Epilogue
Introduction

The overarching aim of this thesis was to enhance our knowledge about some of the factors that influence the ability to regain and maintain walking after unilateral lower limb amputation. While in the previous individual chapters specific aims related to this general aim have been investigated and discussed, this Chapter combines the obtained results and by critically reflecting on these results, determines if, and how, these studies have helped us to better understand the factors associated with prosthetic ambulation. Based on this synthesis, we will formulate recommendations for future research and clinical implications for prosthetic rehabilitation interventions and prosthetic design. To correctly value the conclusions drawn it is important to understand the considerations and implications of the methodology chosen. Hence, this Chapter starts by providing some general considerations regarding the research methods used.
Methodological considerations

In the Chapters 2, 3 and 4 a group of older subjects aged between 50 and 75 participated in all three studies. Using the same group of subjects in all three studies could have biased the results limiting generalizability. Rationale behind choosing older subjects was that these subjects typically experience the greatest difficulty regaining and maintaining walking after undergoing lower limb amputation. In part this is related to the fact that most of the older people are amputated due to vascular deficiency. However, to date surprisingly few experimental studies have been performed that specifically focused on the elderly vascular amputee. Possible reasons for the paucity might be that comorbidity is thought to influence the outcome parameters, moreover, mortality rates one year post-amputation are very high. Also a large group is not fitted with a prosthesis but will ambulate using a wheelchair. To amend the limited knowledge about the specific challenges that these people face, a group of vascular amputees was included in the first three studies described in this thesis. This group is compared to a group of traumatic amputees and able-bodied control subjects in each of the three Chapters. These groups were matched on age because age is known to substantially influence the outcome parameters (e.g. aerobic capacity) of the experiments summarized in this thesis. However, as most of the trauma related amputations are performed on adolescents or young adults, matching subjects on age yielded a significant difference between groups in the time since their first prosthesis; i.e. traumatic amputees had walked with a prosthesis for significantly more years. The time since their first prosthesis may have influenced the measured aerobic load while walking with the prosthesis, with higher physical strain values found in the relatively inexperienced vascular amputees. Unfortunately, longitudinal studies examining the time and process of adaptation to a prosthesis and the influence on biomechanical outcome parameters are scarce. Because the presence of a traumatic amputation and the time since first prosthesis are highly correlated, multicollinearity posed a problem in the regression analysis, rendering statistical adjustments impossible. However, all subjects in the current study were familiar with their prosthesis and able to ambulate for four consecutive minutes on a treadmill, therefore, it was believed that possible differences due to a different time since the first prosthesis were substantially smaller than the difference caused by level or etiology, and subsequently, did not influence the conclusions.

Subjects recruited to participate in the studies were either informed about the study by their physician or prosthetist, or responded to advertisements in a local magazine or on the Internet. As participation was voluntary, there will
have been a selection bias towards the more physically fit, limiting generalization to the overall population. However, the sample bias most likely resulted in an underestimation of the effects found in Chapters 2, 3 and 4. Conclusions drawn in Chapters 5 and 6 were neither influenced by a difference in time since amputation nor by a selection bias because in the repeated measurement approach subjects functioned as their own controls.

Aside from a possible biased sample in Chapters 2, 3 and 4, the number of subjects in each group was unequal. Moreover, the number of subjects with a vascular trans-femoral amputation was relatively low. This might have precluded detecting differences present among groups. In this regard it is important to mention that the differences found among groups for the different outcome parameters were large and indeed clinically relevant, while other outcome parameter that were borderline significant (e.g. the level of amputation) were substantially smaller and it is questionable whether these latter differences have clinical relevance.

**Walking ability explained?**

Whilst taking into account the methodological considerations, the question to answer in this thesis was how relative aerobic load affected subjects’ walking ability in terms of walking speed and walking economy. From the experiments conducted in Chapter 4 one can derive that having sufficient aerobic capacity could be a prerequisite in order to regain walking at a certain speed. For example, vascular amputees are unable to walk at a walking speed similar to that of the able-bodied controls as this would require an aerobic effort that is beyond the aerobic capacity as measured during the cycling exercise test. Reducing walking speed is a method to ensure that the effort while walking (expressed as the relative aerobic load) does not surpass a predefined acceptable limit \[^{71, 139}\]. In addition to being a prerequisite that enables walking at a certain speed it might be speculated that the relative aerobic load is an important factor governing the choice of walking speed. This speculation is based on the fact that subjects lower their walking speed even though it negatively affects walking economy (i.e. the slower walking speed requires more oxygen per distance walked) and prevents them from keeping up with able-bodied peers. Moreover, traumatic amputees reduced their walking speed to such an extent that it matches the relative aerobic load of the able-bodied controls. These results are interesting, as apparently the generally considered notion that walking speed is governed by walking economy \[^{28, 141}\] is refuted for older people who walk with a lower limb prosthesis. However, these conclusions ought to be interpreted with care, as the association found between the relative aerobic load and the reduction in walking speed does not
necessary imply causality. More importantly, relative aerobic load might be only one of the total sum of factors defining subjects’ walking ability.

This study used a biophysical approach to understand the underlying mechanisms influencing subjects’ walking ability. This approach is mechanistic in origin and excludes any cognitive or psychosocial factors, and therefore, cannot fully explain subjects’ walking ability. Retrospective research provides strong evidence that the level and cause of amputation, cognition, functional level prior to amputation, and age are important predictive factors. While moderate evidence exists for the presence of stump and/or phantom pain, motivation, co-morbidity, smoking and social support as predictive factors for subjects’ ability to regain walking ability [80, 99, 137, 165, 172, 184, 188, 214, 216]. Though these factors might in different proportions predict subjects walking ability, the reason for their association with walking ability is not determined. On the other hand we know from the studies presented in this thesis that relative aerobic load is a prerequisite for regaining and maintaining walking ability.

To recapitulate, subjects’ walking ability is, amongst other factors, associated with the relative aerobic load. The higher the relative aerobic load while walking the smaller the spectrum of functional walking speeds at which an individual with an amputation can comfortably walk. Moreover, understanding the (relative) aerobic load provides relevant information about the importance of adequate aerobic capacity, and therefore, provides evidence that prosthetic rehabilitation ought to also focus on improving aerobic capacity. However, to determine causality future studies should focus on the prospective association between the relative aerobic load, aerobic capacity and subjects’ walking ability.

**Discovering aerobic capacity**

Improvement of the relative aerobic load during walking in persons with a lower limb amputation can be accomplished by either reducing the absolute aerobic load or by increasing the aerobic capacity. To do so, requires fundamental knowledge about both the causes for the increased aerobic load (Chapters 5 and 6) and the peak aerobic capacity of the people walking with a prosthesis (Chapters 2 and 3). To obtain fundamental knowledge about the peak aerobic capacity a discontinuous, graded, one-legged, peak exercise test was developed. This exercise test proved to be both feasible and valid when testing older adults with either a traumatic or vascular amputation. Because it targets the lower limb muscles, it provides important information about the aerobic capacity while walking. However, it can be postulated that when subjects are to a large extent wheelchair bound and physical activity primarily involves the upper extremities,
an exercise test which uses both the arm and legs is a more functional evaluation \cite{12, 76}. However, electrocardiogram disturbances and coordination difficulties might hamper the safety and feasibility of a combined arm-leg exercise test. Which test is most appropriate is dependent on the purpose of the test, the ability of the subject to perform the test and the available equipment.

As noted in Chapter 3, remarkably little information about the exercise capacity of amputees was known. Chapter 3 provides evidence for the intuitive notion that the peak aerobic capacity is substantially reduced in people with a lower limb amputation. In older subjects the reduced muscle mass \cite{72} and mitochondrial capacity, result in a reduced muscle oxidative capacity \cite{71} and concomitantly, a reduced peak aerobic capacity \cite{73}. This reduction due to age is aggravated when combined with limited physical activity \cite{200}. In healthy elderly a reduced peak aerobic capacity limits walking ability \cite{71}, but in older people with an amputation this natural decline in peak aerobic capacity is superimposed on the already present capacity limitation due to behavioral characteristics (i.e. food intake, sedentary lifestyle or smoking) and preexisting medical conditions \cite{137}. Consequently, efforts to improve the aerobic capacity during rehabilitation must indeed be encouraged.

**Improving aerobic capacity**

It might be speculated that due to the deconditioned status of the older subjects, small improvements in the aerobic capacity might result in large effects on the functional performance and walking ability. In Chapter 4 a data-driven theoretical model was developed which helped to gain some insight into the magnitude of the potential effects that can be reached when aerobic capacity is theoretically improved. Based on this model it was predicted that an increase of 10% in peak aerobic capacity in the older vascular amputee resulted in a 9.1% reduction in walking effort, a 17.3% higher walking speed and an improvement in walking economy of 6.8%. These improvements are statistically significant and most likely lead to clinically relevant improvements in subjects’ walking ability. Moreover, these effects are larger than the effect reached by a reduction in aerobic load through the use of currently commercially available state-of-the-art prosthetic devices.

Though the above clearly demonstrates the importance of an optimal aerobic capacity, several guidelines either do not mention aerobic training as a rehabilitation intervention \cite{14-15}, or fail to provide specific guidelines for aerobic training \cite{157, 205}. Fortunately, some awareness of the importance of physical
capacity exists as more than 80% of users and professionals in the field of prosthetics rate this aspect as an important predictor of prosthetic use. Despite the awareness, strikingly few longitudinal studies have been performed that investigate the effect of aerobic training on subjects’ peak aerobic capacity and walking ability \(^{30,216}\). Those studies that have been performed involve traumatic amputees and report increases varying between 27.2% and 41.2% \(^{22-23,170}\). Some evidence for the trainability of older vascular amputees might be based on studies in older patients diagnosed with symptomatic peripheral arterial disease. These studies have shown that aerobic exercise training, either through walking or arm- or leg cycling, resulted in an increase in walking distance through improvements in peripheral circulation, walking economy and peak aerobic capacity \(^{4,245}\). These results, together with the knowledge that aerobic exercise is beneficial in older adults with a wide range of pathologies \(^{142}\), vindicates the notion that also in the vascular amputees improvements in peak aerobic capacity are possible. Future training studies specifically focusing on this growing group of patients are highly needed.

One might pose the question whether aerobic training is also beneficial for the traumatic amputee with no comorbidity. For people recently amputated due to trauma, the post-operative period of inactivity leaves them prone to a reduced peak aerobic capacity, and therefore, they are likely to benefit from aerobic training to ease prosthetic ambulation. Clearly, aerobic exercise training must not to be restricted to those recently amputated. Based on the results presented in Chapter 4, and the prediction equation presented therein, we know that although the relative aerobic load (i.e. the walking effort) is the same in the traumatic and able-bodied control subjects, traumatic amputees walk slower and below their theoretically most economical walking speed. Consequently, these people would benefit from having a peak aerobic capacity above that of healthy able-bodied controls as this will allow them to adopt a faster and more economical walking speed while maintaining to walk at the same relative aerobic load.

To conclude, the reduced peak aerobic capacity and the high relative aerobic load together with the substantial improvement in walking ability that can potentially be attained by small improvements in peak aerobic capacity, underscores the importance of aerobic exercise training as an integrated part of prosthetic rehabilitation in the vascular amputees. Positive, though more moderate, effects are also expected for the traumatic population. The current lack of knowledge about effective training regimes and the concurrent effect on walking ability is at least remarkable, and the need for future longitudinal studies targeted to improve subjects’ peak aerobic capacity are needed.
Factors influencing the aerobic load

In the final two Chapters the effect of different prosthetic designs on the mechanical cost while walking (Chapter 5) and the effect of different balance control strategies on the overall metabolic energy cost (Chapter 6) were investigated. In the following paragraphs the implications of these findings for overall walking ability in amputees are reviewed.

The prosthesis

Based on the results from Chapter 5 it is made evident that the energy storage and return (ESAR) foot reduces the mechanical energy cost necessary for the step-to-step transition. Unraveling of the causes for this reduction revealed that the improved push-off power and longer roll-over arc length of the ESAR prosthesis positively contributed to this reduction. A reduction in the step-to-step transition cost is assumed to be associated with a reduction in the overall metabolic cost required for walking \([55, 110, 192]\). Remarkably however, no convincing evidence is present in the literature supporting the notion that the metabolic energy cost is lower when walking with the ESAR foot \([88, 104, 212, 219]\). This discrepancy might be a result of the simplifications on which the dynamic walking approach is based. Apparently, the model overlooks important metabolic costly compensational strategies to deal with the demands imposed when walking with the ESAR prosthesis \([131, 148, 215]\). The dynamic walking model proved to be able to differentiate between different prosthetic feet and provides helpful and useful information about the center of mass work. However, it fails to fully explain the metabolic cost associated with prosthetic gait as improvements in step-to-step transition cost do not directly translate to corresponding reductions in the metabolic energy cost \([98, 192]\).

Balance control

The challenge we are facing is to decipher which other factors may contribute to the overall metabolic energy cost. One possible candidate is the energy required for balance control. From Chapter 6 it can be deduced that conscious placement of the feet in a designated position has a distinct metabolic energy cost. This is the case even if the position of the feet and the associated mechanical constraints are no different than walking unconstrained. The question that arises is how this translates to the metabolic energy cost associated with balance control in people walking with a prosthesis. The mechanical restrictions and the loss
in motor control at the ankle precludes the use of the normally applied ankle strategy \[^{102}\]. Moreover, people with a lower limb amputation have lost part of their somato-sensory system and, therefore, need to revert to other, possibly more costly control strategies to ensure adequate stability. Possible examples of these strategies are: placement of the prosthetic foot well within the margins that ensure stability \[^{102}\], an increased activation of the contra-lateral intact ankle and hip, a wider stride and/or a slower walking speed \[^{50}\]. Finally, it might be postulated that due to the lack of feedback provided by the somato-sensory system subjects more tightly control their gait in order to ensure a feeling of safety and to eventually prevent a fall despite a possible metabolic penalty \[^{233}\].

In Chapter 6 the conscious control of walking is manipulated by turning a largely automatic task like walking into a task which requires constant cognitive guidance. For people with an amputation, and especially the older people \[^{96}\], maintaining balance might already consume substantial cognitive resources. By redirecting part of these resources away from the walking task alteration in the gait pattern \[^{86}\] and dynamic stability \[^{49}\] are expected to occur. Some support for this hypothesis is provided in this patient group while studying standing balance. For example, Geurts and colleagues (1991) \[^{82}\] concluded that at the start of rehabilitation, standing balance control requires substantial central information processing and during rehabilitation a central reorganization process takes place resulting in a restoration of the automaticity of balance control. In a similar experiment this conclusion was substantiated as dynamic measures of regularity (which are said to be indicative for the amount of automaticity of a task) decreased during rehabilitation \[^{178}\]. Interestingly, Hof and colleagues demonstrated that in the small group of relatively young amputees performing a concurrent secondary task while walking did not affect spatio-temporal gait parameters \[^{102}\]. However, unraveling the complex balance control system while walking might entail that analysis ought to surpass purely spatio-temporal signal analysis. It has been advocated that more dynamic measures ought to be applied to gain additional information about the inherent stochastic structure of the dynamic control of the human movement system \[^{58, 134}\]. Previous studies in a small group of traumatic amputees revealed that amputees indeed responded differently to a perturbation than healthy controls on these dynamic measures \[^{134}\]. Combining dynamic measures with measured of metabolic energy consumption while balance control is perturbed using a concurrent secondary task might provide valuable information about the metabolic cost related to balance control. Possible effects might be ameliorated when the secondary task involves a visual task which interferes with foot vision \[^{10-11}\]. These speculations might form the basis of interesting fundamental scientific studies. Additionally, dual task research more closely mimics the daily life situation during which subjects are also continuously confronted with concurrent tasks that direct attention away from the primary walking task \[^{82, 238}\].
To sum, the latter two studies described in this thesis provide evidence that the aerobic load while walking with a prosthesis originates, in part, from the inefficient and inadequate push-off power resulting in an increased step-to-step transition cost and from possible alterations in the balance control strategy applied. While improvements in subjects’ walking ability can be attained using state-of-the-art prostheses, improving subjects’ walking ability to that of healthy controls involves more than developing a prosthetic ankle and knee that provides appropriate propulsion. Amongst other prerequisites, inefficient balance control strategy, especially in challenging situations, can ameliorate any positive effect of an improved propulsion power.

The prosthesis of the future

To date, technical developments in the prosthetic design have resulted in a wide range of different prosthetic feet aside from the relatively simple energy storage and return prosthesis often prescribed and studied in this thesis. The majority of these newly developed prosthetic ankle and knee components aim to reduce the aerobic load while walking. Unfortunately, the prosthetic devices commercially available often show only marginal improvements in the required metabolic energy expenditure while walking. For example, literature investigating the effects of a micro-processor knee (C-leg®) on walking economy in people with a trans-femoral amputation varies between no differences \cite{20} to a reduction in energy expenditure of 6-7\% depending on the speed walked at \cite{100, 187, 195}. Greater reductions in aerobic load might be expected from the so-called 'bionic' prostheses, which are powered systems who emulate the function of the biological ankle \cite{98, 219}. To date, these devices are still being developed; however, studies are promising as reductions between 8\% and 14\% in the cost of walking have been found compared to conventional prostheses \cite{6, 98}. Sophisticated and exciting new developments are currently happening involving prostheses developed for upper extremities. For example, upper arm prostheses have been developed that provide somato-sensory feedback which result in a reduction in phantom limb pain and an increase in functionality \cite{45}. Another new and exciting advancement in the field of upper arm prosthetic rehabilitation, is targeted re-innervation of residual nerves that aims to amplify the information still present in the nerves and use this information to control the prosthetics \cite{127}, which might improve subjects balance control. There is hope that in the future these technologies can also be applied to lower limb amputees \cite{2}. Merging these new technologies with the knowledge gathered from the current thesis and previously performed research, might provide fruitful soil for significant improvements in prosthetic design that can result in an improvement in the functioning and quality of life of people with a lower limb amputation.
Future research directions

Prosthetic development and rehabilitation is an exciting research area which has become increasingly important due to the unfortunate growing numbers of people currently with a lower limb amputation. This thesis provides a starting point for a number of additional scientific studies that can contribute to the overarching aim to improve our knowledge of prosthetic gait.

Using a longitudinal research design the proposed beneficial effects, as predicted in Chapter 4, on relative aerobic load and walking ability after aerobic training could (and should) be experimentally evaluated. Moreover, using this research design information about the effectiveness of specific training regimes can be investigated. Both from a scientific and clinical perspective it is interesting to investigate whether, aside from people currently undergoing rehabilitation, people who have finished clinical rehabilitation also experience beneficial results of aerobic training in terms of walking ability, functioning and quality of life.

Despite many years of research and an abundant number of articles published on the topic we still cannot fully explain the origin of the increased metabolic energy requirement when walking with a prosthesis. Applicability of relatively simple models like the dynamic walking model can provide valuable and interpretable information about the mechanical energy requirement when walking with the newly developed state-of-the-art prostheses. Moreover, future studies might determine whether these models can provide a useful tool to guide prosthetic prescription. However, quite possibly the greatest challenge we face is to disentangle the underlying mechanisms which cause the metabolic costly compensational strategies seen when walking with a prosthesis. To do so, implies altering the line of thought from a prosthetic oriented perspective to a more human orientated research perspective. More specifically, if we want subjects to restore their daily functioning without additional metabolic energy cost, a prosthesis needs to be developed that facilitates balance control and provides adequate adaptability to cope with the continuous changing environment in which subjects ambulate. To enable this we need to understand the importance of balance control to the overall metabolic energy cost. Investigations in which the attention, normally directed towards ensuring balance control, is diverted away from the walking task might provide helpful insights into the effect of conscious control on the walking ability and overall metabolic energy cost. Besides information about the underlying mechanisms and the implications on metabolic energy cost, future research ought to focus on how balance can best be improved in people with a lower limb amputation.
Implications for rehabilitation

Based on the results from this thesis it is made eminent that in order to walk subjects need to have sufficient aerobic exercise capacity. This is most pronounced in those patients whom are deconditioned due to a long period of inactivity, comorbidity and/or a sedentary lifestyle. Therefore, rehabilitation ought to include some form of aerobic training aimed to improve the peak aerobic capacity in these patients.

Due to the paucity of longitudinal studies conducted to date, limited information is available on the efficacy of general rehabilitation programs in this specific patient population. A recent study into the relative effort experienced by stroke, spinal cord injured and amputee subjects during rehabilitation revealed marked differences in aerobic strain between subjects [125]. This underscores the importance of tailor made exercise programs. To ensure continued successful prosthetic ambulation also after rehabilitation it is important to educate subjects on the importance of increasing and maintaining a good level of physical activity [213]. Moreover, in subjects with a lower limb amputation quality of life is to a high degree related to social acceptability [239]. Therefore, the likelihood of regaining and maintaining a physical active life style is largest when physical activity is implemented within a social supportive network [42].

In addition to improving the physical capacity, health care professionals ought to realize that balance control can influence subjects’ walking ability [188]. This study provides some evidence that an improved balance control might potentially reduce the metabolic energy cost while walking. Some weak evidence exists that balance training can be moderately effective in improving the balance of older subjects [112, 243]. With regards to the amputee population positive effects have been found in balance performance during mirror feedback training [101]. To conclude, balance control might be trained using real-life situations during which (like in daily life) conscious control is directed away from the walking task. Another approach is by providing biofeedback through, for example, a mirror or computer screen.


References


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References


Introduction

Undergoing a lower limb amputation is a life-changing surgery. Unfortunately, a substantial number of people undergo amputation of part of the lower limb. Due to the aging population and a rising number of people diagnosed with diabetic mellitus or peripheral vascular disease this number is expected to grow in the coming years. The ability to walk greatly influences subject’s functional independence and quality of life. Not surprisingly, regaining walking ability is one of the primary goals during prosthetic rehabilitation. Within the group of lower limb amputees it is the older person amputated due to vascular deficiency that often experiences the largest difficulties regaining and maintaining walking. In this thesis some of the underlying mechanisms causing these difficulties are investigated using a biophysical approach in which walking is regarded to require an adequate balance between aerobic capacity and aerobic load. The aim of this thesis was to gain insight into the aerobic capacity that subjects possess and relate this to the aerobic load imposed when walking. Additionally, insight is obtained about some of the underlying factors causing the increased aerobic load when walking with a prosthesis.
In Chapter 2 a method to measure peak aerobic capacity in people with a lower limb amputation is described. The peak aerobic capacity is defined as the highest peak oxygen consumption obtained during maximal exercise. In order to measure peak aerobic capacity in a safe and valid manner in people after lower limb amputation requires special consideration of the exercise mode and protocol used. In this Chapter the feasibility and validity of a discontinuous, graded, one-legged, peak exercise test was determined. In total 36 older amputees and 21 healthy controls performed the one-legged exercise test. The healthy controls performed an additional two-legged exercise test. All participants were able to complete the test and blood pressure and electrocardiogram tracings could be adequately monitored to allow for a safe assessment. The exercise test proved to stress the cardio-vascular system to a sufficient extent in both the amputee and control group. With regard to validity it was determined that the one-legged exercise test had both a high construct and a high concurrent validity. To sum, the results of the research presented in Chapter 2 show that the one-legged exercise test provides a feasible and valid assessment of the peak aerobic capacity in older people with a lower limb amputation.

The one-legged exercise test was used in Chapter 3 to determine the magnitude of the peak aerobic capacity and how this was related to the presence, level and cause of the amputation in people with a lower limb amputation. People with an amputation had a 13.1% lower peak aerobic capacity. Differentiation between etiologies revealed that traumatic amputees did not differ to controls, whereas the vascular amputees had a 29.1% lower peak aerobic capacity. Interestingly, no association between peak aerobic capacity and the level of amputation was found. The results corroborated the limited existing evidence and the intuitive notion that the peak aerobic capacity is reduced in people with a vascular amputation.

The lower peak aerobic capacity combined with the increased aerobic load while walking with a prosthesis can result in a high relative aerobic load. In Chapter 4 the relative aerobic load was investigated and the associated effects of level and cause of amputation were determined in the same group of subjects as investigated in Chapter 3. Based on the results, it was concluded that when walking at their preferred walking speed, older vascular amputees walked at a 44.6% higher relative aerobic load than healthy controls. Traumatic amputees compensated for the increased aerobic load by reducing their preferred walking speed to such an extent that the relative aerobic load equaled that of able-bodied controls. They did this even though this entailed walking at a lower walking economy. A data-based model was constructed to determine the potential effect of an increased aerobic capacity on subjects’ walking ability in terms of relative aerobic load, walking speed and walking economy. This model denotes that, for example, in vascular amputees a relatively modest increase in peak aerobic
Summary

capacity of 10% can result in 9.1% reduction in relative aerobic load, a 17.3% improvement in walking speed and a 6.8% improvement in walking economy. These results denote that aerobic training must indeed be considered an essential component of prosthetic rehabilitation.

Whereas in Chapters 2, 3 and 4 the focus was on determining the peak aerobic capacity and the associated relative aerobic load, in Chapters 5 and 6 information is obtained about potential factors causing the increased aerobic load while walking with a prosthesis. In Chapter 5 the mechanical energy cost while walking was investigated using a dynamic walking model. A total of 15 subjects walked both with an energy storage and return (ESAR) prosthetic foot and a solid ankle cushioned heel (SACH) prosthetic foot. Both prosthetic feet were compared with regard to the required step-to-step transition cost while walking. The ESAR foot required the least mechanical work during the step-to-step transition. This was explained by an increased push-off power and a larger forward progression of the center of pressure during single stance in the ESAR foot. Interestingly, previous studies comparing these two prosthetic feet found no convincing evidence that the ESAR feet also required less metabolic cost while walking. To sum, though the ESAR foot is able to reduce the step-to-step transition cost other factors outside those related to step-to-step transition cost influence the overall metabolic energy cost while walking with a prosthesis.

One of the possible factors influencing the overall metabolic energy cost while walking might be an altered balance control. Differentiating between the mechanical energy required for the walking movement and that associated with balance control is a challenge. In Chapter 6 we tried to do this by having nine able-bodied healthy controls walk at an instrumented treadmill while following a projected step pattern composed of either their averaged step pattern (periodic trial), or a step pattern that was an exact copy, including variability of their unconstrained walking trial (variable trial). The novelty of this approach is that we were able to investigate whether balance control strategies can contribute significantly to the overall metabolic energy cost, independent from alteration in the global gait characteristics. Results showed that walking an enforced gait pattern resulted in a metabolic oxygen increase of 8% in the periodic and 13% in the variable trial. It was postulated that the increased metabolic energy cost is related to increased preparatory muscle activation and a more active ankle strategy to control for lateral balance. This Chapter shows that metabolic energy cost can be associated with alterations in balance control strategies that do not alter global gait characteristics.
Conclusion

The overarching aim of this thesis was to enhance our understanding of some of the factors that influence the ability to regain and maintain walking after unilateral lower limb amputation. Based on the results presented in this thesis we can deduce that the peak aerobic capacity plays an important role in subjects’ walking ability. This peak aerobic capacity is reduced in vascular amputees, which makes walking a strenuous activity for these patients. The work presented in this thesis shows that relatively small improvements in peak aerobic capacity could potentially lead to significant and clinically relevant improvements in subject's walking ability. Furthermore, this thesis showed that the development of prosthetic feet with adequate and correctly timed push-off power together with an optimal roll-over shape can decrease the step-to-step transition cost. However, the energy required for balance control seems an important factor contributing to the overall metabolic energy cost while walking.

Implication for rehabilitation

In this thesis we postulate that future research ought to involve longitudinal studies with a heterogeneous group of amputees in order to investigate the efficacy of different training protocols and to determine what effect an increased peak aerobic capacity has on subject’s walking ability. Additionally, simple dynamic models can be used to gain helpful insight into the mechanical work on the center of mass while walking on different state-of-the-art prosthesis. Though insightful, future studies must be designed that face the challenge of disentangling the metabolic energy cost associated with the mechanical work needed to perform the walking movement and that associated with preserving balance. Information about these underlying causes for the increased metabolic energy cost while walking with a prosthesis will help and aid the development of more efficient and functional prostheses. Moreover, health care professionals must realize that both aerobic and balance training can substantially improve subjects' walking ability, and therefore, ought to be an integrated part of prosthetic rehabilitation.
Optimale loopvaardigheid met een prothese
Balanceren tussen capaciteit en belasting

Samenvatting
**Introductie**

Het ondergaan van een beenamputatie is een drastische chirurgische ingreep, die grote gevolgen heeft voor het functioneren. Jaarlijks ondergaan een aanzienlijk aantal mensen een amputatie van een deel van het been. Naast trauma, is vasculaire deficiëntie, vaak als gevolg van diabetes, de belangrijkste reden voor een beenamputatie. Omdat de levensverwachting in Nederland stijgt, en met veroudering de kans op diabetes en dus vasculaire deficiëntie toeneemt, zal het aantal mensen met een beenamputatie naar verwachting de komende jaren verder stijgen.

Mensen, die na een amputatie in staat zijn om te lopen met een prothese, zijn functioneel onafhankelijker, en hebben een hogere kwaliteit van leven dan mensen die in een rolstoel belanden. Het is daarom niet verrassend dat het herwinnen van de loopvaardigheid één van de voornaamste doelen is tijdens de revalidatie na een beenamputatie.

Het zijn de oudere mensen die een amputatie hebben ondergaan als gevolg van vasculaire deficiëntie, die de meeste problemen ondervinden in het herwinnen, dan wel handhaven van de loopvaardigheid. In dit proefschrift is vanuit een biofysische benadering een aantal van de mogelijke onderliggende oorzakelijke mechanismen voor de problemen bij deze categorie mensen onderzocht. In de gehanteerde biofysische benadering wordt er vanuit gegaan dat een goede loopvaardigheid een adequate balans vereist tussen de aerobe capaciteit en de aerobe belasting. Het doel van dit proefschrift was om inzicht te verkrijgen in de aerobe capaciteit van mensen die lopen met een beenprothese, en om deze aerobe capaciteit vervolgens te relateren aan de aerobe belasting die het lopen met een prothese vergt. Daarnaast geeft dit proefschrift inzicht in de onderliggende mechanismen die verantwoordelijk zijn voor de verhoogde aerobe belasting tijdens het lopen met een beenprothese. In de hierop volgende paragrafen wordt een samenvatting gegeven van de verschillende studies die in het kader van dit proefschrift zijn uitgevoerd. De samenvatting eindigt met een aantal concrete aanbevelingen voor de revalidatiepraktijk.
Samenvatting

In hoofdstuk 2 van dit proefschrift wordt een methode beschreven waarmee de piek aerobe capaciteit van mensen met een beenamputatie bepaald kan worden. De piek aerobe capaciteit is gedefinieerd als de maximale hoeveelheid zuurstof die verbruikt wordt tijdens een maximale inspanning. Het op een veilige en valide manier meten van de piek aerobe capaciteit bij mensen met een beenamputatie vergt een weloverwogen keuze wat betreft de te gebruiken inspanningstest. In hoofdstuk 2 wordt de uitvoerbaarheid en de validiteit van een discontinue, gradeerde, éénbenige, piek-inspanningstest beschreven. In totaal hebben 36 personen, allen tussen de 50 en 75 jaar, die een beenamputatie hebben ondergaan en 21 gezonde personen, die de controlegroep vormden, de éénbenige piek-inspanningstest uitgevoerd. Alle deelnemers waren in staat de éénbenige piek-inspanningstest te volbrengen. Zowel de bloeddruk als het elektrocardiogram kon accuraat worden afgenomen tijdens de test. De inspanningstest bleek zowel in de amputatie- als in de controlegroep het cardiovasculaire systeem in voldoende mate te activeren. Daarnaast was zowel de construct en concurrent validiteit hoog bij de éénbenige inspanningstest. De conclusie van het onderzoek, beschreven in hoofdstuk 2, is dan ook dat de éénbenige fietstest een uitvoerbare en valide methode is om de piek-aerobe capaciteit te bepalen van oudere mensen die een beenamputatie hebben ondergaan.

De éénbenige inspanningstest, zoals beschreven in hoofdstuk 2, is in hoofdstuk 3 toegepast om te bepalen of de piek aerobe capaciteit gerelateerd is aan het wel of niet hebben ondergaan van een amputatie, de hoogte van de amputatie of de oorzaak van de amputatie. Dezelfde mensen, beschreven in de vorige paragraaf, participeerde ook in dit onderzoek. Uit de resultaten blijkt dat de proefpersonen die een beenamputatie hebben ondergaan, gemiddeld een 13,1% lagere piek aerobe capaciteit hadden dan de controlegroep zonder beenamputatie. Wanneer onderscheid gemaakt werd naar de oorzaak van de amputatie, bleek dat de proefpersonen die een amputatie hebben ondergaan als gevolg van vasculaire deficiëntie, gemiddeld een 29,1% lagere piek aerobe capaciteit hadden dan de proefpersonen die vanwege een trauma een amputatie hebben ondergaan. De piek aerobe capaciteit van de door trauma geamputeerde groep verschilde niet met die van de controlegroep. Interessant is dat er geen relatie is gevonden tussen piek aerobe capaciteit en de hoogte van de amputatie. De resultaten van deze studie onderschrijven de beperkte bestaande bewijslast dat de piek aerobe capaciteit van personen met een amputatie door vasculaire deficiëntie lager is dan die van personen zonder beenamputatie.

Een lagere piek aerobe capaciteit, gecombineerd met de verhoogde aerobe belasting tijdens het lopen met een beenprothese, kan resulteren in een dermate verhoogde relatieve aerobe belasting dat de loopvaardigheid wordt beïnvloed. De relatieve aerobe belasting wordt bepaald door de aerobe belasting te delen door de aerobe capaciteit. In hoofdstuk 4 is de relatieve aerobe belasting
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tijdens het lopen met een beenprothese bepaald. Vervolgens is er gekeken of de relatieve aerobe belasting gerelateerd is aan de hoogte, dan wel de oorzaak van de amputatie. De resultaten laten zien dat wanneer personen die een amputatie hebben ondergaan door vasculaire deficiëntie op hun voorkeurssnelheid lopen, zij een relatieve aerobe belasting hebben welke gemiddeld 44,6% hoger is dan die van personen zonder een beenprothese. De personen met een aan trauma gerelateerde amputatie compenseerden voor de verhoogde aerobe belasting door hun loopsnelheid zodanig te verlagen dat de relatieve aerobe belasting gelijk werd aan die van de controlegroep. Dit deden ze ondanks dat de lagere loopsnelheid resulteerde in een lagere economie van het lopen.

Om te bepalen wat het mogelijke effect zou kunnen zijn van een verhoogde aerobe capaciteit op de loopvaardigheid in termen van relatieve aerobe belasting, loopsnelheid en economie van het lopen, is in hoofdstuk 4 een op data gebaseerd model beschreven. Dit model laat zien dat bij personen met een amputatie als gevolg van vasculaire deficiëntie, een relatief geringe verhoging van de piek aerobe capaciteit met 10% kan leiden tot een reductie in de relatieve belasting van 9,1%, een verhoging van de loopsnelheid met 17,3% en een verbetering in de economie van het lopen van 6,8%. Deze resultaten laten zien dat bij personen met een amputatie door vasculaire deficiëntie, aerobe training een essentieel onderdeel zou moeten zijn van het revalidatietraject als het gaat om het herwinnen van de loopvaardigheid.

Waar in hoofdstuk 2,3 en 4 de focus van het onderzoek lag op de piek aerobe capaciteit en de daaraan gerelateerde relatieve aerobe belasting, zijn in hoofdstuk 5 en 6 de mogelijke factoren onderzocht die bijdragen aan de verhoogde aerobe belasting tijdens het lopen met een beenprothese. In hoofdstuk 5 worden de mechanische kosten van het lopen met een beenprothese onderzocht door gebruik te maken van een dynamisch loopmodel. In totaal liepen 15 mensen met zowel een prothesevoet die energie kan opslaan en weer kan teruggeven (Energy Storage and Return; ESAR), als ook met een conventionele prothesevoet (Solid Ankle Cushioned Heel; SACH). Met behulp van het model kan de mechanische kosten die nodig zijn tijdens de dubbel support fase (de stap-naar-stap transitiekosten) worden berekend. Uit hoofdstuk 5 blijkt dat er met de ESAR-voet minder mechanische arbeid nodig is voor de stap-naar-stap transitie dan met de SACH-voet. Dit wordt verklaard door het feit dat er met de ESAR meer afzetkracht gegenereerd kan worden, en omdat er een meer optimale afwikkeling plaatsvindt. Desondanks biedt eerder onderzoek onvoldoende bewijs dat de ESAR voet ook daadwerkelijk de aerobe belasting tijdens het lopen reduceert ten opzichte van de conventionele SACH voet. Resumerend kan worden gesteld dat ondanks dat de ESAR-prothesevoet in staat is de mechanische arbeid van de stap-naar-stap transitie te reduceren, er andere factoren zijn die de aerobe belasting tijdens het lopen met de prothesevoet beïnvloeden.
Eén andere mogelijke factor, die het aerobe belasting tijdens het lopen met een beenprothese kan beïnvloeden, is de energie die nodig is voor de balanscontrole. Door een gebrek aan proprioceptieve informatie tijdens het lopen met een beenprothese, zijn mensen aangewezen op andere wellicht minder efficiënte mechanismen om de stabiliteit tijdens het lopen te waarborgen. Tot op heden is het lastig om te gebleken dat de mechanische energie die nodig is voor loopbeweging te onderscheiden van de energie die nodig is om de balans te handhaven. In hoofdstuk 6 is getracht om inzicht te krijgen in het metabole energieverbruik voor balanscontrole door negen gezonde personen (27.6 jaar [SD = 9.9]) te laten lopen op een loopband waarbij ze een geprojecteerd looppatroon moesten volgen. Normaliter wordt een balansverstoring in de ene stap opgevangen door een corrigerende voetplaatsing tijdens de volgende stap. Maar wanneer de voetoestand wordt opgelegd worden mensen gedwongen om alternatieve, en wellicht minder efficiënte, balanscorrecties uit te voeren (bv. door activering van enkel musculatuur). Het geprojecteerde looppatroon welke de deelnemers moesten volgen, representeerde een gemiddelde van het eigen looppatroon (regelmatige conditie), of het was een exacte kopie was hun eigen looppatroon, dus inclusief de inherente variatie normaal aanwezig tijdens het lopen (variabele conditie). Door deze onderzoeksopzet was het mogelijk om te bepalen of een verandering in de balanscontrole leidt tot een significante verandering in het totale metabole energieverbruik, onafhankelijk van veranderingen in het globale looppatroon. De resultaten van het onderzoek laten zien dat tijdens het lopen op een geprojecteerd looppatroon het metabole energieverbruik met 8% en 13% toenam, in respectievelijk de regelmatige en de variabele conditie, vergeleken met het lopen zonder een opgelegd looppatroon. Mogelijke oorzaken voor dit verhoogde metabole energieverbruik zouden een verhoogde voorbereidende spieractiviteit, en een grotere bijdrage van de spieren rond het enkelgewricht voor het handhaven van vooral de laterale stabiliteit kunnen zijn. Hoofdstuk 6 laat zien dat een verhoging van het metabole energieverbruik tijdens het lopen met een beenprothese mogelijk veroorzaakt wordt door veranderingen in de balanscontrole, zonder dat dit direct invloed heeft op het globale looppatroon.

Conclusie

Het overkoepelende streven van dit proefschrift was om inzicht te krijgen in een aantal van de factoren die van invloed kunnen zijn op het herwinnen en behouden van de loopvaardigheid na een beenamputatie. Op basis van de resultaten, gepresenteerd in dit proefschrift, kunnen we stellen dat de piek aerobe capaciteit van personen die een beenamputatie hebben ondergaan door vasculaire deficiëntie, verlaagd is. Voor deze mensen is lopen een inspannende activiteit. Het gepresenteerde werk laat zien dat een relatief kleine verbetering
in de piek aerobe capaciteit kan leiden tot significante en klinisch relevante veranderingen in de loopvaardigheid van personen met een beenprothese. Bovendien laat dit proefschrift zien dat een prothesevoet, die een adequaat getimede afzetkracht kan genereren en die een optimale afwikkeling van de voet geeft tijdens de standfase, de mechanische energie tijdens de stap-naar-stap transitie kan verlagen. Echter, de mechanische energetische kosten voor de stap-naar-stap transitie kunnen niet het verhoogde metabole energieverbruik van het lopen met een beenprothese verklaren. Mogelijk dragen ook de energetische kosten voor de balanscontrole bij aan het verhoogde energieverbruik tijdens het lopen met een beenprothese.

Implicaties voor de revalidatie

In dit proefschrift wordt de aanbeveling gedaan dat toekomstig onderzoek zich zou moeten richten op longitudinale studies met een heterogene groep van mensen met een beenprothese. Met behulp van deze longitudinale studies kan worden onderzocht wat de effectiviteit is van verschillende trainingsprogramma’s op de loopvaardigheid bij verschillende subgroepen binnen de populatie van mensen met een beenprothese. Daarnaast kunnen simpele dynamische modellen inzicht verschaffen in de mechanische arbeid tijdens het lopen met verschillende prothesevoeten. Voor toekomstig onderzoek ligt er een grote uitdaging om de energetische kosten voor de loopbeweging en de kosten die gerelateerd zijn aan de balanscontrole, van elkaar te scheiden. Informatie over de onderliggende oorzaken van de verhoogde energetische kosten tijdens het lopen met een beenprothese vormt de basis voor verdere ontwikkeling van meer efficiënte en functionele prothesen. Binnen de revalidatie na een beenamputatie is het van belang dat men zich realiseert dat zowel aerobe training als balanstraining een substantiële bijdrage kan leveren aan het optimaliseren van de loopvaardigheid. Om die reden zouden beide facetten dan ook een geïntegreerd onderdeel van de revalidatie moeten zijn.
Samenvatting
Dankwoord
No duty is more urgent than that of returning thanks.

- James Allen -
Oke, dit wordt een makkie! Ik mag een stuk schrijven waarbij ik me niet hoef te houden aan enige consensus of wetenschappelijke regels. Dan breek ik gelijk maar met een gewoonte en start ik met het bedanken van alle mensen, die ik hieronder niet expliciet zal noemen. Bedankt, en sorry dat ik je niet bij naam noem. Je moet maar zo denken: nu ben je (soort van) alsnog als eerste genoemd.

Maar eigenlijk is er natuurlijk maar één iemand die ik als eerste wil en moet noemen. Han, zoals het promotietraject voor mij een sprong in het diepe was, heb jij je ook begeven op onbekend terrein. Ik ben je eerste promovendus en enorm trots dat ik samen met jou dit project heb mogen vormgeven. Jou expertise als wetenschapper staat buiten kijf. Ik ben enorm dankbaar dat ik uit jouw bron van kennis heb mogen tappen. Je hebt, door je vertrouwen, je ongekend positieve instelling, enthousiasme en belangstelling, mij als wetenschapper en als persoon de ruimte gegeven om te groeien. Ik had me geen betere begeleider kunnen wensen. En je hebt inderdaad gelijk gekregen met dat vertrouwen! Mijn dank is enorm. Al jouw toekomstige promovendi mogen zich in de handen wrijven met jou als begeleider.

Arnold, als promotor stond je wat verder van het project af, maar je hebt door je adequate manier van reageren en je frisse blik op de resultaten zeer zeker bijgedragen aan de inhoudelijke en organisatorische totstandkoming van dit proefschrift. Luc, jeetje wat baalde ik toen je naar Groningen ging. Jij bracht de rust en het overzicht in het project en jouw kennis binnen het veld van de revalidatie is onuitputtelijk. Gelukkig verdween je niet volledig uit het zicht en heb ik altijd een beroep kunnen blijven doen op jouw kennis en ervaring. Luc, je bent een enorm belangstellend en fijn persoon en ik prijs me gelukkig met jouw betrokkenheid bij mijn project.

Dear Joseph Czerniecki, Andrea Cutti, Jan Geertzen, Coen van Bennekom en Melvyn Roerdink, I am truly grateful for the effort you all have put into reading my thesis and being present at the defense. It is a great honor (though I can't deny, also a bit scary) to have such a great opposition.

Andrea, grazie per la tua ospitalità al centro INAIL. Non ho idea come sia sopravvissuta ogni giorno sul kamikaze-bus. Mi hai dato l'opportunità di imparare tanto e ho apprezzato molto la nostra cooperazione in questo progetto.

Beste collega's in Heliomare, mijn project heeft zich, zeker de laatste jaren (waarvoor excuses), veelal op de VU afgespeeld, maar desondanks hebben jullie me altijd weten te betrekken bij de dagelijkse gang van zaken. Expliciet wil ik toch zeker Richard, Judith, Coen en Linda bedanken, die mij vanaf het begin gesteund hebben. Maar ook alle nieuwe collega's, waaronder Justine, Janneke, Timo, Elmar en Maaike bedankt voor alle interesse en discussies. Daarnaast wil ik de bijdrage van Woji, Irene, Mark, Hans, Willemijn en de arts-assistenten niet
Dankwoord

onopgemerkt laten. Bedankt voor de inhoudelijke discussies tijdens het opzetten van het onderzoek en de hulp bij het screenen van de patiënten. Heliomare is een enorm inspirerende omgeving en ik heb er altijd met trots en veel plezier gewerkt.

Ik had niet alleen geluk wat betreft Heliomare als plezierige werkomgeving, ook op de Faculteit der Bewegingswetenschappen heb ik het geluk gehad om met geweldige collega’s samen te mogen werken en te kunnen ontspannen. Maarten, Menno, Lex, Bernadette, Nienke en Pieter, ik snap nog steeds niet dat jullie mij als totaal niet nuttige teamgenoot toch blijven vragen voor de verschillende pubquiz-avonden. Huub, Bernadette, Jaap, Trienke en Andreas, bedankt voor de rondjes die we samen hebben hardgelopen. Bedankt ook alle overige collega’s voor de oprechte interesse, gezelligheid en onuitputtelijke behulpzaamheid.

Proefpersonen, jullie waren en zijn onmisbaar in de wereld van het revalidatieonderzoek. En ik ben jullie dan ook eeuwig dankbaar dat jullie je voor dit onderzoek letterlijk in het zweet hebben willen werken. Dit gezegd hebbende, wil ik ook nog graag even sorry zeggen: sorry! Sorry dat ik jullie ‘amputees’ heb genoemd in de inleiding en discussie. Het spijt me en ik heb ook eigenlijk geen excuus behalve dan dat ‘amputees’ beduidend minder plek inneemt dan de langere ‘people who have undergone amputation of the lower limb due to vascular deficiency or trauma’-variant. Ik weet het, dit is totaal niet in overeenstemming met de ‘people first’-terminologie. Het spijt me…een beetje ;).

En ja, ik weet dat dit het hoofdstuk is dat het meest gelezen wordt (dat is me vaak genoeg verteld tijdens de lunch [dank je Jeroen]). Vandaar dat ik dankbaar ben voor de hulp van de (door mij zo benoemde) expert in het becommentariëren van Nederlandse teksten a.k.a. Kirsten. Hierdoor maak ik in ieder geval niet de vergissing, die mijn co-promotor ooit beging! En wie denkt dat ik goed ben in tekenen, die kent mij niet goed genoeg voor alle illustraties ben ik Dave en Theo enorm dankbaar. Theo de voorkant is geweldig! En Theo mijn oprechte spijt voor de stress die ik je bezorgd heb! Theo, maar ook Dennis, jullie zijn onmisbaar geweest in de afrondingsfase. En dat is vier ;)!

Zoals elke promovendus kan beamen, zijn er pieken en dalen tijdens het promotietraject. Zo stijgt soms de belasting terwijl de capaciteit daalt; m.a.w. de ballon komt steeds meer op spanning te staan.\(^1\) Op dit soort momenten kon ik altijd terugvallen op mijn vrienden. Iris, het leven is een achtbaan. Ik ben enorm dankbaar dat je samen met mij de rit wil maken, je bent een topvriendin! Trienke, heerlijk die nuchterheid van jouw kant en ik koester de (soms inhoudelijke) gesprekken en discussies samen. Meiden, bedankt dat jullie mijn paranimf willen zijn. En Katja, Achterhoeker, je bent mijn “oudste” vriendin en nu we zo dicht bij

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1. Snap je de vergelijking met de ballon niet? Dat krijg je ervan als je alleen het dankwoord leest!
Dankwoord

eelbaar wonen, hoop ik dat we steeds vaker de deur bij elkaar gaan platlopen! Ik prijs me gelukkig met een groep vrienden waarmee ik kan sporten, feesten en praten. Het liefst noem ik iedereen persoonlijk maar ja, dan doe ik de gewonnen woorden (zie boven) weer teniet. Laat ik gewoon bij dezen beloven dat we snel weer eens ouderwets gezellig afspreken!

James, these words might be the most difficult ones to write of the whole thesis. The completion of this thesis is to a large part dependent on your support and coping behaviour. I owe you a lot, and I will forever treasure the fantastic times we have had together.

Beste pa en ma, misschien was het jullie niet altijd helemaal duidelijk wat ik precies deed, maar jullie hebben me altijd gesteund. Jullie vertrouwen, maar ook het doorzettingsvermogen dat ik van jullie heb meegekregen, hebben mij gevormd tot wie ik nu ben. Rick, broertje, ik ben super trots op jou! Wel een beetje jammer dat je je skivakantie plant tijdens mijn verdediging. Loop je toch mooi een feestje op mijn kosten mis!

Hmm... zo makkelijk was het toch niet om dit te schrijven...
About the author
About the author

Daphne Wezenberg (1982) was born in Doetinchem, the Netherlands. In 2009 Daphne graduated from the Windesheim University of Applied Sciences after attaining her Bachelor degree as a Physical Education Teacher. She continued her studies at the VU University Amsterdam where she attained her Masters degree in Human Movement Sciences in 2006. In the same year she finished the Teaching Training Program. In 2006 she started working at the University of Applied Sciences in Leiden at the department of Physiotherapy. In 2008 she returned to the Faculty of Human Movement Sciences to start her Ph.D. project on the relationship between walking ability and physical capacity in people with a lower limb amputation. This project was a collaboration between the VU University and Heliomare Rehabilitation. From September 2012 she is combining her research activities at the VU University with a position at the Hague University of Applied Sciences at the department of Human Movement Technology. In the future Daphne aims to conduct future research within the field of prosthetic ambulation and hopes to inspire both students and professionals to engage, and explore the field of rehabilitation and movement science.
About the author

Publication in peer reviewed journals


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