen, hoe beperkter iemand is in zijn of haar arm-hand activiteit.

De ULAM is relatief nieuw en de meettechniek verschilt duidelijk van wat tot nu toe gebruikt werd in onderzoek en kliniek met betrekking tot methodologische en praktische criteria. Daarom hebben we bepaald hoe de ULAM uitkomstmaten zich verhouden tot vier vragenlijsten welke ook beogen de gevolgen van een ziekte op het dagelijks functioneren te meten ***(hoofdstuk 7)***. Dertig patiënten met CRPSI in een arm of hand werden in een vergelijkingsstudie in hun thuissituatie eenmalig gemeten met de ULAM en vier vragenlijsten werden afgenomen. Dit betrof ten eerste twee generieke vragenlijsten: de ´Sickness Impact Profile´ bestaande uit 68 items op verschillende gebieden van het menselijk functioneren (SIP68) en de uit 36 items bestaande ´RAND 36-item Health Survey` (RAND36). De andere twee vragenlijsten waren zogenaamde lichaamsdeel specifieke vragenlijsten: de ´Disabilities of Arm Shoulder and Hand Questionnaire´ (DASH) en de ´Radboud Skills Questionnaire´ (RASQ). Deze laatste vragenlijsten vragen specifiek naar beperkingen in activiteiten van de bovenste extremiteit. Om de mate van samenhang tussen de verschillende instrumenten te bepalen werden Spearman correlatie coefficiënten uitgerekend. Het bleek dat 87% van de onderlinge correlaties tussen de vragenlijsten significant waren, terwijl 39% van de correlaties tussen de ULAM en de vragenlijsten significant waren. Het aantal en de hoogte van de correlaties tussen de ULAM en de vragenlijsten was afhankelijk van de mate waarin dezelfde aspecten van het functioneren werden gemeten. Dus alle vijf de instrumenten meten tot op zekere hoogte vergelijkbare aspecten van het functioneren, maar het niet ondubbelzinnige patroon van correlaties wijst erop dat de ULAM aanzienlijk anders het functioneren meet dan de vragenlijsten. We concludeerden dat de ULAM een duidelijk een aparte positie heeft wanneer het gaat om de enorme hoeveelheid uitkomstmaten die er zijn om het functioneren te meten. Omdat de ULAM objectief beperkingen kan meten biedt het op een alternatieve maar enorm belangrijke manier inzicht in de invloed die

een aandoening (zoals bijvoorbeeld CRPSI) kan hebben op het functioneren van een persoon.

In de laatste klinische studie werden, in tegenstelling tot eerdere studies bij chronische CRPSI patiënten, metingen verricht bij personen met acute CRPSI. In deze studie werd gekeken naar het verloop van arm-hand activiteit in de tijd bij vier patiënten met acute CRPSI in één arm of hand ***(hoofdstuk 8)***. Hiervoor hebben we het verloop van arm-hand activiteit zoals gemeten met de ULAM vergeleken met het verloop van andere uitkomstmaten voor (beperkingen in) activiteiten en stoornissen. De vier personen werden op vier momenten tijdens een behandelprotocol gemeten. Er werden een aantal (eerder beschreven) ULAM uitkomstmaten voor arm-hand activiteit en mobiliteit-gerelateerde activiteiten gebruikt, evenals 3 vragenlijsten naar activiteiten en functioneren (RASQ, DASH, RAND36) en zes uitkomstmaten voor stoornissen (VAS-pijn na inspanning, VAS-pijn op dit moment, volume, temperatuur, AROM en kracht). De resultaten lieten zien dat de objectief gemeten arm-hand activiteit vaak verbeterde in de loop der tijd; verbeteringen van >5% werden gevonden voor het merendeel (63%) van de ULAM uitkomstmaten bij de laatste (vierde) meting, gemiddeld 3½ maand na het ontstaan van CRPSI. Het verloop in de tijd van de ULAM uitkomstmaten kwam meer overeen met de CRPSI èn lichaamsdeel specifieke vragenlijst RASQ dan met de andere twee vragenlijsten. Het verloop in de tijd van de stoornissen in temperatuur van de aangedane hand kwam het meest overeen met veranderingen in de tijd zoals gemeten met de ULAM in deze patiënten met acute CRPSI. Minder vaak kwamen veranderingen in volume, AROM en kracht overeen met het verloop in de tijd zoals gemeten met de ULAM. De minste overeenkomst met de ULAM vertoonden de beide VAS pijn scores. Samengevat vonden we dus duidelijke veranderingen in de tijd in arm-hand activiteit objectief gemeten met de ULAM. Daarnaast waren de relaties tussen het verloop in de tijd van de ULAM uitkomstmaten en de andere uitkomstmaten voor (beperkingen in) activiteiten en stoornissen verklaarbaar. De conclusie was dat de ULAM in zijn huidige vorm de potentie heeft om op valide wijze het verloop van arm-hand gebruik in de tijd te bepalen bij personen met CRPSI in een arm of hand.

In de algemene discussie ***(hoofdstuk 9)*** werden een aantal onderwerpen uit de verschillende hoofdstukken bij elkaar gebracht en vanuit een algemeen standpunt bediscussieerd. Ook werden een aantal nieuwe onderwerpen geïntroduceerd.

List of publications

Schasfoort FC, Bussmann JBJ, Stam HJ.
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Curriculum Vitae

Fabiënne Schasfoort werd geboren op 4 maart 1974 in Arnhem. De eerste 7 jaren van haar leven heeft ze doorgebracht in Heteren, waarna ze met haar ouders en jongere broer Remco verhuisde naar Hengelo in het oosten van Nederland. Daar heeft ze de basisschool opleiding voortgezet en heeft van 1986 tot 1992 VWO gevolgd op het Twickel College Hengelo. Vervolgens is ze in september 1992 begonnen met de studie Bewegingswetenschappen aan de Rijks Universiteit Groningen (RUG), welke in september 1997 afgerond werd (differentiatie revalidatie en gehandicaptenzorg).

Na een rondreis in zuidelijk Afrika met haar vriend Frank begon Fabiënne in maart 1998 als Assistent in Opleiding (AiO) onder begeleiding van Hans Bussmann en Henk Stam aan een promotieonderzoek bij het Instituut Revalidatiegeneeskunde van (toen nog) de medische faculteit van de Erasmus Universiteit Rotterdam (EUR, inmiddels samen met het voormalig Academisch Ziekenhuis Rotterdam Dijkzigt het Erasmus MC, Universitair Medisch Centrum Rotterdam). De resultaten van dit promotie onderzoek, waarvoor de financiële middelen voornamelijk verzorgd werden door het Algesiologisch Instituut, zijn beschreven in dit proefschrift.

Naast haar werk als AiO, heeft Fabiënne in de periode 1999-2002 een verkorte opleiding fysiotherapie gevolgd en afgerond en heeft ze periode 2000-2003 als docent de verplichte nascholings module ‘Evidence Based Practice’ gegeven aan fysiotherapeuten. Momenteel werkt ze als wetenschappelijk onderzoeker aan de projecten ‘MAPS, Monitoring amputee progress with a sensor socket’ en 'RealProf, Real world intelligent monitoring of prosthesis and footwear´ op de afdeling Revalidatie van Erasmus MC. MAPS en Realprof zijn projecten die gefinancierd worden door de Europese Unie waarin onderzoek gedaan wordt naar de mogelijkheden om ambulant een aantal parameters (activiteiten patroon en ‘heelcontact/toe-off’ uit versnellingssignalen van het aangedane been, druk tussen stomp en prothese, zuurstof saturatie oppervlakkig weefsel stomp) bij patiënten met een onderbeen amputatie te meten.

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Nando Liem en Annemarie Zandbergen hebben met hun stage en afstudeer onderzoeken voor geneeskunde en bewegingswetenschappen zeker een belangrijke bijdrage geleverd aan dit proefschrift en mogen in dit dankwoord dan ook niet

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