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.