Summary
With today’s specialized medical care, life expectancy of people with spinal cord injury (SCI) has considerably improved. However, many people with long-term SCI show a seriously inactive lifestyle, associated with deconditioning and secondary health complications (e.g. cardiovascular disease, osteoporosis and muscle atrophy), resulting in a reduced participation and quality of life. It is important to avoid this downward spiral that threatens persons with long-term SCI. To get more insight in the long-term impact of SCI on fitness, physical activity and secondary health complications, and to examine interventions to improve these facets, the multicenter and multidisciplinary research program ‘Active LifestyLe Rehabilitation Interventions in long-term Spinal Cord injury (ALLRISC)’ was developed. The work described in this thesis is part of ALLRISC and focuses on the lower-body disuse paradigm.

Due to the lower-limb paralysis, exercise in people with long-term SCI predominantly involves activities of the non-paralyzed upper body (e.g. handcycling). However, several physiological factors related to SCI and upper-body exercise alone, including the relatively small active muscle mass, inactivity of the skeletal muscle pump of the legs and insufficient cardiovascular reflex responses, may reduce desired (aerobic) training effects. Moreover, due to the specificity principle, it is likely that upper-body training alone would not notably contribute to the prevention or improvement of several secondary complications in the lower limbs, such as osteoporosis, muscle atrophy and vascular dysfunction.

Functional electrical stimulation (FES) can be used to reactivate the paralyzed lower-limb musculature and consequently reduce some of the above-mentioned problems. During hybrid exercise (e.g. cycling or rowing), FES-induced leg exercise is combined with voluntary arm exercise. The potential greater beneficial effects of hybrid exercise over upper-body exercise alone on fitness, physical activity and health in people with long-term SCI requires further investigation.

Therefore, the main aim of this thesis was to evaluate the integrated effects of hybrid cycling versus handcycling on fitness, physical activity and health related parameters (i.e. cardiovascular disease risk factors, lower-body soft tissue composition, and proximal tibia and distal femur bone mineral density) in physically inactive people with long-term SCI. To achieve this goal, a 16-week multicenter randomized controlled trial (RCT) was conducted. Parallel to this RCT, two cross-sectional studies were performed to (1) examine the metabolic and cardiorespiratory response during hybrid cycling versus
handcycling at equal subjective exercise intensity levels, and (2) assess the reliability of a standardized method to measure proximal tibia and distal femur bone mineral density using dual-energy X-ray absorptiometry (DXA).

In chapter 2, the experimental design of the 16-week multicenter RCT was extensively described. Briefly, in this RCT, physically inactive people with long-term SCI (time since injury ≥ 10 years; age at onset SCI ≥ 18 years, aged 28–65 years, wheelchair-dependent) were eligible for inclusion. Participants were randomly assigned to either the experimental (hybrid cycle) or control (handcycle) group. During 16 weeks, both groups trained twice a week for 18–30 minutes at an intensity of 65–75% of their heart rate reserve and/or a score of 4–7 on a 10-point rating of perceived exertion scale. Training sessions were performed in a rehabilitation center with a specialized SCI unit (Reade Amsterdam or Sint Maartenskliniek Nijmegen) under the supervision of a trainer. The outcome measures were obtained in the week before the training program (T1), after 8 weeks of training (T2), in the week after (T3), and 26 weeks after the training program (T4).

The purpose of the cross-sectional study described in chapter 3 was to compare the metabolic and cardiorespiratory response during hybrid cycling versus handcycling at equal subjective exercise intensity levels in people with SCI. On separate days, nine people with SCI performed 5-minute bouts of hybrid cycling (day 1) and handcycling (day 2) at moderate (level 3 on a 10-point rating of perceived exertion (RPE) scale) and vigorous (RPE level 6) subjective exercise intensity. The results of this study showed that hybrid cycling induced higher metabolic and cardiorespiratory responses at equal RPE levels than handcycling, suggesting that hybrid cycling is more suitable for fighting obesity and increasing cardiorespiratory fitness in people with SCI.

In chapter 4, the effects of the 16-week RCT on fitness and physical activity were examined in 20 individuals with long-term SCI. Fitness was defined as the peak power output and peak oxygen consumption (measured during a peak exercise test in a manual wheelchair), and resting heart rate. Physical activity was defined as the ‘Physical Activity Scale for Individuals with Physical Disabilities (PASIPD)’ score, and the distance travelled in the wheelchair during seven consecutive days. Overall, ~40% and 65% of the participants showed (non-significant) improvements in peak power output and peak oxygen consumption following the 16-week training program, respectively. Furthermore, a significant overall reduction in resting heart rate, and a significant overall increase in
PASIPD score were found after 16 weeks of training. Since for all outcome measures there were no significant differences over time between the two training groups, it was concluded that there were no additional benefits of the FES-induced leg exercise over handcycling alone.

The aim of chapter 5 was to examine the effects of the 16-week multicenter RCT on cardiovascular disease risk factors (i.e. metabolic syndrome components, inflammatory status and visceral adiposity) in 19 individuals with long-term SCI. Following the 16-week training program, significant overall reductions were found for several metabolic syndrome components (i.e. waist circumference, diastolic blood pressure and insulin resistance), inflammatory status, and visceral adiposity. However, for all outcome measures, no significant differences over time between the two training groups were found. In this chapter, it was concluded that both the hybrid cycle and handcycle exercise program led to similar positive effects on the investigated cardiovascular disease risk factors, indicating that there were no additional benefits of the FES-induced leg exercise over handcycle exercise alone.

The purpose of the cross-sectional study described in chapter 6 was to assess the intra- and inter-rater reliability of a standardized protocol for measuring proximal tibia and distal femur bone mineral density using dual-energy X-ray absorptiometry (DXA). Ten able-bodied persons participated in this study. During one measurement session, the knee of each participant was scanned twice by rater 1 using DXA. Both scans were analyzed twice by rater 1 as well as once by a second rater. Intraclass correlation coefficients (ICCs), standard error of measurements (SEMs) and smallest detectable differences (SDDs) were calculated for proximal tibia and distal femur bone mineral density. The results of this study showed high intra- and inter-rater ICCs, and low intra- and inter-rater SEMs and SDDs for both proximal tibia and distal femur bone mineral density, indicating that these outcome measures can be reliably assessed with this method.

In chapter 7, the effects of the 16-week RCT on lower-body soft tissue composition, and proximal tibia and distal femur bone mineral density were investigated in 20 people with long-term SCI. Following the 16-week program, lean mass of the legs was significantly increased in the hybrid cycle group, and significantly decreased in the handcycle group. For fat mass of the legs, there was a significant overall reduction, but there were no significant differences over time between the two training groups. For proximal tibia and distal femur BMD, no significant main effects for time or time ×
group interactions were observed. From these results, it was concluded that the hybrid cycle intervention led to improvements in soft-tissue composition of the legs, but did not improve proximal tibia and distal femur bone mineral density.

In **chapter 8**, the main findings of this thesis were summarized and discussed, and implications for clinical practice and recommendations for future research were provided. The main finding of this thesis was that both the 16-week hybrid cycle and handcycle exercise intervention led to positive effects on different aspects of fitness, physical activity and health. However, except for lean mass of the legs, there were no notable additional benefits of the hybrid cycle intervention over the handcycle intervention. The results of this thesis may provide future implications for exercise prescription that prevent deconditioning and secondary health complications in people with SCI.